

Provincial epidemiology of invasive pneumococcal disease in South Africa, 2019–2024: Findings from laboratory-based surveillance in the Eastern, Northern, and Western Cape provinces

Neo Legare^{1*}, Kate Bishop^{1,2*}, Ghowa Booley^{3,4}, Siphon Dlamini⁵, Angela Dramowski⁶, Brian Eley⁷, Nondumiso Khoza⁸, Denise Kyazze^{9,10}, Siyazi Mda¹⁰, Loyiso Mngokoyi¹¹, Uafulufhedzea Ndou¹², Arifa Parker¹³, Elizabeth Prentice^{3,4}, Kessendri Reddy^{12,14}, Anthea Ryan^{3,4}, Hafsah Tootla^{3,4,15}, Linda de Gouveia⁸, Sibongile Walaza⁸, Cheryl Cohen^{8,16}, Anne von Gottberg^{4,8,17}, Vanessa Quan¹ and Susan Meiring¹, for GERMS-SA.

¹Division of Public Health Surveillance and Response, National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.

²Division of Epidemiology and Biostatistics, School of Public Health, University of Cape Town, Cape Town, South Africa.

³Groote Schuur Microbiology Laboratory, NHLS, Cape Town, South Africa.

⁴Division of Medical Microbiology, Department of Pathology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa.

⁵Division of Infectious Diseases & HIV Medicine, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Groote Schuur Hospital, Cape Town, South Africa.

⁶Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital, Cape Town, South Africa.

⁷Department of Paediatrics and Child Health, University of Cape Town, Red Cross War Memorial Children's Hospital, Cape Town, South Africa.

⁸Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.

⁹Livingstone Tertiary Hospital, Infectious Diseases Unit, Department of Internal Medicine, Gqeberha, South Africa.



¹⁰Nelson Mandela University Medical School, Gqeberha, South Africa.

¹¹Port Elizabeth Microbiology Laboratory, National Health Laboratory Service, Gqeberha, South Africa.

¹²Tygerberg Microbiology Laboratory, National Health Laboratory Service, Cape Town, South Africa.

¹³Unit for Infection Prevention and Control, Department of Medicine, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital, Cape Town, South Africa.

¹⁴Department of Pathology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg Hospital, Cape Town, South Africa.

¹⁵Medical Microbiology, National Health Laboratory Service, Red Cross War Memorial Children's Hospital, Cape Town, South Africa.

¹⁶School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

¹⁷School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

*corresponding authors



Summary

The introduction of pneumococcal conjugate vaccines (PCVs) into South Africa's Expanded Programme on Immunisation in 2009 led to a substantial decline in overall disease incidence, yet invasive pneumococcal disease (IPD) continues to occur. This report describes the IPD epidemiological trends in the Eastern Cape (EC), Northern Cape (NC), and Western Cape (WC) provinces from 2019–2024, using laboratory-confirmed cases reported through surveillance. Clinical data were collected at enhanced surveillance sites (ESS). Incidence rates were calculated using Thembisa population estimates. Data were analysed descriptively. A total of 5 108 IPD cases was reported (EC: 1 335; NC: 225; WC: 3 548), with the highest annual average incidence in the WC (8.3/100 000), followed by EC (3.3/100 000) and NC (3.1/100 000). Infants aged <1 year consistently had the highest incidence. Non-vaccine serotypes (i.e. serotypes not included in current 10- and 13-valent PCVs) accounted for >60% of cases, with serotype 8 (13%, 522/4 181) the most common. Among cases with clinical data from ESS (84%, 1 357/1 616), underlying conditions were common: 53% (717/1 357) had >1 co-morbidity; 34% (393/1 142) individuals aged ≥15 years were smokers; and 52% (700/1 357) were living with HIV. In-hospital mortality remained high at 31% (424/1 357). These findings identify high-risk groups for severe disease, so as to guide targeted vaccinations and support HIV management. Strengthened laboratory capacity and surveillance are important to monitor serotype shifts following PCV changes and inform public health interventions. Inter-provincial differences in IPD highlight the importance of province-specific data to guide local strategies.

Introduction

Invasive pneumococcal disease (IPD), caused by *Streptococcus pneumoniae*, is a major cause of morbidity and mortality worldwide, including in South Africa (SA), particularly among young children, the elderly, and the immunocompromised.¹⁻⁴ IPD is largely vaccine-preventable, and the introduction of pneumococcal conjugate vaccines (PCVs) into SA's Expanded Programme on Immunisation (EPI) for infants in 2009 resulted in decreased IPD incidence in both vaccinated and unvaccinated populations.⁵ With continued use of PCV in infants nationally, IPD incidence was estimated at 3.02 cases per 100 000 persons in 2023, with the highest incidence occurring among children aged less than one year (14.90 cases per 100 000 persons), nearly five times higher than in any other age group.⁶ This occurred against a background of a PCV13 coverage rate estimate of 84% in 2023 (slightly below the national EPI target of ≥90%) for the third and final dose of PCV13, administered at nine months of age.⁷

A major decline in national IPD incidence was observed during the COVID-19 pandemic during 2020–2021 (from 4.07/100 000 in 2019 to 2.13/100 000 in 2020), largely attributed to non-pharmaceutical interventions. Incidence then rebounded toward pre-pandemic estimates during 2022–2023 (from 2.14/100 000 in 2020 to 3.02/100 000 in 2023), similar to trends reported in other countries.^{6, 8} The recent change in the EPI schedule, replacing 13-valent PCV (PCV13, Pfizer, or Wyeth) with 10-valent PCV (PCV10, Serum Institute of India [SII]) in 2024, may further influence circulating IPD serotypes and epidemiology, as PCV10 provides less serotype coverage than PCV13.⁵ These recent shifts in IPD epidemiology and changes in vaccine formulation raise concern for a potential increase in disease caused by non-vaccine serotypes (NVTs) and necessitate ongoing surveillance of IPD to inform management and policy.⁵



While national data on IPD, collected through laboratory-based surveillance, are useful to guide National Department of Health (NDoH) policy, provincial data are also important to assist the Provincial Departments of Health in identifying vulnerable populations, informing targeted interventions, and allocating resources efficiently. Differences in governance structure and population demographics across provinces further emphasise the need to interpret IPD trends at the provincial level. Laboratory-based surveillance data have shown that IPD incidence varies across provinces: in 2023, the Western Cape (WC) reported rates nearly three times that of the national average (8.76/100 000). Only the Eastern Cape (EC) province's rate was similar to the national average (3.65/100 000), while the Northern Cape (NC) was below the national average (2.32/100 000).⁶ These inter-provincial differences suggest that not only the incidence but also the clinical characteristics of IPD cases may vary by province. Understanding provincial trends and case characteristics may be useful to optimise IPD prevention strategies across provinces.^{9, 10}

We used laboratory-based surveillance data to describe IPD epidemiology in the EC, NC, and WC provinces from 2019–2024. Specifically, we described IPD: (i) annual and age-specific IPD incidence, (ii) serotype and specimen type distribution, and (iii) clinical characteristics collected through enhanced surveillance at sentinel sites.

This study aimed to provide detailed provincial-level data to inform public health planning and guide vaccine strategy at a local level.

Methods

Study design and population

Data were prospectively collected through GERMS-SA, a national infectious disease surveillance platform conducting laboratory-based, population-based, and enhanced surveillance. All methods, including the prospective and retrospective clinical data collection at selected enhanced surveillance sites (ESS), are standardised and have been described previously. For this study, we selected three geographically adjacent provinces in SA (EC, NC, and WC) to provide detailed provincial-level analyses, with data from other provinces reported separately. From 2019 through 2024, all laboratory-confirmed cases of IPD in these provinces were included.

Case definition

A case of IPD was defined as *S. pneumoniae* isolated or detected from a normally sterile site specimen (including cerebrospinal fluid [CSF], blood, pleural fluid, peritoneal fluid, joint fluid, or tissue) using culture, latex agglutination, or polymerase chain reaction (PCR). Duplicate isolates, defined as laboratory-confirmed *S. pneumoniae* detected within 21 days of the initial specimen, were excluded. When multiple specimens from the same patient were collected on the same day, classification was based on specimen type, prioritising CSF, blood, and then other specimen types, to avoid duplication.

Laboratory-based surveillance

All private and public clinical microbiology laboratories within the three provinces (EC, NC, and WC) submitted *S. pneumoniae* isolates (cultured on Dorset slopes) or PCR-positive but culture-negative



samples to the National Institute for Communicable Diseases' (NICD) Centre for Respiratory Disease and Meningitis (CRDM) if they met the IPD case definition. At the CRDM, identification of *S. pneumoniae* was confirmed, and isolates underwent phenotypic and genotypic characterisation, including molecular methods (PCR and whole genome sequencing [WGS]) and serotyping. Serotypes were determined using the Quellung reaction (SSI Diagnostica A/S, Hillerød, Denmark). Audits were conducted for all National Health Laboratory Service (NHLS) laboratories using the Surveillance Data Warehouse to identify any isolates or PCR-positive but culture-negative samples not submitted to the CRDM. Data for these audit cases were captured and included in the analysis.

Data collection at enhanced surveillance sites

Seven ESS participated across the three provinces: EC (Dora Nginza, Livingstone, and Port Elizabeth provincial hospitals); NC (Kimberley/Robert Mangaliso Sobukwe Hospital); and WC (Groote Schuur, Red Cross War Memorial Children's, and Tygerberg hospitals). ESS are selected hospitals in which trained surveillance officers (registered nurses) collect additional clinical information on patients with IPD. At each ESS, surveillance officers identified IPD cases in the laboratory and collected clinical data via an electronic case report form (CRF) in Research Electronic Data Capture, a secure, web-based platform for electronic data collection. Clinical data collected included demographic information, HIV status, vaccination history, co-morbidities, and in-hospital outcomes. If the patient was still admitted, informed consent was obtained from the patient or guardian to conduct an interview. If the patient had been discharged or had died before being seen, only a medical record review was conducted (with a waiver of individual informed consent). Patients were followed up until discharge from hospital. For cases in the NC, clinical data were primarily collected retrospectively from medical records, as no dedicated surveillance officer was present at the site during most of the study period.

Surveillance data analysis

IPD incidence rates by age group and provinces were calculated using population estimates from the Thembisa (version 4.7) model for the years 2019–2024.¹² All isolates were first analysed by specimen type, and then those that had serotyping results were included in serotype-specific analyses. Continuous variables were summarised as median and interquartile range (IQR). Categorical variables were summarised using frequencies and proportions. Serotypes were grouped according to their inclusion in PCV formulations. The currently in-use PCV10 (SII) serotypes included 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, and 23F, and three additional PCV13 serotypes, 3, 4, and 18C. NVTs included all other serotypes not in PCV13.

Vaccination analyses included only children old enough to have received each dose as per the EPI schedule (six weeks, 14 weeks, and nine months) with protection expected two weeks post-vaccination (i.e., ≥ 8 weeks for PCV1, ≥ 16 weeks for PCV2, and ≥ 38 weeks for PCV3); those aged < 8 weeks were classified as not vaccinated. All statistical analyses were conducted using Stata statistical software (version 19.0; StataCorp, College Station, TX).

Results

Between January 2019 through to December 2024, 5 108 laboratory-confirmed IPD cases were reported to the GERMS-SA surveillance programme in the three provinces overall; 71% (3 647/5 108) of cases were



confirmed on blood culture, ranging from 55% in the EC to 78% in the WC (Table 1). Demographic characteristics, including median age and sex distribution, were similar between provincial IPD cases and those captured through ESS (Table 2).

The overall average annual IPD incidence was 3.3 per 100 000 persons in the EC, 3.1 per 100 000 persons in the NC, and 8.3 per 100 000 persons in the WC (Figure 1). Infants aged <1 year had the highest incidence (EC: 12.7; NC: 7.6; WC: 24.6 per 100 000 persons). In the EC and NC provinces, incidence next peaked in adults aged 45–64 years (5.3 and 6.0 per 100 000 persons, respectively), while in the WC it peaked next in adults aged ≥64 years (15.7 per 100 000 persons) (Figures 2A–C).

The CRDM received 85% (4 361/5 108) of isolates or PCR-positive but culture-negative samples, ranging from 56% (127/225) in the NC to 90% (3 204/3 548) in the WC. Among cases of IPD with serotyping data (82%, 4 181/5 108), NVTs (i.e., those not included in PCV10 [SII] or PCV13) predominated, comprising 68% (644/954) in the EC, 63% (76/120) in the NC, and 66% (2 062/3 107) in the WC (Figure 3). Serotype 8 (NVT) was the leading serotype causing disease overall: 11% (105/954) in the EC, 13% (16/120) in the NC, and 13% (401/3 107) in the WC. The next most common serotypes were 3 (PCV13) (9%, 85/954) and 6C (NVT) (7%, 63/954) in the EC; 3 (13%, 15/120) and 4 (PCV13) (5%, 6/120) in the NC; and 19A (PCV10 [SII]) (12%, 371/3 107) and 3 (7%, 212/3 107) in the WC.

Table 1. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type in the Eastern, Northern, and Western Cape provinces, 2019–2024 (N=5 108).

Province	Total	Blood		CSF		Other*	
	N	n	%	n	%	n	%
Eastern Cape	1 335	739	55.4	474	35.5	122	9.1
Northern Cape	225	128	56.9	77	34.2	20	8.9
Western Cape	3 548	2 780	78.4	535	15.1	233	6.6
Total	5 108	3 647	71.4	1 086	21.3	375	7.3

CSF=cerebrospinal fluid.; *Includes specimens from normally sterile other than blood or CSF e.g. joint or pleural fluid

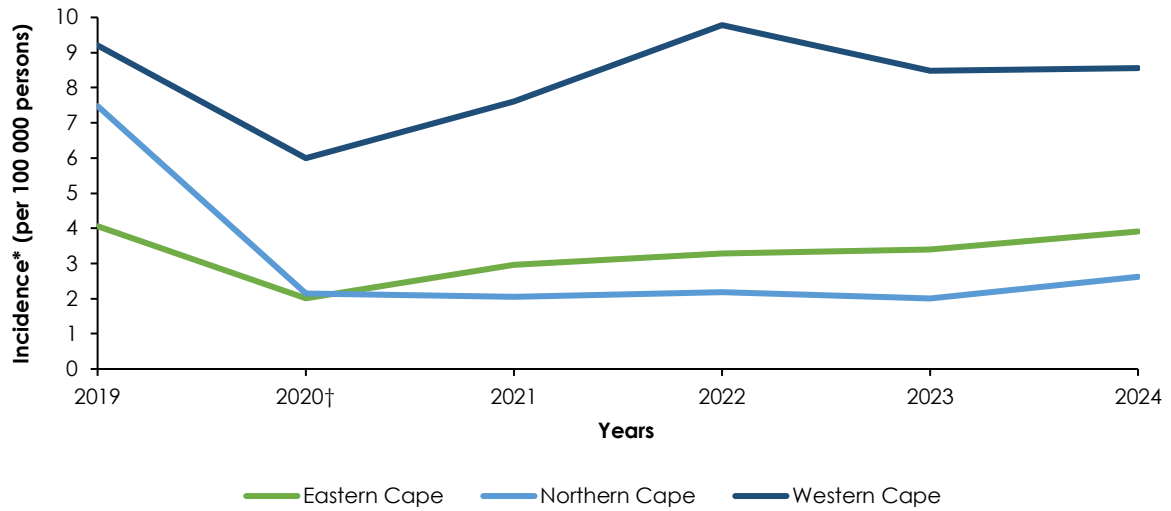


Figure 1. Incidence of invasive pneumococcal disease in the Eastern, Northern, and Western Cape provinces, 2019–2024 (N=5 108).

*Rate calculation based on population denominators provided by the Thembisa model.

†Decline in IPD incidence observed during the COVID-19 pandemic in 2020.

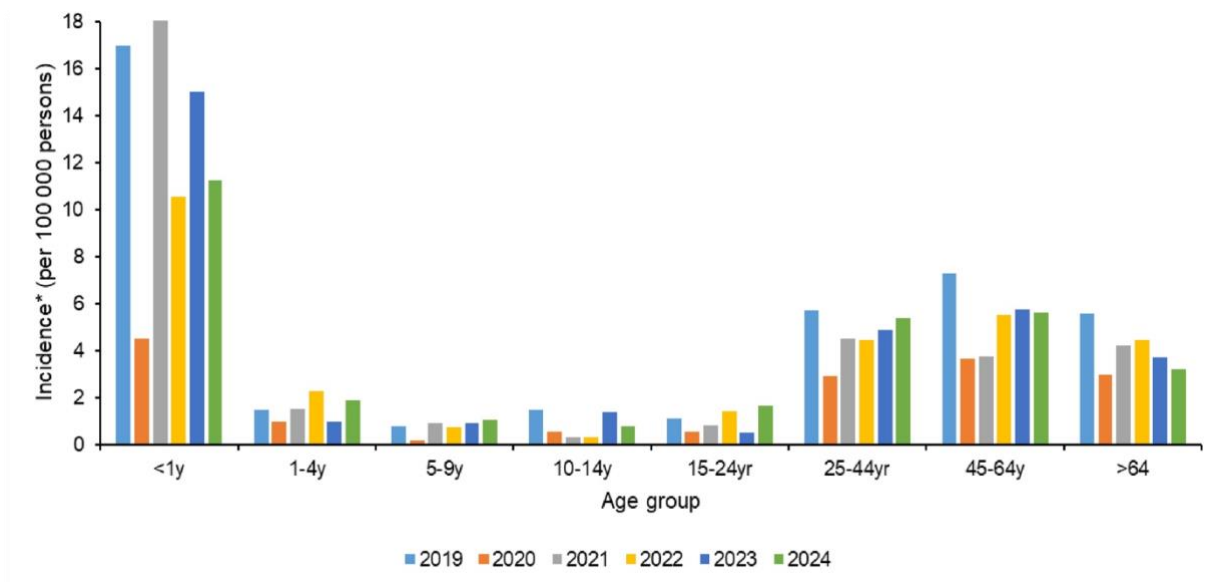


Figure 2A. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the Eastern Cape province (N=1 291; 44 with unknown age not included in the figure).

*Rate calculation based on population denominators provided by the Thembisa model.

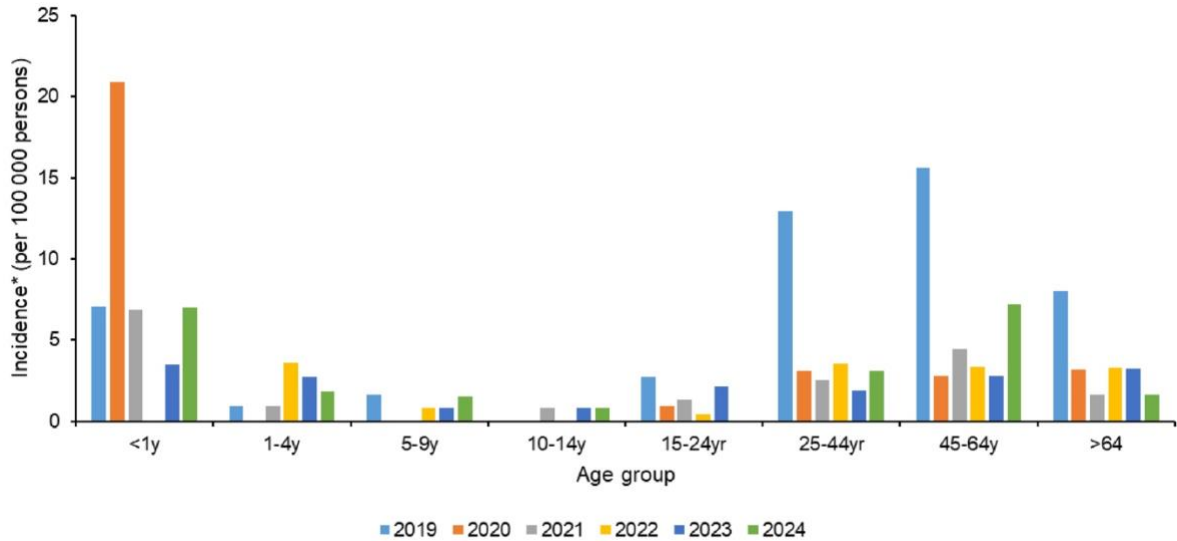


Figure 2B. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the Northern Cape province (N=225).

*Rate calculation based on population denominators provided by the Thembisa model.

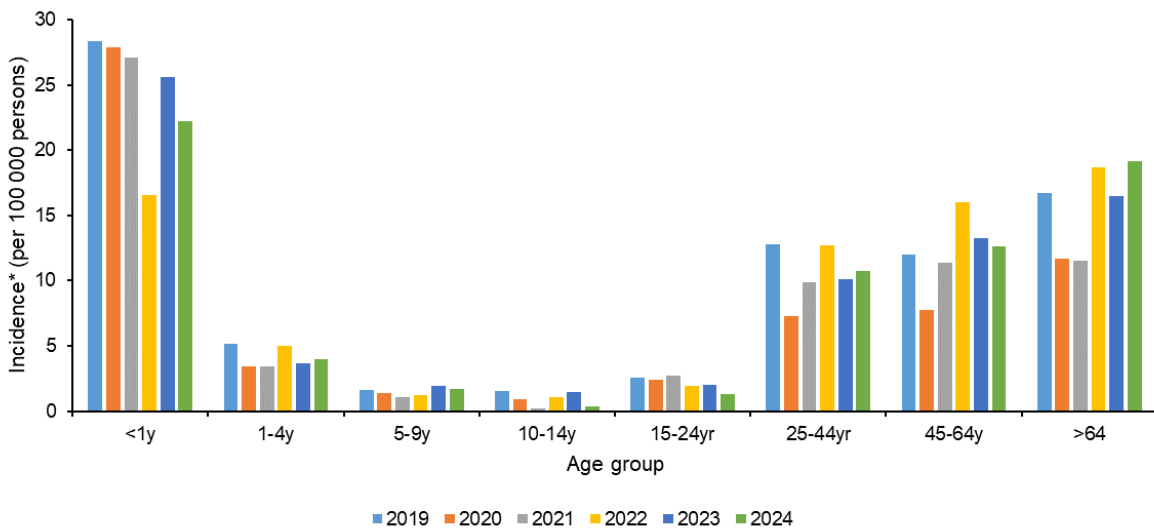


Figure 2C. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the Western Cape province (N=3 548; 57 with unknown age not included in the figure).

*Rate calculation based on population denominators provided by the Thembisa model.

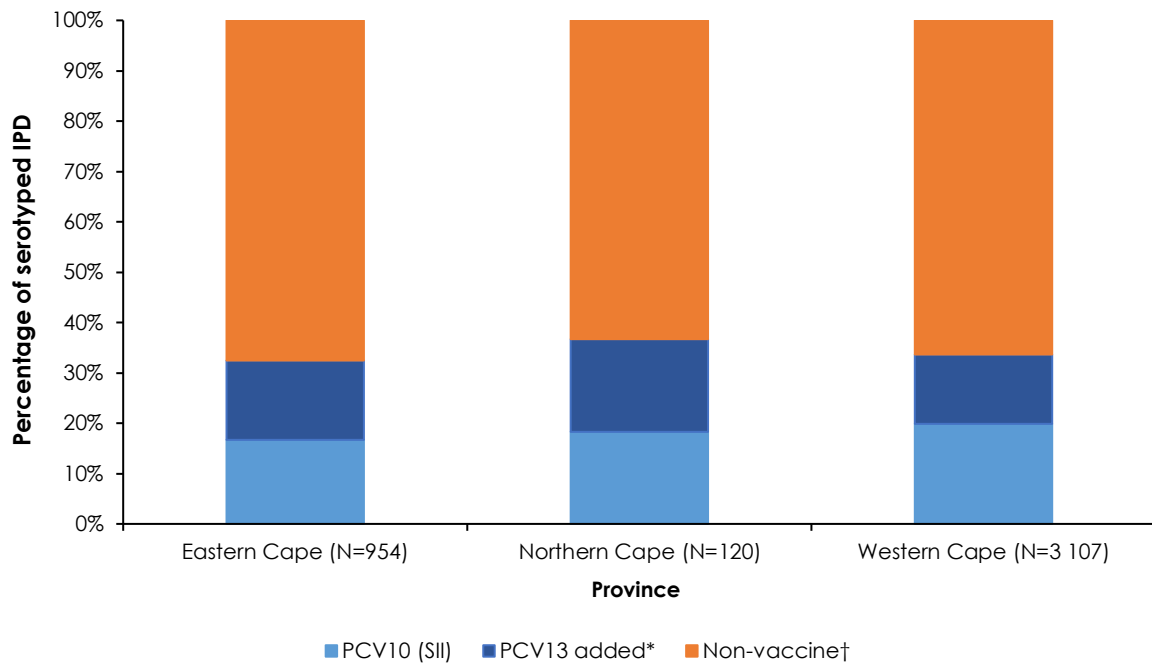


Figure 3. Pneumococcal serotype classification of laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, by relevant pneumococcal conjugate vaccines in the Eastern, Northern, and Western Cape provinces, 2019–2024, (N=4 181; n=927 cases not serotyped).

IPD: invasive pneumococcal disease; PCV: pneumococcal conjugate vaccine.

*Three additional serotypes included in PCV13 but not in PCV10 (SII).

†All other serotypes not included in PCV13.

A total of 32% (1 616/5 108) of all IPD cases was detected at ESS, with clinical data available for 84% (1 357/1 616) of these cases. Pneumonia was the most common clinical presentation across all three provinces. One or more co-morbidities (excluding HIV) were documented in 55% (335/604) of cases in the EC, 38% (28/74) in the NC, and 52% (354/679) in the WC (Table 2).

In-hospital fatality was substantial in all provinces (Table 2). Where the outcome was known (99%, 1 339/1 357), in-hospital fatality was higher in individuals aged ≥ 5 years compared to children aged < 5 years in the EC (35% vs 14%) and NC (22% vs 10%). In the WC, in-hospital fatality was higher in children aged < 5 years compared to those aged ≥ 5 years (35% vs 29%). By clinical presentation of IPD, in-hospital fatality was $> 40\%$ among meningitis cases in both the EC (41%) and NC (47%), and $> 40\%$ among pneumonia cases in the EC (42%) and WC (57%).

Among IPD cases at ESS with known HIV status (93%, 1 257/1 357), HIV infection was commonly observed, ranging from 40% in the WC to 71% in the EC (Table 2). Among those people living with HIV, more than half showed evidence of severe immunosuppression ($CD4 \leq 200$ cells/ μL) in all three provinces.



Table 2. Overview of patient characteristics among invasive pneumococcal disease (IPD) cases admitted to enhanced surveillance sites in the Eastern, Northern, and Western Cape provinces, 2019–2024 (N=1 616).

Characteristic	EC	NC	WC
	N=669 n (% or IQR)	N=174 n (% or IQR)	N=773 n (% or IQR)
Median age (years)	39 (31–51)	40 (28–53)	38 (22–53)
Age group (years)			
<1	23 (3.4)	10 (5.8)	79 (10.2)
1–4	22 (3.3)	6 (3.5)	40 (5.2)
5–9	12 (1.8)	3 (1.7)	24 (3.1)
10–14	14 (2.1)	2 (1.2)	14 (1.8)
15–24	33 (4.9)	12 (6.9)	38 (4.9)
25–44	295 (44.1)	75 (43.1)	264 (34.2)
45–64	190 (28.4)	55 (31.6)	196 (25.4)
65+	54 (8.1)	11 (6.3)	79 (10.2)
Unknown	26 (3.9)	–	39 (5.1)
Sex			
Female	328 (49.0)	74 (42.3)	356 (46.1)
Male	316 (47.2)	97 (55.6)	393 (50.8)
Unknown	25 (3.7)	3 (1.7)	24 (3.1)
Specimen type			
Blood culture	502 (75.0)	117 (67.2)	564 (73.0)
CSF	125 (18.7)	42 (24.1)	110 (14.2)
Other	42 (6.3)	15 (8.6)	99 (12.8)
Clinical data available	604 (90.3)	74 (42.5)	679 (87.8)
Clinical presentation			
Pneumonia	314 (52.0)	31 (41.9)	424 (62.4)
Meningitis	174 (28.8)	27 (36.5)	123 (18.1)
Bacteraemia	105 (17.3)	11 (14.9)	69 (10.2)
Other	11 (1.8)	5 (6.8)	63 (9.3)
Co-morbidities* (excl. HIV)			
No co-morbidities	178 (29.5)	34 (46.0)	252 (37.1)
1 co-morbidity	242 (40.1)	22 (29.7)	217 (32.0)
2 co-morbidities	65 (10.8)	5 (6.8)	75 (11.1)
≥3 co-morbidities	28 (4.6)	1 (1.4)	62 (2.8)
Unknown	91 (15.1)	12 (16.2)	101 (14.8)
High risk behaviours (aged ≥15 years)	(n=542)	(n=60)	(n=540)
Smoker	179 (33.0)	19 (31.7)	195 (36.1)
Alcohol dependency†	155 (28.6)	–	36 (6.7)
In-hospital fatality			
Died	205 (33.9)	15 (20.3)	204 (30.0)
Alive	386 (63.9)	59 (75.7)	470 (69.2)
Unknown	13 (2.2)	–	5 (0.7)
HIV status (aged ≥5 years)	(n=566)	(n=64)	(n=573)
HIV infected	402 (71.0)	43 (67.2)	231 (40.3)



HIV uninfected	146 (25.8)	19 (29.7)	286 (49.9)
Unknown	18 (3.2)	2 (3.1)	56 (9.7)
HIV status (aged <5 years)	(n=38)	(n=10)	(n=106)
HIV infected	11 (29.0)	1 (10.0)	12 (11.3)
HIV exposed uninfected	6 (15.8)	2 (20.0)	16 (15.1)
HIV unexposed uninfected	19 (50.0)	7 (70.0)	56 (52.8)
Unknown	2 (5.3)	–	22 (20.8)
People living with HIV (all ages)	413 (68.4)	44 (59.5)	243 (35.8)
ART treatment experience			
Current	101 (24.4)	14 (31.8)	95 (39.1)
Previous	192 (46.5)	18 (40.9)	59 (24.3)
None	98 (23.7)	9 (20.5)	81 (33.3)
Unknown	22 (5.3)	3 (6.8)	8 (3.3)
CD4 count (cells/μL)			
≤ 200 cells/ μ L	290 (70.2)	25 (56.8)	137 (56.4)
> 200 cells/ μ L	104 (25.2)	14 (31.8)	76 (31.3)
Unknown	19 (4.6)	5 (11.4)	30 (12.4)
Viral load (copies/mL)			
≥ 400	287 (69.5)	22 (50.0)	82 (33.7)
< 400	82 (19.6)	4 (9.1)	60 (24.7)
Unknown	44 (10.7)	18 (40.9)	101 (41.6)

EC: Eastern Cape; NC: Northern Cape; WC: Western Cape; n: numerator; CSF: cerebrospinal fluid; IQR: interquartile range; ART: antiretroviral therapy.

*Includes chronic medical conditions (cardiovascular, pulmonary, renal, hepatic, neurologic, haematologic, immunosuppressive, or endocrine [e.g., diabetes]); HIV excluded.

†Defined as problematic alcohol use in the past year, including loss of control, binge drinking, or dependence, with classification guided by a validated 4-question screening tool (CAGE - Cut-down, Annoyed, Guilty, Eye-opener).

Among children aged <5 years at ESS with available serotyping data (80%, 122/154), NVTs predominated across all vaccination categories and provinces, with serotype 8 being most common (13%, 16/122), followed by serotype 10A (7%, 8/122) (Figure 4A–C). Breakthrough infections were observed in fully vaccinated children, with serotype 3 (PCV13) in the EC and serotype 19F (PCV10[SII]) in the WC. Among individuals aged ≥ 5 years, vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV23) was rare (1%, 8/743).

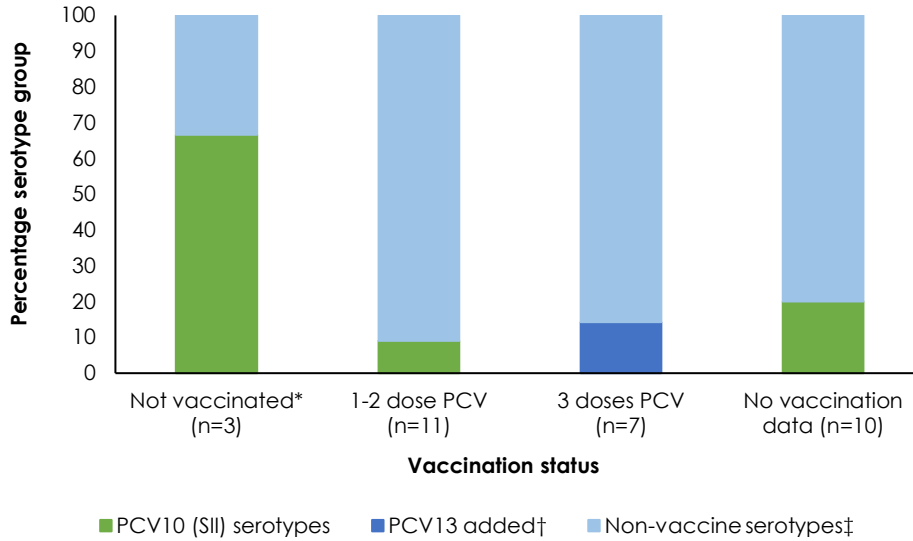


Figure 4A. Distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in the Eastern Cape province, 2019–2024, N=31.

PCV: pneumococcal conjugate vaccine; SII: Serum Institute India.

*Infants aged <8 weeks or those ≥8 weeks with no history of PCV vaccination.

†Three additional serotypes included in PCV13 but not in PCV10 (SII).

‡Non-vaccine serotypes: All other serotypes not included in PCV13.

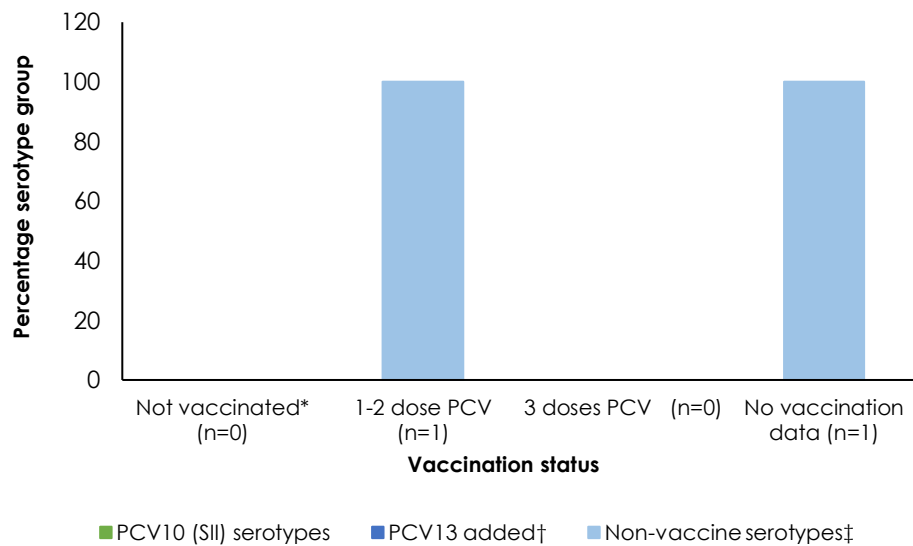


Figure 4B. Distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in the Northern Cape province, 2019–2024, N=2.

PCV: pneumococcal conjugate vaccine; SII: Serum Institute India.

*Infants aged <8 weeks or those ≥8 weeks with no history of PCV vaccination.

†Three additional serotypes included in PCV13 but not in PCV10 (SII).

‡Non-vaccine serotypes: All other serotypes not included in PCV13.

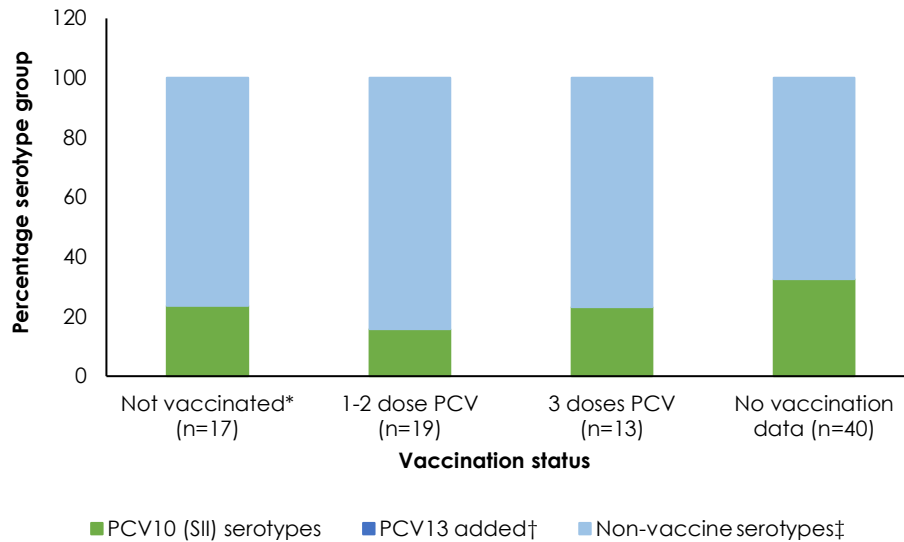


Figure 4C. Distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in the Western Cape province, 2019–2024, N=89.

PCV: pneumococcal conjugate vaccine; SII: Serum Institute India.

*Infants aged <8 weeks or those ≥8 weeks with no history of PCV vaccination;

†Three additional serotypes included in PCV13 but not in PCV10 (SII).

‡Non-vaccine serotypes: All other serotypes not included in PCV13.

Discussion

Between 2019 and 2024, laboratory-confirmed IPD in the EC, NC, and WC showed the highest burden among infants aged <1 year and adults with underlying co-morbidities. A secondary burden of IPD was observed among adults aged 45–64 years in the EC and NC and in those aged >64 years in the WC. Pneumonia was the most common clinical presentation, and in-hospital fatality was substantial (EC: 34%, NC: 20%, WC: 30%). NVTs were the leading cause of disease (EC: 68%, NC: 63%, WC: 66%), with PCV10 (SII) and PCV13 serotypes accounting for a smaller proportion of cases. HIV infection was common among individuals aged ≥5 years (EC: 71%, NC: 67%, WC: 40%) and substantial among children aged <5 years (EC: 29%, NC: 10%, WC: 11%). More than 50% of people living with HIV across all ages had severe immunosuppression (CD4 ≤200 cells/μL).

These findings align with national and international surveillance reports showing persistent IPD burden in infants and immunocompromised adults despite longstanding implementation of infant PCV programmes, and an increasing role of NVTs post-PCV introduction.² Persistent serotype replacement after vaccine rollout remains an important driver of ongoing disease and highlights the need for sustained serotype surveillance to assist with future vaccine formulations.

The COVID-19 pandemic temporarily reduced IPD incidence, probably due to non-pharmaceutical interventions and reduced healthcare access, with only the WC showing a clear rebound toward pre-pandemic levels. In the EC, the increase in IPD has been gradual, while the NC has not returned to pre-



pandemic levels. In addition to these differences, the WC consistently reported higher incidence of IPD across all age groups compared to the EC and NC. These inter-provincial differences may reflect a combination of local factors, including population density, household crowding, healthcare access, clinical and sampling practices, laboratory capacity, and HIV prevalence and management. Because these factors differ between provinces, province-specific surveillance data are important, as national reports risk masking local epidemiological patterns. Further studies are needed to explore how these factors contribute to the inter-provincial disparities observed in IPD.

Disease prevention efforts should focus on achieving high infant immunisation coverage (>90%), continued monitoring of NVTs, and incorporating adult vaccination recommendations into NDoH guidelines, including higher valency vaccines for adults at increased risk, such as people living with HIV, individuals with chronic illnesses, and the elderly. Additional strategies could include promoting sustained antiretroviral therapy adherence among people living with HIV and implementing smoking cessation education programmes, since more than 30% of IPD cases aged ≥ 15 years were smokers. Strengthening surveillance systems and laboratory capacity for the submission of isolates and PCR-positive but culture-negative samples will enhance monitoring and support future evaluations of serotype distribution and vaccine effectiveness, particularly following the 2024 switch from PCV13 to PCV10 (SII). Integrating HIV care with IPD prevention and focusing resources on vulnerable populations are essential to reducing morbidity and mortality.

This analysis has several limitations that should be considered when interpreting the findings. Firstly, the use of laboratory-confirmed cases only underestimates the true burden of IPD, as patients who were not tested or lacked access to microbiology services would not have been captured. Clinical and HIV-related data were incomplete in some provinces, particularly in the NC, where limited surveillance capacity resulted in retrospective data collection and potential information gaps. Some information may not have been captured by clinicians, while other data were available in medical records, leading to variability in completeness and quality of clinical history across provinces. Serotype data were unavailable for isolates or PCR-positive but culture-negative samples not submitted, which may have influenced the accuracy of serotype distribution estimates. The descriptive nature of this report limits our ability to determine causal relationships or adjust for confounding factors. In addition, health-seeking behaviour may have been delayed during the COVID-19 pandemic, which may have affected case detection and reporting trends during 2020–2022.

Conclusion

IPD remains a preventable yet significant cause of morbidity and mortality in the EC, NC and WC provinces. Infants, adults with co-morbidities, smokers, and people living with HIV were most affected. The predominance of NVTs highlights ongoing serotype replacement and reinforces the need for continued surveillance with improved laboratory capacity, particularly following the recent switch to PCV10 (SII). Strengthening integration of IPD prevention within HIV care pathways and targeting high-risk groups are essential to reduce the IPD burden.



Recommendations

Based on the findings of our surveillance, we recommend the following for the three provinces:

- Identify districts with low infant PCV vaccination coverage (<90%) to target outreach interventions aimed at improving PCV vaccine coverage to ≥90%, with leadership from provincial and district EPI co-ordinators.
- Ensure that 100% of patients presenting with IPD at any age with an unknown HIV status are tested during hospitalisation, with linkage to care within seven days for those newly diagnosed and implementation by patient-facing clinicians and oversight by provincial/district HIV programme managers.
- Incorporate risk-based pneumococcal vaccination in NDoH guidelines with PCV13 and PPV23 for people living with HIV and adults ≥64 years of age, including integrating vaccination into HIV and non-communicable diseases (NCD) clinics, under guidance of the National and Provincial DoH immunisation and NCD programmes.
- Encourage complete documentation of PCV vaccination history in Road-to-Health Cards (RTHCs), including dose dates and batch numbers, to support surveillance and investigation of breakthrough vaccine-type IPD and future evaluations following vaccine formulation changes, with support from provincial and district primary healthcare managers, in collaboration with Maternal and Child Health directorates and EPI programme managers.
- Conduct annual GERMS-SA refresher training for NHLS laboratories regarding the submission of IPD isolates or PCR-positive but culture-negative samples, aiming for ≥95% isolate/specimen submission completeness, led by the GERMS-SA/NICD staff involved in laboratory surveillance.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

The protocol was approved by local Human Research Ethics Committees (HRECs): The University of the Witwatersrand HREC (M1809107; M230985) for the NC and EC; the University of Cape Town Faculty of Health Sciences HREC (115/2009) and Stellenbosch University Faculty of Health Science HREC (N04/10/001) for the WC. Furthermore, the surveillance study is registered on the provincial National Health Research Databases (NHRDs) for each participating province and facility. Informed consent and assent, where applicable, were obtained from participants or their legal guardians for the collection of clinical data through surveillance interviews.



References

1. Meiring S, Cohen C, Quan V, et al. HIV Infection and the epidemiology of invasive pneumococcal disease (IPD) in South African adults and older children prior to the introduction of a pneumococcal conjugate vaccine (PCV). *PLoS One*. 2016;11(2):e0149104. Epub 20160210. doi: 10.1371/journal.pone.0149104. PubMed PMID: 26863135; PubMed Central PMCID: PMC4749259.
2. Ochoa-Gondar O, Torras-Vives V, de Diego-Cabanes C, et al. Incidence and risk factors of pneumococcal pneumonia in adults: a population-based study. *BMC Pulm Med*. 2023;23(1):200. Epub 20230608. doi: 10.1186/s12890-023-02497-2. PubMed PMID: 37291502; PubMed Central PMCID: PMC10251659.
3. Maimaiti N, Ahmed Z, Md Isa Z, et al. Clinical burden of invasive pneumococcal disease in selected developing countries. *Value Health Reg Issues*. 2013;2(2):259-63. Epub 20130913. doi: 10.1016/j.vhri.2013.07.003. PubMed PMID: 29702874.
4. Billings ME, Deloria-Knoll M, O'Brien KL. Global burden of neonatal invasive pneumococcal disease: A systematic review and meta-analysis. *Pediatr Infect Dis J*. 2016;35(2):172-9. doi: 10.1097/inf.0000000000000955. PubMed PMID: 26517330.
5. von Gottberg A, Kleynhans J, de Gouveia L, et al. Long-term effect of pneumococcal conjugate vaccines on invasive pneumococcal disease incidence among people of all ages from national, active, laboratory-based surveillance in South Africa, 2005-19: a cohort observational study. *Lancet Glob Health*. 2024;12(9):e1470-e84. doi: 10.1016/s2214-109x(24)00263-8. PubMed PMID: 39151982.
6. Maluleka C, Shuping L, Meiring S, et al. 2023 GERMS-SA: Annual surveillance review. Annual report. Johannesburg: National Institute for Communicable Diseases. Available from: <https://www.nicd.ac.za/wp-content/uploads/2024/12/GERMS-Annual-Review-2023.pdf>
7. WHO. Pneumococcal vaccination coverage: South Africa Geneva: World Health Organization; 2023 [cited 2025 12 September]. Available from: <https://immunizationdata.who.int/global/wiise-detail-page/pneumococcal-vaccination-coverage?CODE=ZAF&ANTIGEN=PCV3&YEAR=>.
8. Chan KF, Ma TF, Fang H, et al. Changes in the incidence, viral coinfection pattern and outcomes of pneumococcal hospitalizations during and after the COVID-19 pandemic. *Pneumonia (Nathan)*. 2025;17(1):9. Epub 20250425. doi: 10.1186/s41479-025-00164-0. PubMed PMID: 40275411; PubMed Central PMCID: PMC12023597.
9. Kiakuvue YN, Mall S, Govender N, et al. Demographic and pathogen characteristics of incident bacterial meningitis in infants in South Africa: A cohort study. *PLoS One*. 2024;19(9):e0310528. Epub 20240925. doi: 10.1371/journal.pone.0310528. PubMed PMID: 39321191; PubMed Central PMCID: PMC11423971. <https://journals.plos.org/plosone/article/file?id=10.1371/journal.pone.0310528&type=printable>.



10. Wolzak NK, Cooke ML, Orth H, et al. The changing profile of pediatric meningitis at a referral centre in Cape Town, South Africa. *J Trop Pediatr*. 2012;58(6):491-5. Epub 20120712. doi: 10.1093/tropej/fms031. PubMed PMID: 22791086.

11. von Mollendorf C, Cohen C, de Gouveia L, et al. Risk factors for invasive pneumococcal disease among children less than 5 years of age in a high HIV prevalence setting, South Africa, 2010 to 2012. *Pediatr Infect Dis J*. 2015;34(1):27-34. doi: 10.1097/inf.0000000000000484. PubMed PMID: 24992122; PubMed Central PMCID: PMC11632609.
<https://pmc.ncbi.nlm.nih.gov/articles/PMC11632609/>

12. Johnson LF, Chiu C, Myer L, et al. Prospects for HIV control in South Africa: a model-based analysis. *Glob Health Action*. 2016;9:30314. Epub 20160608. doi: 10.3402/gha.v9.30314. PubMed PMID: 27282146; PubMed Central PMCID: PMC4901512