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Laboratory-based surveillance of invasive pneumococcal disease in the Free State, KwaZulu-Natal, and Mpumalanga provinces, South Africa, 2019–2024

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Summary

Invasive pneumococcal disease (IPD) continues to cause illness and death in South Africa. Following the introduction of infant pneumococcal conjugate vaccines (PCVs) into the Expanded Programme of Immunisation (EPI), overall incidence declined, but residual cases have persisted across provinces. In this second report of a three-part series, we describe the IPD epidemiology in the Free State (FS), KwaZulu-Natal (KZN), and Mpumalanga (MP) provinces from 2019–2024. Laboratory-confirmed IPD cases were reported through laboratory-based surveillance. Additional clinical details were collected at enhanced surveillance sites (ESS). Incidence rates were calculated using Statistics-South Africa population estimates. A total of 1 710 IPD cases was reported (FS: 416; KZN: 961; MP: 333), with the highest annual average incidence in the FS (2.3/100 000), followed by KZN (1.3/100 000) and MP (1.2/100 000). Infants aged <1 year consistently had the highest IPD incidence. Only 54% (919/1 710) of laboratory-confirmed IPD specimens were submitted; serotyping data were available for 50% (856/1 710). Non-vaccine serotypes (i.e., serotypes not included in current vaccines, up to the 13-valent PCV) accounted for 69% (591/856) of cases, with serotype 8 (13%, 110/856) most common. Among cases at ESS with clinical data (82%, 509/620), 37% (189/509) had ≥1 co-morbidity (excluding HIV). HIV prevalence was 54% (273/509); 13% (64/509) had an unknown status. In-hospital mortality was high (37%, 190/509). These findings identify high-risk groups for IPD to guide targeted life-course vaccinations and optimise HIV testing and care. Ongoing isolate submission for serotyping is important to monitor serotypes following recent EPI PCV changes.

Introduction

Invasive pneumococcal disease (IPD), caused by *Streptococcus pneumoniae*, is a major cause of morbidity and mortality worldwide and in South Africa (SA), with young children, the elderly, and immunocompromised individuals at greatest risk.[1-4] IPD is largely vaccine-preventable, with the introduction of pneumococcal conjugate vaccines (PCVs) in SA's Expanded Programme on Immunisation (EPI) for infants in 2009 resulting in decreasing 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).[6] This occurred against a background of an estimated PCV13 coverage rate of 84% in 2023 (slightly below the national EPI target of 90% or above) 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 in 2020–2021 (from 4.07/100 000 in 2019 to 2.13/100 000 in 2020) as a result of non-pharmaceutical interventions, followed by a rebound towards pre-pandemic estimates in 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] In 2024 the EPI schedule replaced the 13-valent PCV (PCV13, Pfizer/Wyeth) with the 10-valent PCV (PCV10, Serum Institute of India [SII]). PCV10 (SII) provides coverage for 10 serotypes (1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, and 23F) but does not include three serotypes present in PCV13, namely 3, 4, and 18C; notably, serotype 3 in PCVs has not been associated with significant vaccine effectiveness.[9] These recent shifts in IPD epidemiology and changes in vaccine formulation raise concern for a potential increase in disease caused by non-vaccine serotypes and necessitate ongoing IPD surveillance to inform clinical management and policy.[5]

National laboratory-based surveillance provides important data to inform IPD prevention and vaccine policy in SA. However, surveillance data has shown variation in IPD incidence between provinces – for example, in 2023, IPD incidence ranged from 0.83/100 000 in Mpumalanga (MP) to 8.77/100 000 in the Western Cape, with a national average of 3.02/100 000.[6] Provincial analyses may identify epidemiological patterns masked by national aggregation, particularly where HIV prevalence, healthcare access, laboratory capacity, and population characteristics may differ. Given that health service planning, resource allocation, and programme implementation are largely undertaken at the provincial level, understanding local disease epidemiology is important for targeted public health action.[10,11] Despite this, detailed provincial analyses of IPD epidemiology in South Africa are limited.

We used laboratory-based surveillance data to describe IPD epidemiology in the Free State (FS), KwaZulu-Natal (KZN), and MP provinces from 2019 to 2024. Specifically, we described IPD: (i) incidence by year and

age group, (ii) serotype and specimen type distribution, and (iii) clinical characteristics collected at sentinel sites. This study provides detailed provincial data to inform public health planning at a provincial level.

Methods

Study design and population

Data were collected prospectively through GERMS-SA, a national infectious disease surveillance platform conducting laboratory- and population-based surveillance, supplemented by enhanced surveillance at selected sites. All methods for prospective and retrospective clinical data collection are standardised and have been described previously.[5,12] The FS, KZN, and MP provinces were selected for this report as part of a series of provincial-level descriptive analyses covering all nine provinces in SA, with each report providing data to support provincial public health planning. From 2019 through 2024, data were collected on laboratory-confirmed cases of IPD.

Case definition

A case of IPD was defined as *S. pneumoniae* isolated or detected from a normally sterile site specimen (e.g., cerebrospinal fluid [CSF], blood, pleural fluid, peritoneal fluid, or joint fluid) by culture, latex agglutination, or polymerase chain reaction (PCR). Duplicate isolates, defined as laboratory-confirmed *S. pneumoniae* detected within 21 days after the initial case, were excluded. For patients with multiple specimens collected on the same day, classification was based on specimen type in the following order: CSF, blood, and then other specimen types, to avoid duplication.

Laboratory-based surveillance

All private and public clinical microbiology laboratories within the three provinces (FS, KZN, and MP) submitted *S. pneumoniae* isolates (cultured on Dorset slopes), or PCR-positive but culture-negative specimens, to the National Institute for Communicable Diseases' (NICD) Centre for Respiratory Disease and Meningitis (CRDM) from individuals who met the IPD case definition. At the CRDM, identification of *S. pneumoniae* was confirmed, and cases underwent phenotypic and genotypic characterisation, including molecular methods (PCR and whole-genome sequencing) and serotyping. Serotypes were determined using the Quellung reaction (SSI Diagnostica A/S, Hillerød, Denmark) and PCR. 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 specimens not submitted to the CRDM. Data for these audit cases were captured and included in the analyses.

Data collection at enhanced surveillance sites

Eleven enhanced surveillance hospital sites participated across the three provinces: FS (Universitas, National District and Pelonomi hospitals); KZN (Greys', Northdale, Harry Gwala, RK Khan, Addington, and Victoria Mxenge hospitals); and MP (Rob Ferreira and Themba hospitals). Enhanced surveillance sites (ESS) are selected hospitals in which surveillance officers (trained 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.[13,14] 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. Vaccination history was obtained from Road-to-Health cards, where available, supplemented by medical records. If the patient had been discharged or had died before being seen, only a medical record review was conducted. Patients were followed up until discharge from hospital.

Surveillance data analysis

IPD incidence rates by age group and provinces were calculated using midyear provincial population estimates from Statistics South Africa (Stats-SA) for 2019–2024. 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. Non-vaccine serotypes (NVTs) included all other serotypes not in PCV13. Vaccination analyses included only children old enough to have received that 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 and December 2024, 1 710 laboratory-confirmed IPD cases were reported to the GERMS-SA surveillance programme in the three provinces. Just over half (51%; 869/1 710) of cases were confirmed on blood culture (Table 1). Demographic characteristics, including median age and sex distribution, were similar between total IPD cases and those captured through ESS (Table 2).

The overall average annual IPD incidence was 2.3 per 100 000 persons in the FS, 1.3 per 100 000 persons in KZN, and 1.2 per 100 000 persons in MP (Figure 1). Infants aged <1 year had the highest average annual incidence rates (FS: 13.3; KZN: 10.2; MP: 9.2 per 100 000 persons). In all three provinces, incidence next peaked in adults aged 45–64 years (FS: 3.3; KZN: 1.7; MP: 1.6 per 100 000 persons) (Figures 2A–C).

The CRDM received 54% (919/1 710) of isolates or PCR-positive but culture-negative specimens, ranging from 47% (451/964) in KZN to 64% (213/333) in MP. Serotyping data were available for 50% (856/1 710), with 63 cases not successfully serotyped. Across all provinces, the most commonly detected serotype was serotype 8 (FS: 13%, 31/246; KZN: 12%, 48/415; MP: 16%, 31/195). The next two most common serotypes included serotype 3 (FS: nine per cent, 23/246; KZN: eight per cent, 35/415; MP: 14%, 27/195) and 19F (FS: 9%, 21/246; KZN: 12%, 49/415; MP: 8%, 16/195). Non-vaccine serotypes (i.e., those not included in PCV10 [SII] or PCV13) predominated, comprising 73% (180/246) in FS, 68% (282/415) in KZN, and 66% (129/195) in MP (Figure 3).

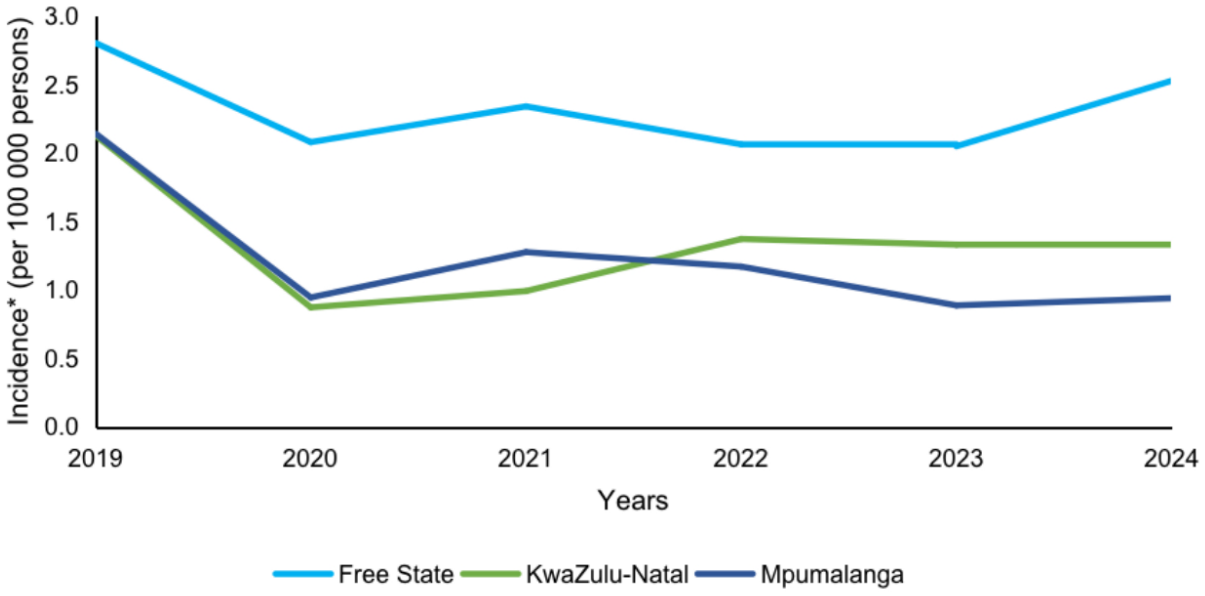

Figure 1. Incidence of invasive pneumococcal disease in the Free State, KwaZulu-Natal, and Mpumalanga provinces, 2019–2024 (N=1 710).

*Rate calculation based on population denominators provided by Stats-SA.

Table 1. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type in the Free State, KwaZulu-Natal, and Mpumalanga provinces, South Africa, 2019–2024 (N=1 710).

Province	Total	Blood		CSF		Other*	
	N	n	%	n	%	n	%
Free State	416	151	36.3	222	53.4	43	10.3
KwaZulu-Natal	961	539	56.1	310	32.3	112	11.7
Mpumalanga	333	179	53.8	129	38.7	25	7.5
Total	**1 710**	**869**	**50.8**	**661**	**38.7**	**180**	**10.5**

CSF = cerebrospinal fluid.

*Includes specimens from normally sterile sites other than blood or CSF, e.g., joint or pleural fluid.

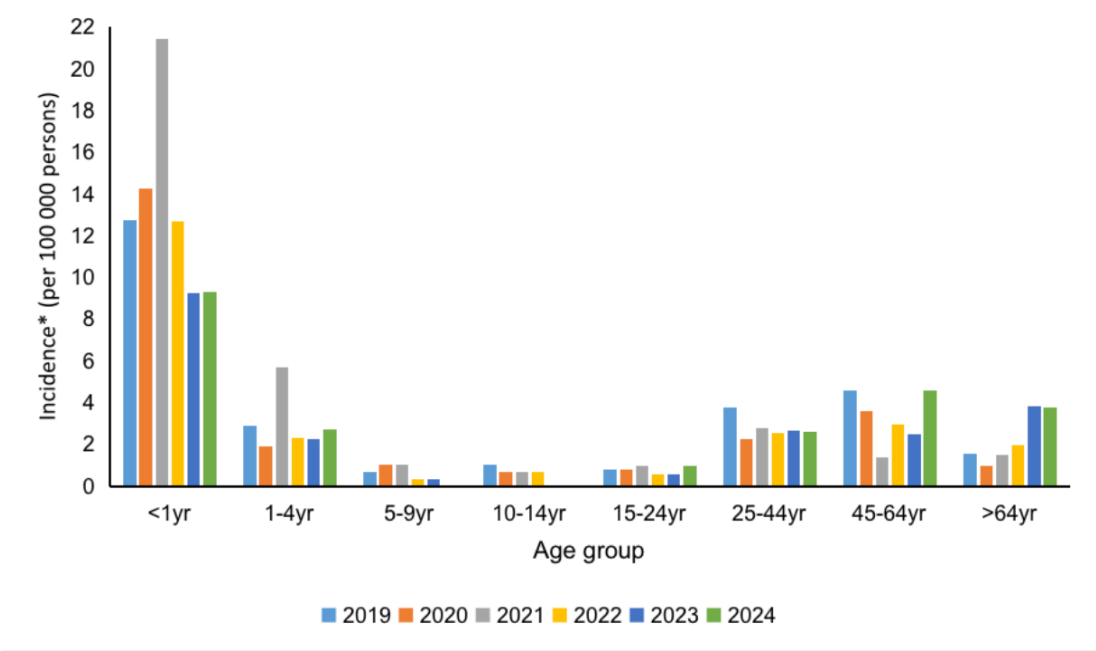

Figure 2A. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the Free State province (N=409; seven with unknown age not included in the figure), 2019–2024.

*Rate calculation based on population denominators provided by Stats-SA.

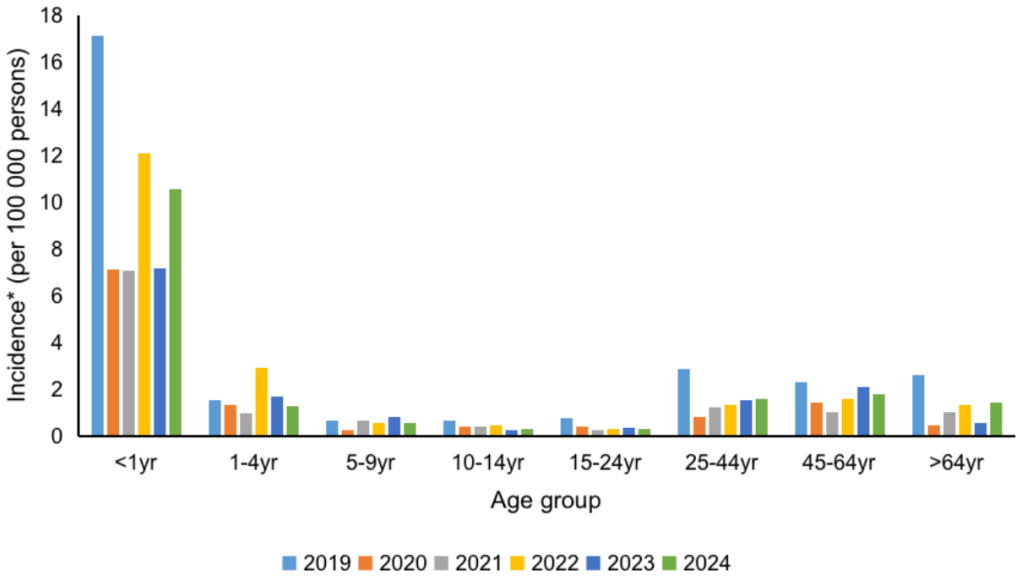

Figure 2B. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the KwaZulu-Natal province (N=946; 15 with unknown age not included in the figure), 2019–2024.

*Rate calculation based on population denominators provided by Stats-SA.

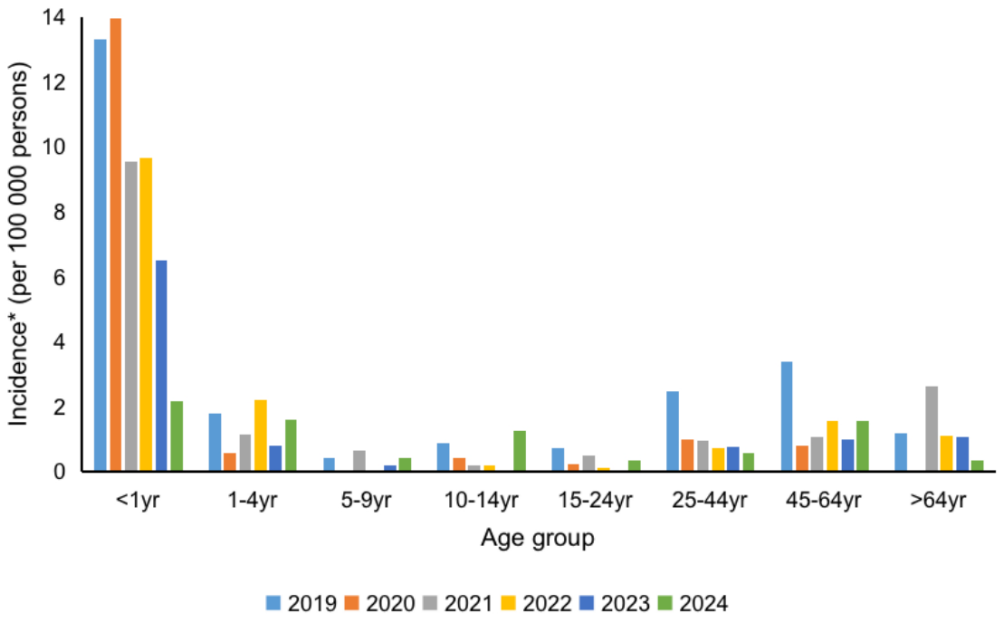

Figure 2C. Age-specific incidence of invasive pneumococcal disease reported to GERMS-SA in the Mpumalanga province (N=312; 21 with unknown age not included in the figure), 2019–2024.

*Rate calculation based on population denominators provided by Stats-SA.

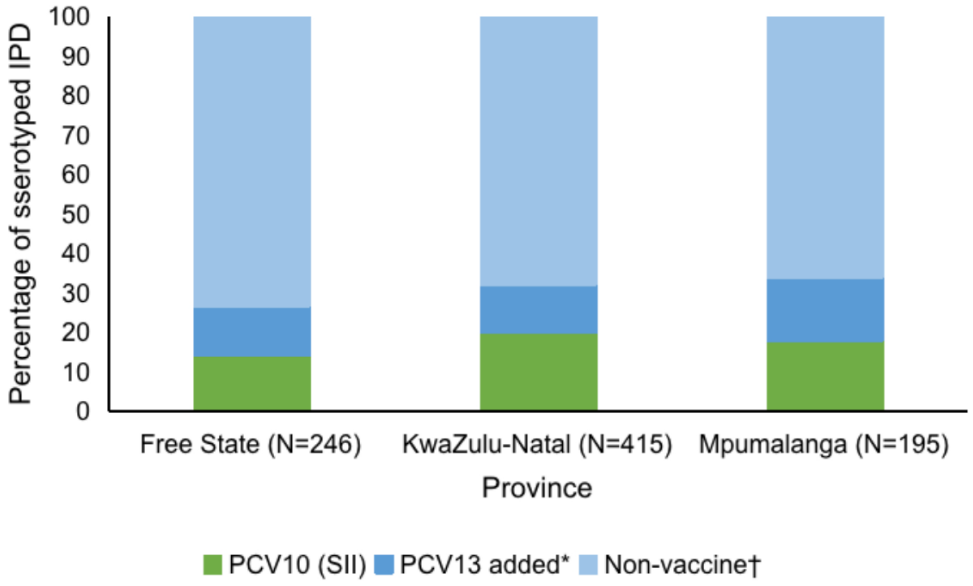

Figure 3. Pneumococcal serotype classification of laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, by relevant pneumococcal conjugate vaccines in the Free State, KwaZulu-Natal, and Mpumalanga provinces, 2019—2024, (N=856; n=854 cases not serotyped excluded from figure).
IPD: invasive pneumococcal disease; PCV: pneumococcal conjugate vaccine.
*Three additional serotypes (3, 4, and 18C) are included in PCV13 but not in PCV10 (SII).
†All other serotypes are not included in PCV13.

Thirty-six per cent (620/1 710) of all IPD cases were detected at ESS. Clinical data were available for 82% (509/620) of these cases (Table 2). Pneumonia was the most common clinical presentation in KZN (49%, 124/253) and MP (45%, 52/115), while meningitis was the most common clinical presentation in the FS (54%, 76/141). One or more co-morbidities (excluding HIV) were documented in 40% (56/141) of cases in the FS, 37% (93/296) in KZN, and 35% (40/115) in MP (Table 2).

Where the outcome was known (99%, 507/509), in-hospital fatality was notably higher in individuals aged ≥5 years compared to children aged <5 years in KZN (43%, 81/190 versus 13%, 8/62) and MP (44%, 37/84 versus 23%, 7/24) (Table 2). By clinical presentation of IPD, in-hospital fatality was high among both meningitis and bacteraemia without focal cases across provinces. In FS, bacteraemia without focus had the highest case fatality (58%, 11/19), followed by meningitis (48%, 36/75) and pneumonia (27%, 10/37). In KZN and MP, meningitis had the highest fatality (KZN: 45%, 36/80; MP: 53%, 19/36), while substantial case fatality was reported among those with bacteraemia without focus (KZN: 41%, 11/27; MP: 30%, 6/20) and pneumonia (KZN: 32%, 40/124; MP: 31%, 16/52).

Among IPD cases at ESS with known HIV status (87%, 445/509), HIV infection was commonly observed, ranging from 58% (130/223) in KZN to 70% in MP (66/94) (Table 2). Among people living with HIV, more than half were currently on antiretroviral therapy (ART), and over a third showed evidence of severe immunosuppression (CD4 ≤200 cells/μL) in all three provinces. Among individuals aged ≥5 years with known HIV status and outcome (51%, 208/409), in-hospital fatality was higher among people living with HIV than among those without HIV infection (FS: 57%, 38/67; KZN: 72%, 72/100; MP: 80%, 33/41).

Table 2. Overview of patient characteristics among IPD cases admitted to enhanced surveillance sites with clinical data available in KwaZulu-Natal, Free State, and Mpumalanga provinces, 2019–2024 (N=509).

Characteristic	FS N = 141 n (% or IQR)	KZN N = 253 n (% or IQR)	MP N = 115 n (% or IQR)
Median age (years)	37 (21—47)	30 (5—43)	30 (3—45)
Age group (years)			
<1	13 (9.2)	41 (16.2)	23 (20.0)
1—4	12 (8.5)	21 (8.3)	8 (7.0)
5—9	5 (3.6)	10 (4.0)	—
10—14	3 (2.1)	8 (3.2)	5 (4.6)
15—24	11 (7.8)	12 (4.7)	9 (7.8)
25—44	56 (39.7)	107 (42.3)	38 (33.0)
45—64	31 (22.0)	43 (17.0)	25 (21.7)
65+	10 (7.1)	11 (4.6)	7 (6.1)
Sex			
Female	52 (36.9)	114 (45.1)	54 (47.0)
Male	87 (61.7)	133 (52.6)	60 (52.2)
Unknown	2 (1.4)	6 (2.4)	1 (0.9)
Specimen type			
CSF	76 (53.9)	69 (27.3)	29 (25.2)
Blood culture	55 (39.0)	150 (59.3)	80 (69.8)
Other	10 (7.1)	34 (13.4)	6 (5.2)
Clinical presentation			
Meningitis	76 (53.9)	80 (31.6)	36 (31.3)
Pneumonia	37 (26.2)	124 (49.0)	52 (45.2)
Bacteraemia without focus	19 (13.5)	27 (10.7)	20 (17.4)
Other	9 (6.4)	21 (8.3)	7 (6.1)
Unknown	—	1 (0.4)	—
Co-morbidities* (excl. HIV)			
No co-morbidities	73 (51.7)	142 (56.1)	71 (61.7)
1 co-morbidity	43 (30.5)	80 (31.6)	26 (22.6)
2 co-morbidities	13 (9.2)	8 (3.2)	12 (10.4)

≥3 co-morbidities	—	5 (2.0)	2 (1.7)
Unknown	12 (8.5)	18 (7.1)	4 (3.5)
High risk behaviours (aged ≥15 years)	(n=108)	(n=173)	(n=80)
Smoker	16 (14.8)	33 (19.1)	5 (6.3)
Alcohol dependency†	1 (0.9)	4 (2.3)	—
In-hospital fatality			
Died	57 (40.4)	89 (35.2)	44 (38.3)
Alive	83 (58.9)	163 (64.4)	71 (61.7)
Unknown	1 (0.7)	1 (0.4)	—
HIV status (aged ≥5 years)	(n=116)	(n=191)	(n=84)
HIV infected	73 (62.9)	117 (61.3)	58 (69.1)
HIV uninfected	33 (28.5)	50 (26.2)	12 (14.3)
Unknown	10 (8.6)	24 (12.6)	14 (16.7)
HIV status (aged <5 years)	(n=25)	(n=62)	(n=31)
HIV infected	4 (16.0)	13 (21.0)	8 (25.8)
HIV exposed uninfected	4 (16.0)	13 (21.0)	9 (29.0)
HIV unexposed uninfected	14 (56.0)	30 (48.4)	7 (22.6)
Unknown	3 (12.0)	6 (9.9)	7 (22.6)
People living with HIV	**77**	**130**	**66**
ART treatment experience			
Current	41 (53.3)	83 (63.9)	30 (45.5)
Previous	19 (24.7)	9 (6.9)	10 (15.2)
None	13 (16.9)	30 (23.1)	23 (34.9)
Unknown	4 (5.2)	3 (2.3)	3 (4.5)
CD4 count (cells/µl)			
≤200 cells/µL	44 (57.1)	47 (36.2)	29 (43.9)
>200 cells/µL	17 (22.1)	43 (33.1)	18 (27.3)
Unknown	16 (20.8)	40 (30.1)	19 (28.8)
Viral load (copies/mL)			
≥400	18 (23.4)	43 (33.1)	20 (30.3)
<400	21 (27.3)	26 (20.0)	10 (15.2)
Unknown	38 (49.4)	61 (46.9)	36 (54.6)

KZN: KwaZulu-Natal; FS: Free State; MP: Mpumalanga; n: numerator; CSF: cerebrospinal fluid; IQR: interquartile range; excl.: excluding; 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 (74%; 87/118), the most commonly detected serotype across all provinces was serotype 8 (16%, 14/87), followed by serotype 19F (12%, 10/87) (Figure 4A–C). Non-vaccine serotypes predominated across all vaccination categories and provinces (72%; 63/87). Eight breakthrough infections (42%; 8/19) occurred in fully vaccinated children, including five due to serotype 19F and one case each of serotypes 19A, 23F, and 3. Seven of the eight children with breakthrough infections had documented underlying co-morbidities, including HIV infection (n=3), HIV exposure without infection (n=4), tuberculosis requiring treatment (n=2), and prematurity (n=4); the remaining child was 15 months old and presented with bacteraemia without an identified focus. Among individuals aged ≥5 years, there were no reports of vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV23), which provides coverage for serotype 8.

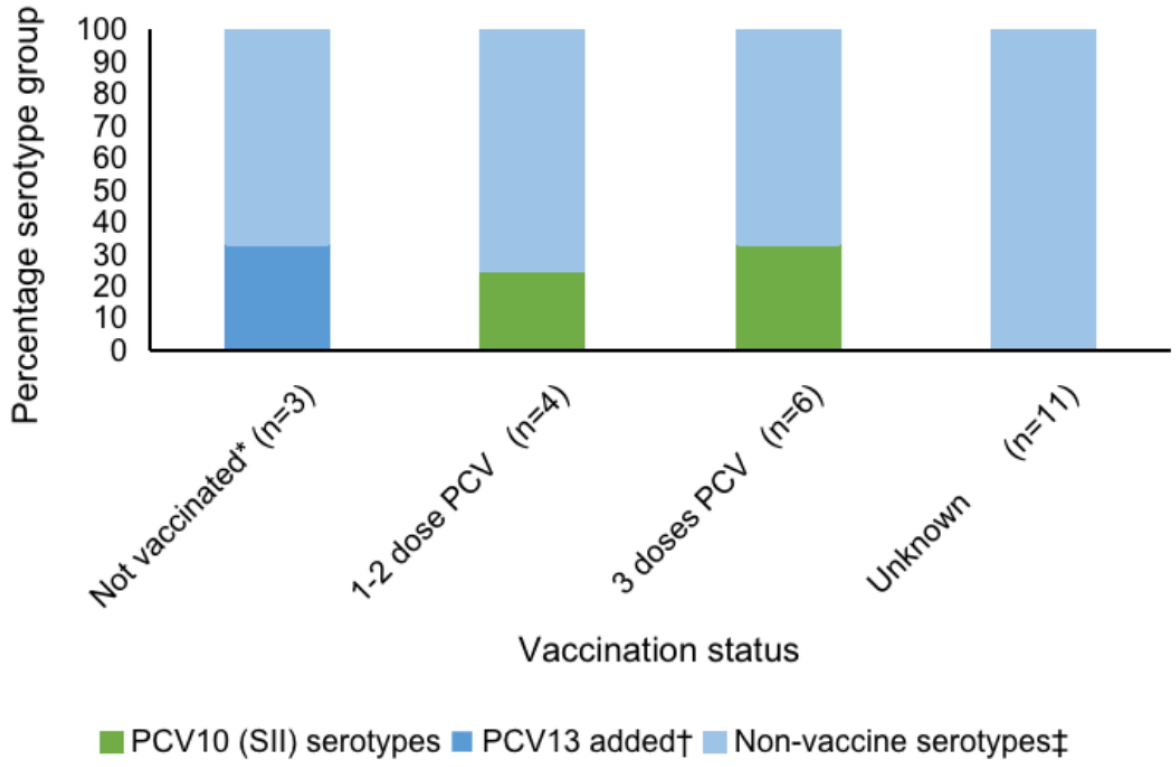

Figure 4A. The distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in the Free State, 2019–2024 (N=24; one case was excluded from the figure due to no serotyping information).

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

*Infants aged <8 weeks (n=3) or those ≥8 weeks (n=0) 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.

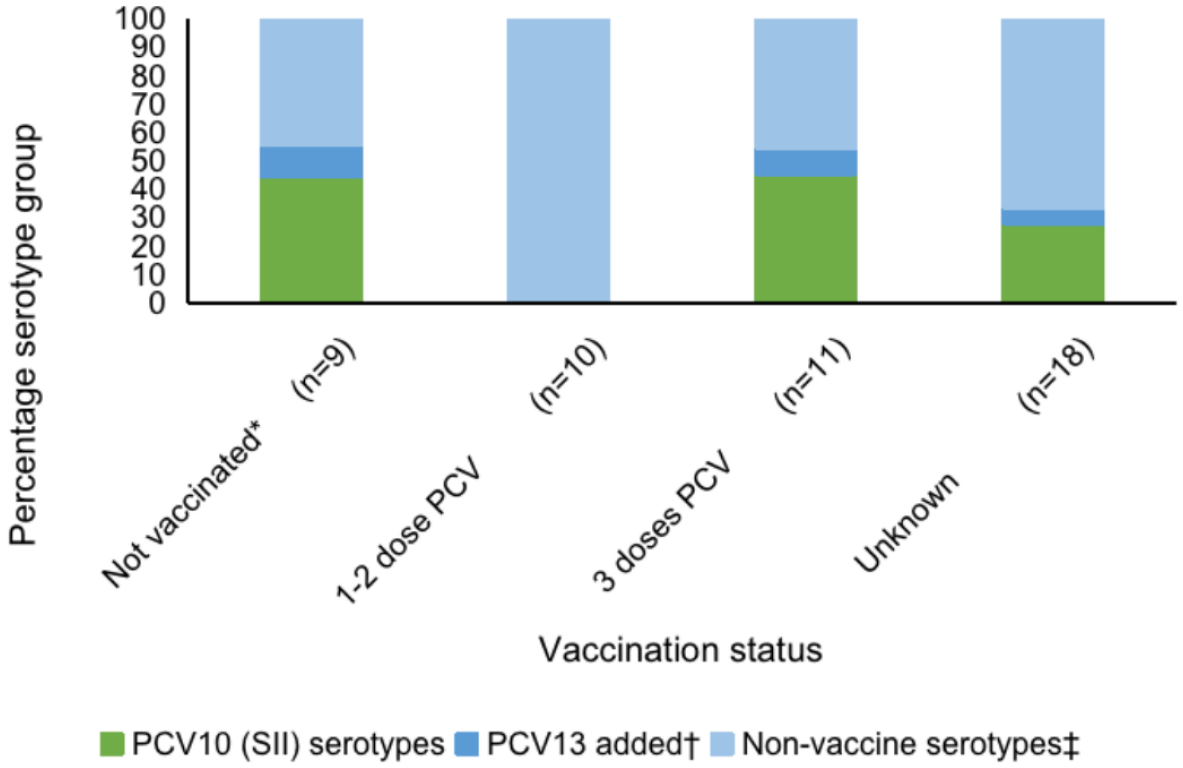

Figure 4B. The distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in KwaZulu-Natal, 2019–2024 (N=48; 14 cases were excluded from the figure due to no serotyping information).

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

*Infants aged <8 weeks (n=8) or those ≥8 weeks (n=1) 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.

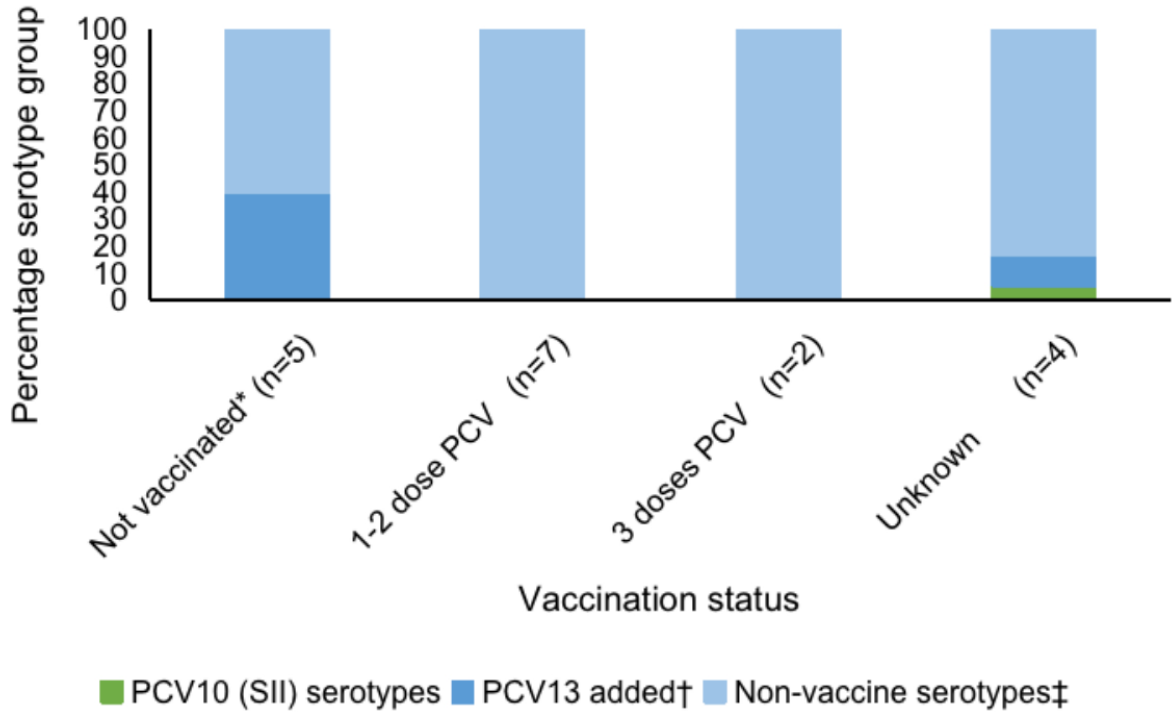

Figure 4C. The distribution of PCV10 (SII)/PCV13 and non-vaccine serotypes by vaccination status among children aged <5 years with invasive pneumococcal disease at enhanced surveillance sites in Mpumalanga, 2019–2024 (N=18; 13 cases were excluded from the figure due to no serotyping information). PCV: pneumococcal conjugate vaccine; SII: Serum Institute India.

*Infants aged <8 weeks (n=4) or those ≥8 weeks (n=1) with no history of PCV vaccination.

†Three additional serotypes are 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 FS, KZN, and MP provinces showed the highest burden among infants aged <1 year and adults with underlying co-morbidities. Pneumonia was the most common clinical presentation in all provinces, except in the FS, where meningitis was most common. In-hospital fatality among IPD cases was substantial (FS: 40%, KZN: 25%, MP: 38%) but not unexpected given the invasive nature of the disease, high prevalence of HIV infection, and other co-morbidities among cases, and the predominance of large referral hospitals among ESS. Non-vaccine serotypes accounted for most disease (FS: 73%, KZN: 68%, MP: 66%). These findings should be interpreted in the context of previous research documenting temporal reductions in vaccine-type IPD following PCV introduction.[2]

Our findings that residual IPD cases are mostly due to non-vaccine serotypes support the need for sustained serotype surveillance.

Provincial variation was observed across several indicators; however, these data were not analysed for inter-provincial comparisons and should be interpreted cautiously, as observed differences may reflect both true epidemiological heterogeneity and variation in surveillance and diagnostic practices. The COVID-19 pandemic was associated with a temporary reduction in IPD incidence, probably due to non-pharmaceutical interventions and reduced healthcare access.[8] Following this, a return towards pre-pandemic levels was observed in the FS, while KZN and MP showed a gradual increase in IPD that has not yet reached pre-pandemic levels, possibly influenced by the NHLS laboratory information system disruption in June/July 2024 that may have led to underreporting. Provincial variation was also noticeable in clinical presentation, with a higher proportion of meningitis and CSF specimens reported in the FS compared with KZN and MP. These findings are not directly comparable between provinces due to differences in surveillance completeness, healthcare access, and laboratory practices, among other factors. Further analytic studies are needed to better understand the contribution of these factors to the observed provincial-level variation in IPD.

HIV infection was common among individuals aged ≥5 years and similarly high across provinces (FS: 63%, KZN: 61%, MP: 69%), although variations were observed in treatment experience and immune status. These observations suggest that differences in HIV disease management, rather than prevalence alone, may contribute to provincial-level variation of IPD burden, although analytical studies would be required to investigate this hypothesis. In-hospital fatality was higher among adults than children aged <5 years, which may potentially reflect a higher prevalence of underlying co-morbidities, including HIV-related immunosuppression. Among children aged <5 years, HIV infection (FS: 16%, KZN: 21%, MP: 26%) and HIV exposure (FS: 16%, KZN: 21%, MP: 29%) were substantial, highlighting vulnerability in this population. This finding suggests potential gaps in early diagnosis, treatment initiation, or retention in care.

Disease prevention efforts should focus on achieving high infant immunisation coverage (>90%), since IPD incidence was highest in this age group, and on continued monitoring of non-vaccine serotypes to inform vaccine strategies, including the potential use of higher-valency vaccines to address non-vaccine-type disease. Almost half (48%) of infant cases occurred within the first three months of age, prior to completion of the primary PCV series, indicating a period of vulnerability that could be reduced through improved PCV coverage and timely completion of all scheduled doses, including the booster, to strengthen indirect protection, with maternal immunisation as a potential future consideration. In our surveillance, only 54% of eligible IPD isolates/specimens were received for further characterisation, which may have influenced serotype estimates and highlights the need to strengthen laboratory participation in IPD surveillance, particularly following the 2024 switch from PCV13 to PCV10 (SII). A large proportion of cases occurred in

people living with HIV and individuals with chronic illnesses, and in-hospital fatality was substantial, emphasising the importance of targeted vaccination and optimal clinical management (e.g., sustained ART adherence) among these high-risk groups to reduce morbidity and mortality. In terms of IPD detection, 12% (109/919) of cases received for further characterisation were culture-negative but PCR-positive, which may reflect prior antibiotic exposure or the fastidious nature of pneumococcus. This finding supports strengthening the use of molecular diagnostics, particularly for culture-negative CSF specimens with elevated cell counts, and reinforcing the referral of such specimens to the CRDM to improve IPD detection and surveillance.

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 without microbiology testing or access to laboratory services would not have been captured. Non-IPD, such as pneumonia without bacteraemia, which contributes substantially to vaccine-preventable disease, was not captured in this surveillance.[15] Serotype data were available for approximately half of IPD cases, which may introduce selection bias if isolates submitted for characterisation are not fully representative of all cases. Previous analyses using the GERM-SA surveillance platform have demonstrated that serotype distributions observed among sampled isolate collections were consistent with those observed in larger surveillance datasets, supporting the utility of submitted isolates for describing pneumococcal serotype epidemiology and vaccine impact despite incomplete isolate submission.[16, 17] Surveillance procedures for isolate submission have remained unchanged over time, although incomplete submission remains a recognised limitation of the system. ESS data may not be fully representative of all provincial cases, potentially limiting the generalisability of our findings. Incomplete clinical and HIV-related data at ESS, partly due to variable recording by clinicians and gaps in medical records, may have affected data completeness and quality. The descriptive nature of this report limits the ability to determine causal relationships or adjust for confounding factors, such as HIV-related factors.

Conclusion

IPD remains a preventable yet significant cause of morbidity and mortality in the FS, KZN, and MP. Infants, adults with co-morbidities, and people living with HIV were most affected. The predominance of non-vaccine serotypes in our surveillance of IPD reinforces the need for continued monitoring of IPD serotype distribution, particularly following the recent switch to PCV10 (SII). Strengthening integration of IPD prevention into HIV care pathways and targeting high-risk groups are essential to reduce the IPD burden.

National IPD surveillance data are available in the GERMS-SA Annual Report (https://www.nicd.ac.za/wp-content/uploads/2025/12/GERMS-Annual-Review-2024.pdf), Public Health Bulletin South Africa GERMS-SA key findings (https://www.phbsa.ac.za/2023-germs-sa annual-surveillance-review-key-findings/), and the

quarterly GERMS-SA surveillance reports (https://www.nicd.ac.za/publications/communicable-diseases-publications/laboratory-surveillance-of-invasive-bacterial-diseases-vaccine-preventable-epidemic-pathogens/).

Recommendations for policy and practice

We recommend the following for the three provinces:

1. **Surveillance strengthening:**

- Strengthen IPD case detection and surveillance through timely identification of suspected IPD and submission of all IPD isolates/specimens for characterisation led by microbiology laboratory teams in collaboration with the GERMS-SA/NICD staff.
- Encourage complete documentation of PCV vaccination history in Road-to-Health Cards to support surveillance, investigation of breakthrough vaccine-type IPD, and future evaluations following vaccine formulation changes, supported by provincial and district primary healthcare managers in collaboration with Maternal and Child Health directorates and EPI programme managers.
- Enhance visibility and accessibility of GERMS-SA surveillance data to clinicians and laboratories to demonstrate the value of serotype information and encourage submission of isolates or specimens for characterisation, driven by the GERMS-SA/NICD staff.

2. **HIV integration:**

- Ensure that all patients presenting with IPD at any age with an unknown HIV status are tested for HIV during hospitalisation, with linkage to care for those newly diagnosed, implemented by patient-facing clinicians and oversight by provincial/district HIV programme managers according to the HIV guidelines.
- Consider risk-based pneumococcal vaccination recommendations in Department of Health (DoH) policy and routine clinical care, prioritising those at increased risk of IPD, including people living with HIV and individuals with co-morbidities, guided by the National and Provincial DoH immunisation and non-communicable diseases programmes.

3. **Vaccination coverage improvement:**

- Identify districts within provinces with low infant PCV vaccination coverage (<90%) to target outreach interventions aimed at improving PCV vaccine coverage to ≥90%, led by provincial and district EPI co-ordinators.

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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 Free State (HSD2018/085810) for FS; the University of KwaZulu-Natal (BF 130/11) for KZN; and the University of the Witwatersrand HREC (M1809107; M230985) for MP. 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.

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