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FOREWORD

This diverse issue presents details of malaria microscopy quality control, two long-term disease monitoring reports and two annual surveillance reports for South Africa.

Light microscopy of blood smears remains the gold standard for diagnosing clinical malaria, and a recent quality assurance assessment of this method shows that malaria parasite microscopy in the Mpumalanga Province malaria control programme performs well, although there is room for skills improvement.

A rare form of pneumonia, Legionnaires' disease, affects South Africa, primarily in Western Cape Province. As this disease is transmitted through the inhalation of contaminated water droplets, ongoing surveillance and improved investigation of cases is important for cluster identification, particularly during the COVID-19 pandemic when lockdown measures have resulted in closure or restricted use of buildings, thereby increasing the risk for Legionella growth in water systems.

Children and adolescents living with HIV in South Africa remain an especially vulnerable population. A report in this issue shows that major advances in paediatric HIV care, in particular retention in care and treatment adherence, will be required if South Africa is to achieve an end to the AIDS epidemic.

Acute flaccid paralysis (AFP) surveillance is used as a proxy for polio incidence. The AFP surveillance report for 2019, presented in this issue, shows that countries in the southern African region, including South Africa, need to strengthen their surveillance efforts and increase routine immunization against polio.

This issue also contains the GERMS-SA report for 2019. This report contains summaries of national surveillance data for laboratory-confirmed invasive meningococcal, *Haemophilus influenzae*, pneumococcal, Group A Streptococcal and Group B Streptococcal infections. These data are routinely collected from the enhanced surveillance sites that cover all nine of South Africa's provinces.

We trust that you will find these important reports informative and useful, and thank all contributors for their inputs.

Basil Brooke, Editor

QUALITY CONTROL OF MALARIA MICROSCOPY SURVEILLANCE, MPUMALANGA PROVINCE MALARIA CONTROL PROGRAMME, SOUTH AFRICA, JANUARY – DECEMBER 2019

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Summary

The prompt diagnosis and treatment of malaria is the most effective way to prevent a mild case from developing into severe disease and potentially, death. All malaria patients must be treated as soon as possible following microscopy and/ or rapid diagnostic test confirmation of malaria. Light microscopy of Giemsa-stained blood smears remains the gold standard for diagnosing clinical malaria.

The South African National Malaria Quality Assurance Guidelines stipulate that microscopy results should be cross-checked for quality assurance purposes. The South African malaria control programme operates primarily in the three malaria-endemic provinces of Mpumalanga, KwaZulu-Natal and Limpopo. Malaria microscopy quality control (QC) was initiated in 2018 for the Mpumalanga provincial malaria control programme (MCP). On at least a monthly basis, smears were sent to the Parasitology Reference Laboratory (PRL) at the National Institute for Communicable Diseases (NICD) for QC. Twenty percent of the received smears and any additional positive smears underwent microscopy quality control; this included microscopy and PCR. The PRL received 4 738 smears in 2019 and microscopy quality control was done on 969 of these. The majority (939) were reported as negative by the MCP. The PRL found two false positive results and three false negative results. Mpumalanga Province MCP microscopy had a sensitivity of 88.9% and a specificity of 99.8% as compared against PRL microscopy. When microscopy results were compared to PCR results, the majority of smears (94%, 781/834) were concordant between the Mpumalanga Province MCP microscopy, PRL microscopy and PRL PCR. This quality control exercise shows that malaria parasite microscopy in the Mpumalanga Province MCP performs well. There is however room for microscopy skills improvement within the Mpumalanga province MCP. The PRL/NICD has recommended that all provincial MCP malaria microscopists attend the Malaria Microscopy Refresher Course offered by the PRL. They will also benefit greatly from the implementation of a proper quality management system.

Background

Malaria is a parasitic disease caused by *Plasmodium* species, and is usually transmitted by an infected female *Anopheles* mosquito.[1] In South Africa, human malaria is caused by four species of the *Plasmodium* parasite*: Plasmodium falciparum*; *P. malariae*; *P. ovale* and *P. vivax*.[2] *Plasmodium knowlesi* is recognised as the fifth human malaria parasite[2] but has not yet been reported in South Africa.

Malaria is preventable and curable but if not diagnosed and treated early, can be fatal. In 2018, an estimated 228 million cases of malaria occurred worldwide with 405 000 reported deaths.[1] The majority of malaria cases (213 million or 93%) and deaths (94%) were in the World Health Organization (WHO) African Region.[1] Children aged under 5 years are the most vulnerable group affected by malaria, accounting for 67% (272 000) of all malaria deaths worldwide.[1]

Ten percent of the population in South Africa is estimated to be at risk of contracting malaria.[3] In South Africa, malaria is seasonal, occurring mainly between September and May, with cases usually peaking after the Christmas and Easter holidays.[4] Over 90% of the reported malaria cases are caused by *P. falciparum*.[4] Malaria has been a notifiable medical condition (NMC) in South Africa since 1956.[5] According to South Africa's National Health Act 61 of 2003, all malaria cases should be reported within 24 hours of diagnosis.[6] Light microscopy of Giemsa-stained blood smears remains the gold standard for diagnosing clinical malaria.[7] Prompt diagnosis and treatment is the most effective way to prevent a mild case of malaria from developing into severe disease and potentially, death.[1]

Between 2000 and 2012, South Africa reduced the burden of malaria by ~90% (64 622 vs. 6 846 cases, respectively) and mortality by ~80% (459 vs. 91 deaths, respectively).[7] In 2012, South Africa adopted a malaria elimination strategy.[4] The broad objectives of the national malaria elimination strategy include strengthening case surveillance, preventing infections and eliminating the parasite reservoir.[5]

An essential component of a malaria surveillance system is the accurate parasitological diagnosis of malaria cases. The WHO Malaria Surveillance, Monitoring and Evaluation Reference Manual recommends that diagnosis should be made with either quality-assured malaria microscopy or WHO-recommended rapid diagnostic tests (RDTs).[8] The WHO Malaria Microscopy Quality Assurance Manual states that: "Blood film microscopy remains the only inexpensive, easily used test for direct measurement of the presence of parasites, distinguishing the infecting parasite species and providing a means of quantifying parasite load."[9] These attributes of malaria microscopy make it an extremely useful tool in any malaria control programme.

South Africa has a decentralised malaria control programme (MCP) with activities at the provincial level.[5] The national malaria programme at the National Department of Health (NDOH) defines policies and guidelines and provides technical support to provinces.[5] The provincial MCPs operate in the three malaria-endemic provinces of KwaZulu-Natal, Mpumalanga and Limpopo. All malaria-positive cases are provided with treatment within 24 hours and treatment is only prescribed when cases are confirmed.[5] Since 2000, all suspected malaria cases in South Africa have been confirmed using microscopy and/or RDTs.[5]

There are two broad types of malaria case surveillance activities conducted by the provincial MCPs in South Africa: passive case detection (PCD) and active case detection (ACD). During the PCD process, patients visit health facilities and, once they are confirmed as having malaria, the health worker notifies the case as per the NMC requirements.[5] Therefore PCD is detection of malaria cases among people who approach a health facility or a community health worker on their own initiative to seek treatment, usually related to fever.[8] On the other hand, ACD locates both symptomatic and asymptomatic malaria cases, who will also be treated according to national malaria treatment guidelines.[5]

The aim of ACD surveillance is to prevent onward malaria transmission by identifying new infections and potential sources of infections.[5] ACD surveillance is further classified into reactive case detection (RACD) and proactive case detection (PACD).[8] RACD is usually a response to an index case that may have been notified through the NMC process. RACD will screen for symptoms and test for malaria in the household of the index case and/or people in the community potentially linked to the index case[8] (Figure 1).

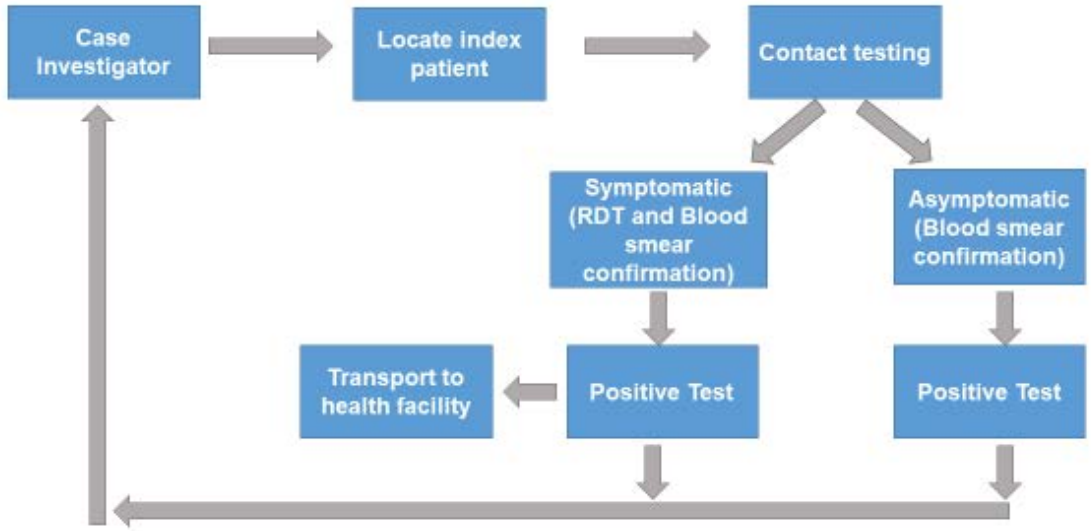

Figure 1. Adapted flow diagram demonstrating the general reactive case investigation and detection plan.[5]

PACD is triggered by the strong likelihood of malaria transmission in a defined area or among high-risk groups of people.[5,8] There is usually limited access to healthcare facilities. PACD is performed regularly at specific times (mainly during the malaria transmission season) to confirm active local transmission in target populations and to detect malaria cases early.[8]

There are dedicated teams of malaria surveillance officers and case investigators working between the health facilities and the communities on a daily basis.[5] The duties of the malaria surveillance teams include conducting malaria-related health education, taking blood smears, collecting malaria-related data in the field and assisting

the team leaders with conducting case investigations.[5] The MCPs have malaria microscopists who work independently of the National Health Laboratory Service (NHLS).[10]

The South African National Malaria Quality Assurance Guidelines stipulate that microscopy results should be cross-checked as quality control (QC) for quality assurance purposes.[11] This is required as South Africa is moving towards malaria elimination, with the target of zero locally-transmitted malaria cases.[12] To assist with malaria microscopy surveillance in South Africa, the Parasitology Reference Laboratory (PRL) at the National Institute for Communicable Diseases (NICD), a specialised institution of the NHLS, has assisted with the required QC for the provincial malaria control programmes. QC was initiated for Mpumalanga Province in 2018, as this MCP's slide procedures were mostly aligned to the processing QC requirements.

Methods

As per the routine malaria testing procedures described above for active surveillance, case investigator teams from the Mpumalanga Province MCP actively screened people who lived with or near to a person who had tested positive for malaria. Once these people were located, the case investigators and their team members collected basic demographic information using a registry form. Blood was collected using the finger prick method with a disposable lancet, an RDT was performed (when indicated), and thick and thin blood smears were prepared on site.

The forms and smears were sent to one of four testing stations in Mpumalanga Province for staining and/microscopy. The testing stations were located in Thulamashe and Cunningmoore in Bushbuckridge District, Masoyi in Mbombela districts and Tonga in Nkomazi District. At the testing stations, the dried blood smears were stained with Giemsa. Thin blood films were first fixed with 100% methanol. MCP microscopists then examined the blood films for *Plasmodium* spp. using light microscopy. Microscopy results were recorded on the forms and any positive results were communicated to the case investigators for further action. On at least a monthly basis, smears were sent to PRL/NICD with copies of the corresponding Mpumalanga Province MCP forms for microscopy QC.

At NICD, smears were checked against the accompanying forms. Any missing smears or forms were noted. Twenty percent (every 5th slide) of the received smears were then selected for QC. Any additional site positives that were not part of the 20% blinded reads were also selected for QC. Each of the selected smears was read by two microscopists independently. The thick blood smears were scanned under 100x magnification first, then under 1000x magnification using immersion oil. At least 100 to 150 high power fields (1000x magnification) were looked at before declaring a smear negative for malaria, where possible. A third microscopy read was done if there were discrepant results between the first two microscopy reads or when compared to the microscopy results from the Mpumalanga Province MCP microscopists. All smears received were also assessed for quality macroscopically and microscopically. Quality areas looked at were thick smear fixing by methanol or heat, presence of a feathered edge on thin smears, presence of stain precipitate, or washing-off of the blood smears. Following microscopy and checking of any discrepant microscopy results, DNA was extracted from the blood smears and a conventional malaria multiplex PCR, which detects the four common human

malaria species in South Africa, was performed.[13] Results were collated, analysed and reports sent to the Mpumalanga Province MCP.

Results

In 2019, 4 738 smears were received. Figure 2 shows the summary of the number of smears that were received by month. Nineteen batches were received (there were a few months where multiple batches were received). Due to occasional delays, smears were not always received in the month after they were completed by the province. Therefore, the number of smears received each month at NICD does not accurately reflect the number of smears done in the previous month from the Mpumalanga Province MCP.

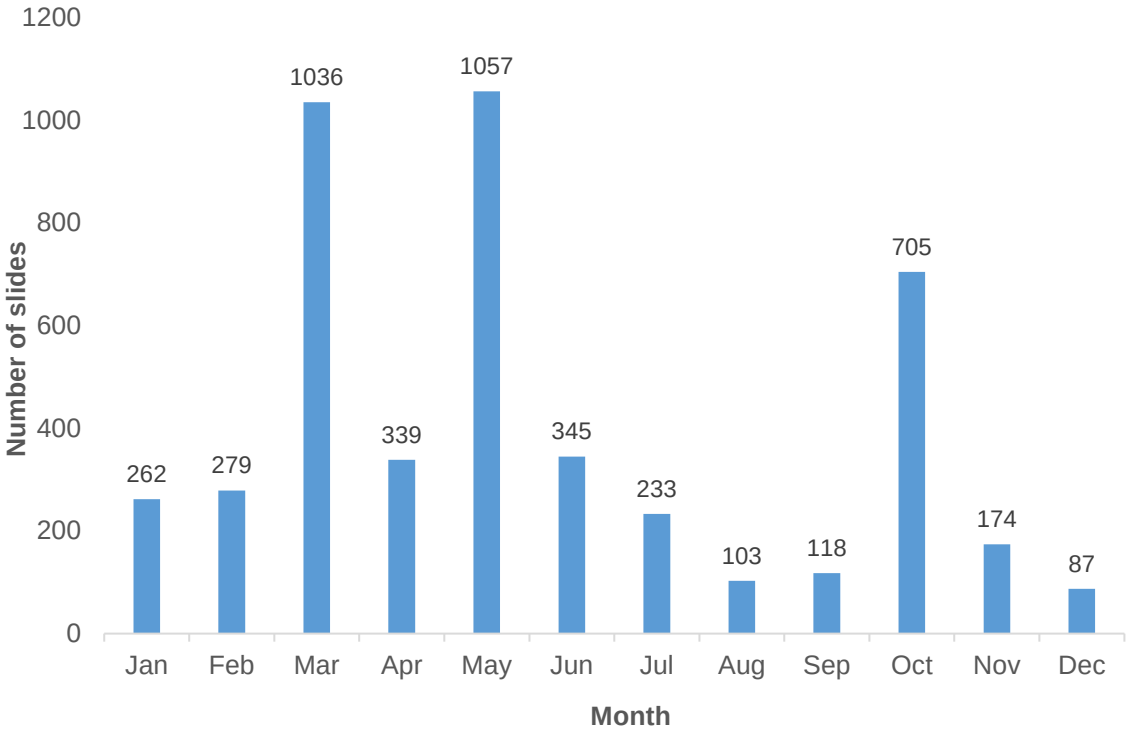

Figure 2. Numbers of malaria smears received by the National Institute for Communicable Diseases for quality control from the Mpumalanga Province malaria control programme, 2019.

Of all the smears received, the Mpumalanga province MCP reported 32 (0.7%) as positive and 4 665 as negative; there were 41 smears that had missing microscopy results or missing forms. All smears received without paperwork (n=37) were assumed to be negative for the purpose of this comparison and were included in the analysis. Table 1 shows a summary of the results, comparing microscopy between the Mpumalanga Province MCP and NICD for the smears that were quality controlled. The Mpumalanga Province MCP microscopy had a sensitivity of 88.9% and a specificity of 99.8%.

Table 1. Summary of the comparison of malaria parasite microscopy between Mpumalanga Province malaria control programme (MCP) and the National Institute for Communicable Diseases (NICD).

		NICD microscopy result	
		Positive	**Negative**
Mpumalanga Province MCP microscopy result	**Positive**	24	2
	Negative	3	936

Of the 969 slides that were microscopically quality controlled by NICD, Mpumalanga Provincial MCP reported 26 smears as positive and 939 as negative. Unfortunately, due to difficulty in interpreting the MCP forms, six smears reported by the Mpumalanga Provincial MCP as positive were accidentally discarded before microscopy QC was done. The results are explained further in Table 2. There were four cases that did have paperwork but had 'RDT positive' recorded as a microscopy result. For these four cases, one was confirmed as *P. falciparum* (1 032 p/µl) and the other three were found to be negative by microscopy QC. These results were excluded from the analysis.

Table 2. Comparison of malaria parasite microscopy results between the Mpumalanga Province malaria control programme (MCP) and the National Institute for Communicable Diseases (NICD).

Mpumalanga Province MCP microscopy result	NICD microscopy result	Number	Comment on the Mpumalanga MCP microscopy result
Positive	Positive	21	100% agreement
Negative	Negative	936	100% agreement
P. falciparum	*P. malariae*	1	Incorrect species identification
Relapsing malaria species	*P. ovale*	1	Acceptable response
Relapsing malaria species	*P. falciparum*	1	Incorrect species identification
Relapsing malaria species	Negative	1	False positive
"Positive"	Negative	1	False positive
Negative	*P. falciparum*	3	False negative

The three false negative slides had low parasitaemias: 16 parasites/microliter (p/µl), 546 p/µl and 417p/µl. To put this in context of percentage parasitaemia, an average of 50 000 p/µl is considered 1% parasitaemia.[14] Therefore, these three false negatives all had percentage parasitaemias of 0.01% or less.

All slides received were also assessed for smear quality (Figure 3). The major problems noted were the lack of a feathered edge on the thin blood films, partial washing off of the blood films and partial autofixing of the thick blood films.

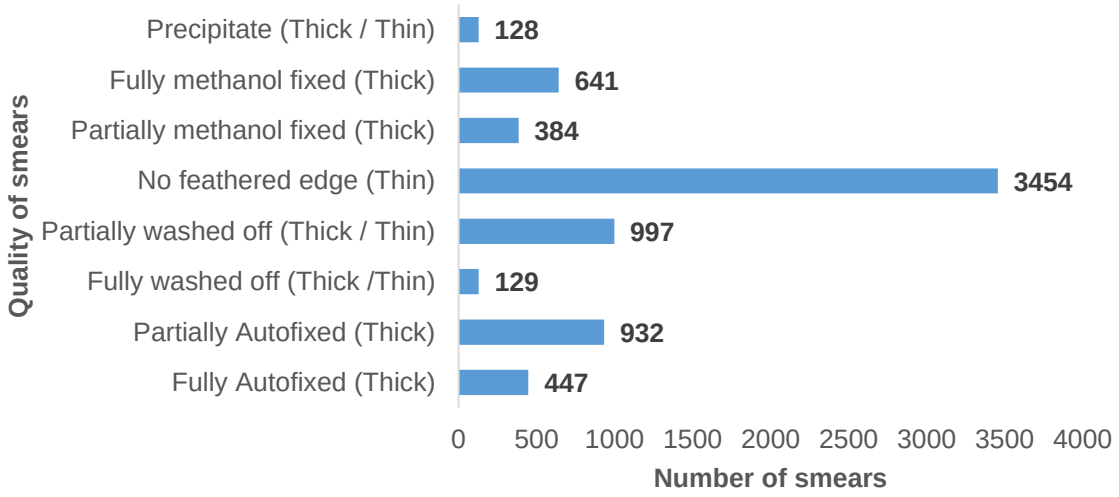

Figure 3. Results of the assessment of the Mpumalanga Province malaria control programme blood smear quality, 2019.

Molecular testing was initiated from slides received at NICD in March 2019. Seventeen of the 19 batches (851 slides) had PCR results available to be compared to the microscopy results and 118 slides were excluded. The majority of slides (94%, 781/834) had concordant results between the Mpumalanga Province MCP microscopy, NICD microscopy and NICD PCR (Table 3). Thirteen slides were quality-controlled microscopically, but accidently discarded before molecular testing could be performed. The four cases whose microscopy results were recorded as 'RDT Pos', were negative on PCR.

Table 3. Comparison between the National Institute for Communicable Diseases (NICD) PCR results and the microscopy results from the Mpumalanga Province malaria control programme (MCP) and the NICD.

Mpumalanga province MCP microscopy result	NICD microscopy result	NICD PCR result	Number
Negative	Negative	Negative	775
Positive	Positive	Positive	6
Positive	Positive	Negative	9
Positive	Negative	Negative	2
Negative	Positive	Negative	1
Negative	Positive	Positive	2
Negative	Negative	Positive	39

Discussion, conclusions and recommendations

The microscopy quality control results for 2019 show good sensitivity and excellent specificity by the Mpumalanga Province MCP microscopists. Very few false positives and false negatives were detected; nevertheless, there is room for improvement of the microscopy skills at the testing stations. Only six of the Mpumalanga province MCP positive smears had quantitation recorded. Quantitation should be determined for all *P. falciparum*-positive samples. Only asexual stages (trophozoites and schizonts) should be counted, as the asexual stages of the parasite contribute to the clinical symptoms of the disease. If gametocytes of *P. falciparum*

are observed, it is important to record this observation, as gametocytes (sexual stages) contribute to the ongoing transmission of malaria.

Concerning the quality issues, we note that it is difficult to prepare perfect smears in the field, i.e. from a fingerprick and often without a table. In April 2018, case investigators were provided with slide boards to assist them in the field. To prevent autofixing of the thick smears, the field teams were requested to deliver the smears to the testing stations for staining in the quickest time possible. The staff at the testing stations were also trained to take care while rinsing the stain off the slides to prevent the smears from washing off. There were major issues with the completion of forms: some data were illegible, missing or filled in incorrectly. These concerns were reported to the province. They will also benefit greatly from implementing a proper quality management system.

The NICD has requested that the batches be sent as soon as possible. Ideally, they should be sent in the month after the testing station has processed the smears. This will allow for a quicker feedback response to the province. As a preventive measure, NICD will store smears that have not undergone microscopy QC for at least six months after receipt.

It is expected that more samples would be identified as positive by PCR as compared to microscopy, as PCR is generally more sensitive than microscopy at very low parasitaemias.[7] However, there were 10 NICD-confirmed microscopy-positive results that were PCR negative. Low concentration of the *Plasmodium* spp. DNA, the sample type that the DNA was extracted from (blood smears) or the presence of inhibitors in the sample, are possible reasons for this.

It is recommended that all the MCP microscopists be given an opportunity to attend the Malaria Microscopy Refresher Training (MMRT) course offered by PRL, NICD. At the end of the course an evaluation will be conducted to determine if the malaria microscopists qualify to attend the National Competence Assessment in Malaria Microscopy (NCAMM). The NCAMM will be a formal certification of their level of skill in malaria microscopy (based on parasite detection, identification and quantification). A certificate of competence reflecting their grading (highest grade A, lowest grade D) will be awarded at the end of the NCAMM and will be valid for two years. This objective assessment of competence will be done according to the Malaria Microscopy Quality Assurance Manual (version 2) published by the World Health Organization.[9]

Acknowledgements

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References

1. World Health Organization, 2019. World Malaria Report 2019. Geneva: World Health Organization
2. South African National Department of Health, 2018, National Guidelines for the Prevention of Malaria – South Africa, Pretoria, NDoH Available at: https://www.nicd.ac.za/diseases-a-z-index/malaria/ [Accessed 17-08-2020]
3. South African National Department of Health, 2015. Malaria Introduction. [online] Health.gov.za. Available at: http://www.health.gov.za/index.php/introduction [Accessed 17 July 2020].
4. Raman J, Morris N, Frean J, Brooke B, Blumberg L, Kruger P, Mabusa A, Raswiswi E, Shandukani B, Misani E, Groepe M Moonasar D. Reviewing South Africa's malaria elimination strategy (2012–2018): progress, challenges and priorities. *Malaria Journal* 2016, 15(1), p.3.
5. Roll Back Malaria Partnership and World Health Organization. 2013. Focus On South Africa. 8th ed. Geneva: World Health Organization. Available at: https://www.mmv.org/sites/default/files/uploads/docs/publications/RBMSouthAfrica_3.pdf [Accessed 17-08-2020]
6. Department of Health (South Africa). 2017. National Health Act, 2003 (Act no. 61 of 2003): Regulations relating to the surveillance and the control of notifiable medical conditions. (Notice no. 1434). Government Gazette, 41330: 4, 15 December
7. Blumberg L, Frean J, Moonasar D and Malaria Elimination Committee. Successfully controlling malaria in South Africa. *South African Medical Journal* 2014, 104(3), pp.224-226
8. World Health Organization. 2018. Malaria Surveillance, Monitoring & Evaluation. Genève: World Health Organization.
9. World Health Organization. 2016. Malaria Microscopy Quality Assurance Manual, version 2. Geneva: World Health Organization.
10. Balawanth R, Ba I, Qwabe B, Gast L, Maharaj R, Raman J, Graffy R, Shandukani M Moonasar D. Assessing KwaZulu-Natal's progress towards malaria elimination and its readiness for sub-national verification. *Malaria Journal* 2019, 18(1), pp.5-6.
11. South Africa National Department of Health, 2011, The National Malaria Quality Assurance Guidelines, Pretoria, NDoH https://www.nicd.ac.za/diseases-a-z-index/malaria/ [Accessed 17/07/2020]
12. National Department of Health (South Africa), 2019, Malaria elimination strategy for South Africa 2019 – 2023, Pretoria, NDoH.
13. Padley D, Moody HA, Chiodini PL, Saldanha J. Use of a rapid, single-round, multiplex PCR to detect malarial parasites and identify the species present. *Annals of Tropical Medicine & Parasitology* 2003, 97 (2) p131-137
14. Malaria Parasite Counting – Malaria Microscopy Standard Operating Procedure – MM-SOP-09. 2016. 1st version. [pdf] Geneva: The World Health Organization. Available at: https://apps.who.int/iris/handle/10665/274382 [Accessed 28 October 2020].

NOTIFIED LEGIONNAIRES' DISEASE IN SOUTH AFRICA, 2018-2020

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Summary

Legionnaires' disease is a rare form of severe pneumonia caused by *Legionella* bacteria, which is transmitted through the inhalation or aspiration of contaminated water droplets. Cases of laboratory-confirmed Legionellosis notified to the National Institute for Communicable Disease's national notifiable medical conditions (NMC) surveillance system between 1 January 2018 and 30 September 2020 are described here. During this period, 93 cases of Legionellosis were notified, with the majority (72/93, 77.4%) of cases reported from the Western Cape Province. Most cases occurred in individuals aged between 40 and 69 years (65/93, 70.0%), in males (61/93, 65.6%), and in individuals with underlying illness (52/64, 81.3%). The case-fatality ratio was 20% (15/74). Whilst difficult to ascertain the source of infection due to poorly completed case investigation forms, Legionellosis cases were largely sporadic. Ongoing surveillance and improved investigation of Legionnaires' disease cases is important for cluster identification, particularly during the COVID-19 pandemic when lockdown measures have resulted in closure or restricted use of buildings, thereby increasing the risk for *Legionella* growth in water systems.

Introduction

Legionnaires' disease is a rare form of severe pneumonia caused by *Legionella* bacteria, most commonly *Legionella pneumophila* serogroup 1. Individuals typically present with an acute consolidating pneumonia, which can be radiologically and clinically indistinguishable from other aetiological causes of pneumonia. Older age (≥50 years), male gender and underlying illnesses such as chronic heart or lung disease, diabetes, cancer or immunosuppression, increase an individual's susceptibility to disease. The disease is associated with severe illness and a high case-fatality ratio of 10-15%.[1]

Although *Legionella* spp. are ubiquitous in natural water sources, transmission predominantly occurs through the inhalation/aspiration of water droplets from man-made water systems such as industrial heating/cooling systems, plumbing systems, whirlpools and fountains which, if not adequately managed, allow the bacteria to proliferate to high levels.[2,3] Warm water temperatures (25°C to 50°C) and poor or no water flow increases the risk of growth and spread of the bacteria.

Approximately 20 of the more than 50 identified species have been known to be pathogenic in humans, with *Legionella pneumophila* identified in 90% of cases in the United States and Europe. [2,4,5] In some countries, such as Australia, *Legionella longbeachae* (also found in compost and potting soil) is predominant. Traditional diagnostic methods include culture and serology and, more recently, the urinary antigen test (only detecting *L. pneumophila* serogroup 1) and polymerase chain reaction (PCR) are being commonly used due to their improved speed and sensitivity, facilitating early diagnosis and treatment.[1,3,6]

The prevalence of Legionnaires' disease is underestimated globally due to a lack of clinical index of suspicion and requests for testing by clinicians (who generally treat empirically for community-acquired pneumonia), inadequate diagnostic tests, and limited surveillance programmes. Many of these concerns are more marked in Africa from where data are severely limited.[7]

From June 2012 to September 2014, among 1805 patients hospitalised with pneumonia and enrolled in the National Institute for Communicable Diseases (NICD) pneumonia surveillance programme, 21 (1.2%) tested positive for *Legionella* spp. by PCR on nasopharyngeal and/or induced sputum specimens.[8] Disease occurred predominantly in chronically ill adults living with human immunodeficiency virus (HIV) and/or tuberculosis infection. The majority of cases were not diagnosed with Legionnaires' disease and were sub-optimally treated. In this report, cases of laboratory-confirmed Legionellosis in South Africa notified to the NMC surveillance system between 1 January 2018 and 30 September 2020 are described.

Methods

Legionellosis is a category 2 notifiable medical condition in South Africa, which requires notification (either paper-based or electronically) by healthcare workers to the NICD's NMC surveillance system within seven days of diagnosis. Upon notification, basic demographic and clinical information are collected. Healthcare workers are also requested to complete and submit to the NICD a Legionnaires' disease case investigation form (CIF), which collects additional information such as underlying illness and potential sources of contaminated water exposure. Patient outcome data were obtained from the CIF where it was not available in the NMC database or had changed following notification.

Results

From 1 January 2018 through 30 September 2020, 93 laboratory-confirmed cases of Legionellosis were notified to the NMC surveillance system; 43 (46.2%) in 2018, 25 (26.9%) in 2019 and 25 (26.9%) in 2020 (Table 1 and Figure 1). The highest number of cases were reported in February 2018 (n=7) and March 2020 (n=7). Cases were observed throughout the year, with no specific seasonality identified. The majority of cases were reported from Western Cape Province (72/93, 77.4%), although the number of provinces reporting cases increased from 3 in 2018 to 5 in 2019 and 6 in 2020 (Figure 1). The majority of cases (81/93, 87.1%) were diagnosed by the urinary antigen test, with nine cases (9.7%) identified by PCR and three (3.2%) by serology.

All Legionellosis cases occurred in adults with the highest number observed in the 50-59 years age group (25/93, 26.9%), and with 70% (65/93) occurring in individuals aged between 40 and 69 years (Table 1 and

Figure 2). The majority of cases were males (61/93, 65.6%). Among patients with known admission status, 98.8% (83/84) were hospitalised. Of 64 cases for whom the CIF was completed, 52 (81.3%) reported having ≥1 underlying illness and 12 (18.8%) were HIV infected. At the time of notification or completion of the CIF, 20.3% (15/74) of individuals had died.

Table 1. Characteristics of notified cases of Legionnaires' disease in South Africa, January 2018 – September 2020 (N=93).

Characteristic	n/N (%)
Year	
2018	43/93 (46.2)
2019	25/93 (26.9)
2020	25/93 (26.9)
Sex	
Male	61/93 (65.6)
Female	32/93 (34.4)
Age group (years)	
<20	0/93 (0.0)
20-39	19/93 (20.4)
40-59	44/93 (47.3)
60-79	28/93 (30.1)
≥80	2/93 (2.1)
Province	
Eastern Cape	5/93 (5.4)
Free State	1/93 (1.1)
Gauteng	9/93 (9.7)
KwaZulu-Natal	2/93 (2.2)
North West	4/93 (4.3)
Western Cape	72/93 (77.4)
Admission status	
Inpatient	83/84 (98.8)
Outpatient	1/84 (1.2)
Diagnostic test	
Urinary antigen test	81/93 (87.1)
PCR	9/93 (9.7)
Serology	3/93 (3.2)
Underlying illness	
Yes	52/64 (81.2)
No	12/64 (18.8)
HIV status	
Infected	12/64 (18.8)
Uninfected	52/64 (81.2)
Outcome	
Died	15/74 (20.3)
Survived	59/74 (79.7)

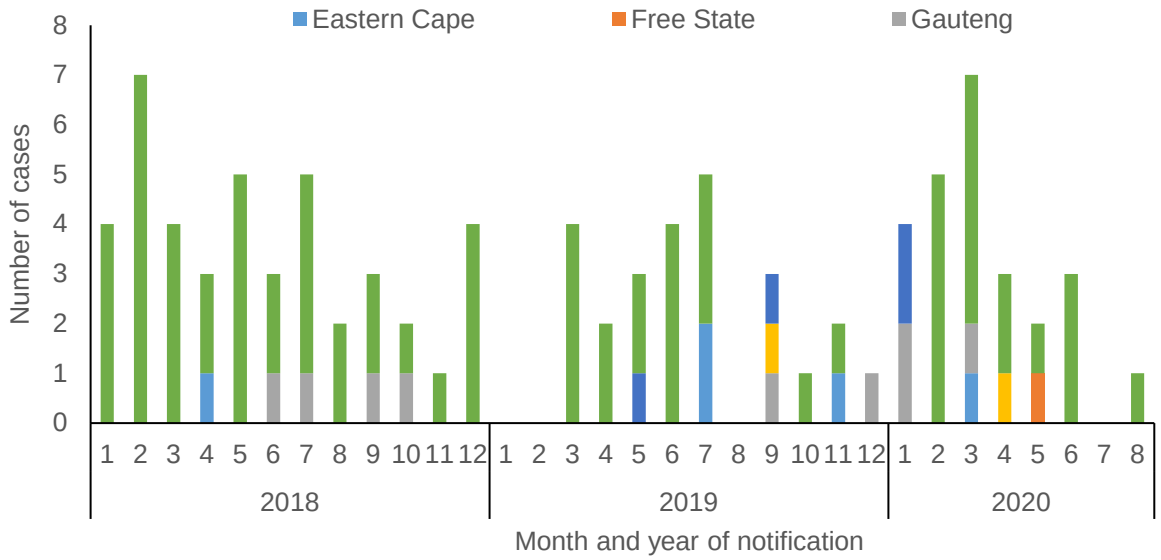

Figure 1. Legionellosis cases notified to the national Notifiable Medical Conditions (NMC) surveillance system by year and province, South Africa, January 2018 – 30 September 2020.

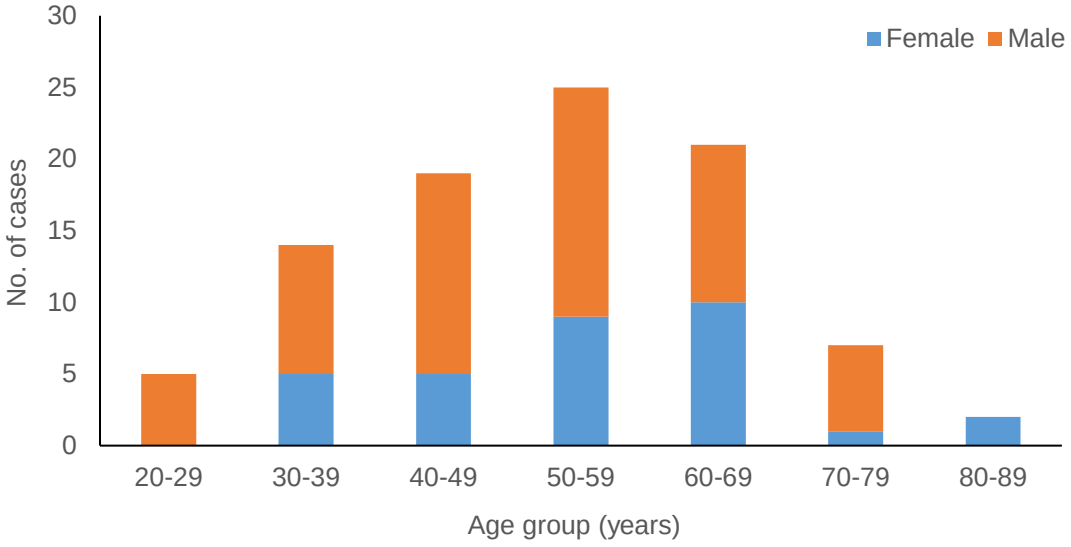

Figure 2. Legionellosis cases notified to the national Notifiable Medical Conditions (NMC) surveillance system by age and gender, South Africa, January 2018 – 30 September 2020.

Discussion

During the surveillance period, 93 cases of Legionnaire's disease were notified to the NMC system. The majority of cases were reported from the Western Cape Province, likely due to increased awareness and increased availability of diagnostic testing there. It should also be noted that the drought and resulting restrictions in water use in the province over recent years may also have had an effect. The increased number of provinces notifying cases over time may represent an increased awareness of the requirement to notify cases. As is typical for Legionnaire's disease[1,9], cases occurred in adults with the majority in older adults and males with underlying

illness. Almost all notified cases were hospitalised individuals, and a high case fatality ratio of 20% was observed.

These data are likely an underestimate of the burden of Legionnaires' disease in South Africa, and only represent cases where the disease was clinically suspected, laboratory testing was performed, and where healthcare workers notified cases to the NMC surveillance system. Most laboratories performed diagnostic testing using the urinary antigen test. While rapid and easy to use, this test only detects *L. pneumophila* serogroup 1 and therefore the prevalence of other *Legionella* species and other *L. pneumophila* serogroups that cause Legionellosis in South Africa are largely unknown. In a previous study from South Africa[8], patients with Legionnaires' disease were likely to be HIV-infected, or chronically ill individuals with suspected or confirmed tuberculosis. Similarly, in this study >80% of individuals reported having at least one underlying illness. Although Legionnaires' disease is associated with a high mortality rate, the case fatality ratio of 20%, which is on the upper boundary of what is expected, likely represents a bias because individuals with severe disease are more likely to be tested for Legionellosis.

Due to the poor quality of data captured during completion of the CIF, potential sources of infection could not be adequately assessed. This may be a result of the CIF being completed by healthcare workers, whereas the environmental investigation is conducted by environmental health practitioners. In addition, individuals with Legionnaires' disease are often severely ill and therefore not able to provide exposure information.

Although Legionnaire's disease remains relatively rare in South Africa, it is important to diagnose and notify cases in order to identify potential clusters of disease and sources of infection for intervention. This has become increasingly important during the coronavirus disease 2019 (COVID-19) pandemic during which many places of work and large buildings such as hotels, offices, gyms and salons have reopened after being closed for extended periods. Closure or restricted use of buildings or parts of buildings can increase the risk for *Legionella* growth in water systems[10], and thereby the risk of Legionnaires' disease. The Centers for Disease Control and Prevention (CDC)[11] and European Society of Clinical Microbiology and Infectious Diseases (ESCMID)[12] have published guidance for the management of water systems during the COVID-19 epidemic. Individuals with Legionnellosis may present with similar signs and symptoms to COVID-19. In addition, SARS-CoV-2 and *Legionella* co-infection has been described[13] and co-infection among patients with COVID-19 should be considered clinically as both pathogens cause more severe illness in the elderly and in males.[14]

Conclusion

Ongoing surveillance and improved investigation of Legionnaires' disease cases is important for cluster identification, particularly during the COVID-19 pandemic when lockdown measures have resulted in closure or restricted use of buildings, thereby increasing the risk for *Legionella* growth in water systems.

Acknowledgements

"We would like to thank Siyabonga Mazibuko and all individuals involved in Notifiable Medical Conditions Surveillance for the collection and management of NMC data".

References

1. Phin N, Parry-Ford F, Harrison T, et al. Epidemiology and clinical management of Legionnaires' disease. *Lancet Infect Dis*. 2014;14(10):1011-1021. doi:10.1016/S1473-3099(14)70713-3
2. Diederen BMW. Legionella spp. and Legionnaires' disease. *J Infect*. 2008;56(1):1-12. doi:10.1016/j.jinf.2007.09.010
3. Mercante JW, Winchell JM. Current and emerging legionella diagnostics for laboratory and outbreak investigations. *Clin Microbiol Rev*. 2015;28(1):95-133. doi:10.1128/CMR.00029-14
4. Fields BS, Benson RF, Besser RE. Legionella and legionnaires' disease: 25 Years of investigation. *Clin Microbiol Rev*. 2002;15(3):506-526. doi:10.1128/CMR.15.3.506-526.2002
5. Joseph CA, Ricketts KD, European Working Group for Legionella Infections. Legionnaires disease in Europe 2007-2008. *Euro Surveill*. 2010;15(8):19493. http://www.ncbi.nlm.nih.gov/pubmed/20197022
6. Murdoch DR, Podmore RG, Anderson TP, et al. Impact of routine systematic polymerase chain reaction testing on case finding for legionnaires' disease: A pre-post comparison study. *Clin Infect Dis*. 2013;57(9):1275-1281. doi:10.1093/cid/cit504
7. Dlamini SK, Mendelson M. Atypical pneumonia in adults in southern Africa. *South African Fam Pract*. 2012;54(4):286-291. doi:10.1080/20786204.2012.10874237
8. Wolter N, Carrim M, Cohen C, et al. Legionnaires' Disease in South Africa, 2012–2014. 2016;22(1):2012-2014.
9. Marston BJ, Lipman HB, Breiman RF. Surveillance for Legionnaires' disease. Risk factors for morbidity and mortality. *Arch Intern Med*. 1994;154(21):2417-2422. http://www.ncbi.nlm.nih.gov/pubmed/7979837
10. De Giglio O, Diella G, Lopuzzo M, et al. Impact of lockdown on the microbiological status of the hospital water network during COVID-19 pandemic. *Environ Res*. 2020;191:110231. doi:10.1016/j.envres.2020.110231
11. Guidance for Reopening Buildings After Prolonged Shutdown or Reduced Operation | CDC. Accessed November 4, 2020. https://www.cdc.gov/coronavirus/2019-ncov/php/building-water-system.html
12. ESCMID Study Group for Legionella Infections ESGLI Guidance for managing Legionella in building water systems during the ESGLI Guidance for managing Legionella in building water systems during the COVID-19 pandemic. Published 2020. Accessed November 4, 2020. https://www.escmid.org/research_projects/study_groups/study_groups_g_n/legionella_infections/
13. Arashiro T, Nakamura S, Asami T, et al. SARS-CoV-2 and Legionella co-infection in a person returning from a Nile cruise. *J Travel Med*. 2020;2020:1-3. doi:10.1093/jtm/taaa053
14. Lai C-C, Wang C-Y, Hsueh P-R. Co-infections among patients with COVID-19: The need for combination therapy with non-anti-SARS-CoV-2 agents? *Immunol Infect*. 2020;53:505-512. doi:10.1016/j.jmii.2020.05.013

PAEDIATRIC & ADOLESCENT HIV VIRAL LOAD MONITORING, 2014-2020

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Summary

Between July 2019 and June 2020, HIV viral load testing coverage among children and adolescents living with HIV aged <15 years and 15-19 years was approximately 51% and 57%, respectively**.** Among all children and adolescents (0-19 years of age) with an HIV viral load, 49.7% (130 952) were virally suppressed (<50 RNA copies per millilitre [cps/ml]), 22.7% (59 779) had low-level viraemia (50–<1 000 RNA cps/ml) and 27.6% (72 774) had a VL >1 000 RNA cps/ml**.** Over the past six and half years, improvement in the overall paediatric and adolescent suppression rate (<50 RNA cps/ml) has been modest at only 7.3%, although some sub-populations (<1 years and 15-19 years) have demonstrated greater improvement than other age groups. Differences in HIV viral load suppression between males and females were apparent among all paediatric and adolescent age groups, with 51.8% of females compared with 46.8% of males 0-19 years of age suppressed between July 2019 and June 2020. There are considerable differences in the volume of HIV viral load testing and suppression rates among South Africa's nine provinces. Whereas KwaZulu-Natal Province has the second highest viral suppression rate, it remains the province with the highest number of unsuppressed children and adolescents living with HIV.

Introduction

In 2014, UNAIDS launched a set of ambitious targets to accelerate the end of the AIDS epidemic, proposing that by 2020 90% of people living with HIV be diagnosed, 90% of those diagnosed be on antiretroviral therapy (ART), and 90% of those on ART be virally suppressed.[1] Importantly, these goals acknowledge the need to achieve equity across diverse patient populations, including children and adolescents who have traditionally lagged behind with regards to accessing diagnosis and treatment services.

Although South Africa has made great strides in reducing the vertical transmission rate to <5%, thanks to a comprehensive Prevention of Mother-to-Child Transmission (PMTCT) programme[2] the absolute burden of paediatric and adolescent HIV remains high. Mathematical modelling estimates suggest more than 400 000 children and adolescents are presently living with HIV in South Africa.[3] This is on account of an extremely high maternal HIV prevalence, which has remained around 30% for over a decade,[4] as well as a high HIV-incidence among adolescent girls and young women, including during pregnancy and breastfeeding periods.[5] Hence, monitoring of the paediatric and adolescent HIV programme has been identified as an essential requirement for

improving overall HIV care.[6] Unless effective measures to reduce the HIV infection rate amongst adolescent girls and young women are rapidly implemented, children and adolescents will remain an important population for targeted intervention in the decades to come.

Routine HIV viral load data provides an opportunity to gauge programmatic outcomes, disaggregated by age and sex, whereby progress towards achieving the second and third 90-90-90 targets can readily be assessed. Here we report on paediatric and adolescent HIV viral load monitoring within the National Health Laboratory Service (NHLS) between 2014 and mid-2020.

Methods

HIV viral load results were evaluated using rolling 12-month periods per calendar quarter, from quarter 4 (31 December) 2014 to quarter 2 (30 June) 2020. Test results were de-duplicated to represent the last viral load result per patient during each 12-month period using the NHLS Corporate Data Warehouse probabilistic patient-linking algorithm. The number of patients with a viral load done was used as a proxy for people on ART (viz. the second 90 target), with viral suppression rates calculated at both the <1 000 RNA cps/ml and <50 RNA cps/ml thresholds.

Results

For the 12-month period between July 2019 and June 2020, 263 505 children and adolescents (aged 0-19 years) had evidence of HIV virological monitoring in South Africa. HIV viral load testing coverage was 51% and 57% among children and adolescents living with HIV aged <15 years and 15-19 years, respectively, as suggested by Thembisa Model prevalence estimates. Among all children and adolescents with an HIV viral load (VL) test, 49.7% (130 952) were virally suppressed (<50 RNA cps/ml), 22.7% (59 779) had low-level viraemia (50-<1 000 RNA cps/ml), and 27.6% (72 774) had a VL >1 000 RNA cps/ml. Figure 1 represents the HIV viral load breakdown per age group for the 12-month period between July 2019 and June 2020, with a total of 7 829 infants increasing to 111 469 adolescents aged 15-19 years having a viral load result.

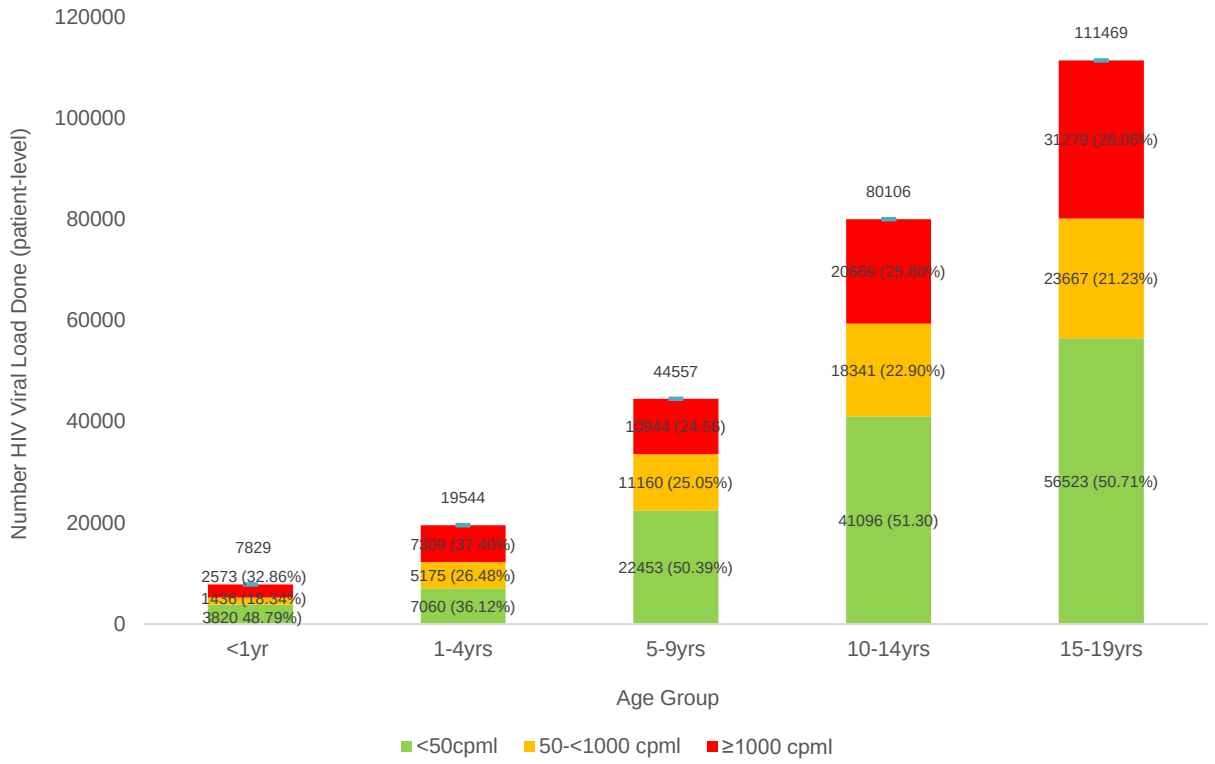

Figure 1. HIV viral load done (VLD) breakdown by result and age group, South Africa, July 2019–June 2020.

Between 2014 and mid-2020, the total antiretroviral therapy (ART) programme showed an improvement in the rolling 12-month suppression rate of 8.2% (from 80.4% to 88.6%) at the <1 000 RNA cps/ml threshold and 15.5% (from 56.3% to 71.8%) at the <50 RNA cps/ml threshold. However, improvements among children and adolescents, in comparison to all age groups, was more modest at 7.2% (from 65.2% to 72.4%) and 7.3% (from 42.4% to 49.7%), respectively (Figure 2). An evaluation of viral load suppression rates among different paediatric and adolescent age groups demonstrates that children aged 1-4 years had the lowest suppression rate (<50 RNA cps/ml) of 36.3%, with an improvement of only 1.5% (from 34.8% to 36.3%) since 2014 (Figure 3). All other paediatric and adolescent age groups converged at an approximate 50% viral suppression rate (<50 RNA cps/ml) in mid-2020. Low-level viraemia (50-<1 000 RNA cps/ml) ranged from 18.3% in infants to 26.5% in 1-4 year olds and high viral loads (>1 000 RNA cps/ml) ranged from 24.6% in the 5-9 year old age group to 37.4% in the 1-4 year olds with 73% (n=51 948) of high viral loads occurring in those aged 10 years and older.

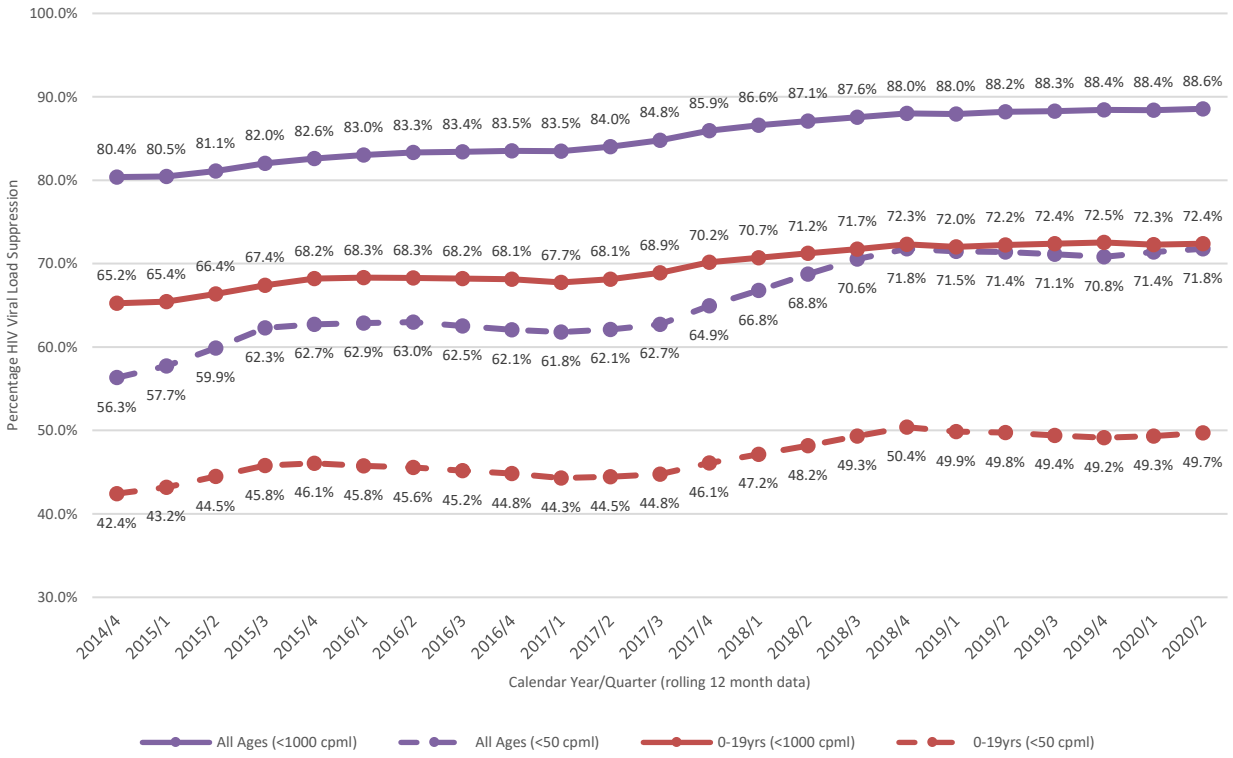

Figure 2. HIV viral load suppression (VLS) trends comparing all ages vs 0-19 years by year and quarter, South Africa 2014-2020.

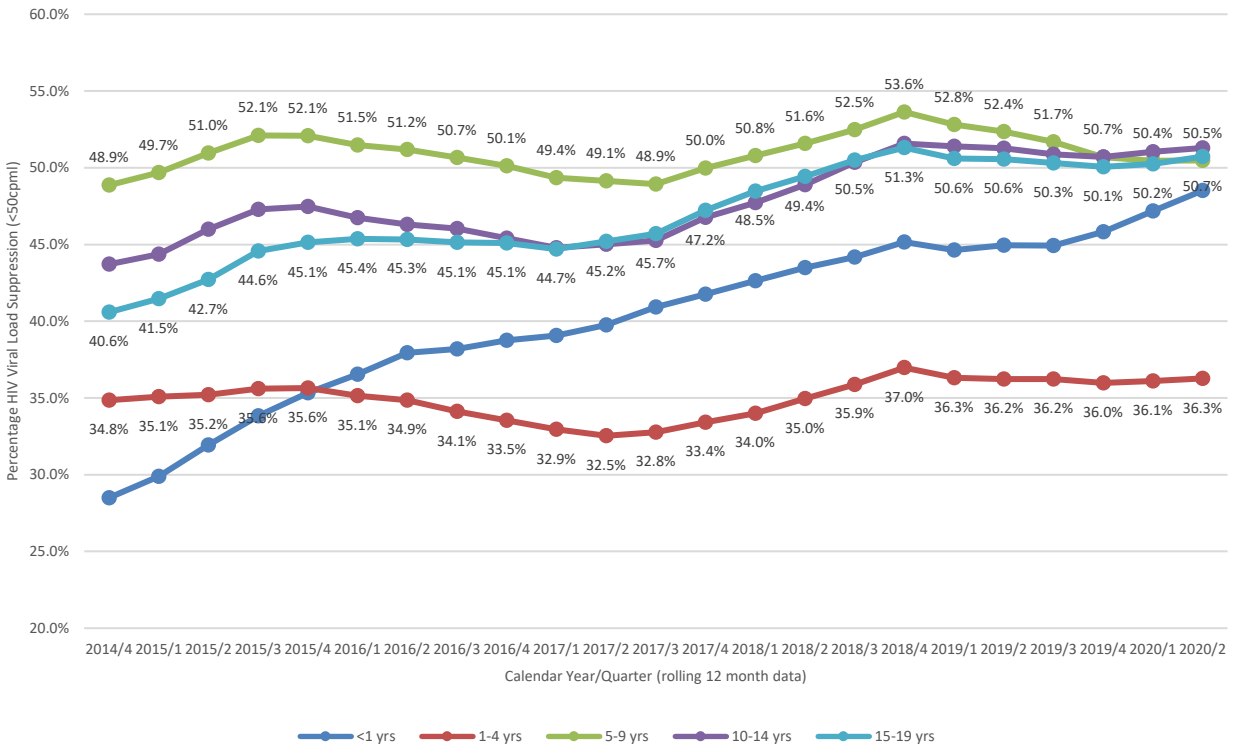

Figure 3. Paediatric and adolescent HIV viral load suppression (<50 cps/ml) trends by age group by year and quarter, South Africa, 2014–2020.

Considerable differences in the volume of HIV viral load testing and suppression rates can be seen among the nine provinces, with similar suppression patterns among those aged <15 years and 15-19 years (Figures 4 and 5). The numbers of children and adolescents aged <15 years with a viral load done between July 2019 and June 2020 per province were as follows: KwaZulu-Natal Province (46 081, 30.3%), Gauteng Province (28 397, 18.7%), Eastern Cape Province (18 296, 12.0%), Mpumalanga Province (17 224, 11.3%) Limpopo Province (14 847, 9.8%), North West Province (8 955, 5.9%), Free State Province (8 659, 5.7%), Western Cape Province (6 979, 4.6%), and Northern Cape Province (2 598, 1.7%). Among adolescents 15-19 years, the provincial breakdowns were as follows: KwaZulu-Natal (37 283, 33.4%), Gauteng Province (19 712, 17.7%), Mpumalanga Province (12 971, 11.6%), Eastern Cape Province (12 830, 11.5%), Limpopo Province (8 582, 7.7%), North West Province (7 005, 6.3%), Free State Province (6 744, 6.1%), Western Cape Province (4 678, 4.2%) and Northern Cape Province (1 664, 1.5%). The province with the highest suppression rate (<50 RNA cps/ml) was Western Cape, with 57.0% and 62.5% <15 year olds and 15-19 year olds suppressed, respectively, followed by Kwa-Zulu Natal and Gauteng provinces. Whereas KwaZulu-Natal Province has the second highest paediatric and adolescent suppression rate, it remains the province with the highest number of unsuppressed patients (Figures 4 and 5).

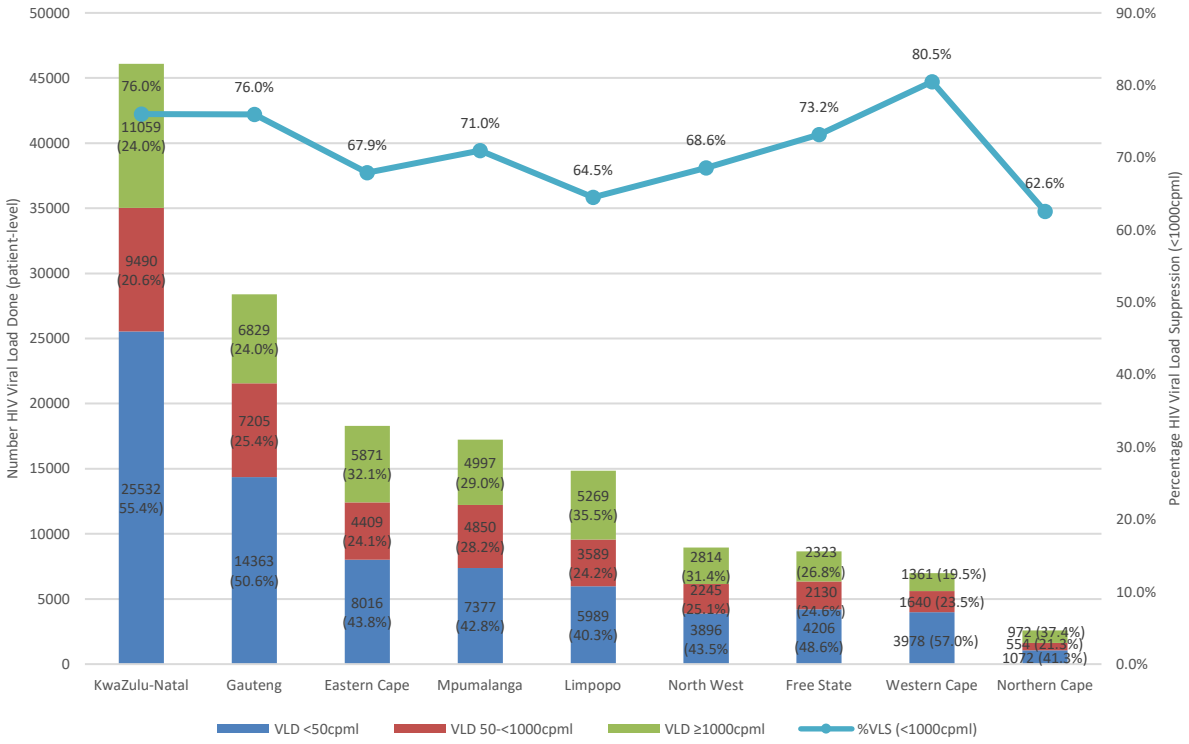

Figure 4. Provincial breakdown of HIV viral load (VLD) and viral load suppression (VLS) among patients <15 years of age, South Africa, July 2019–June 2020.

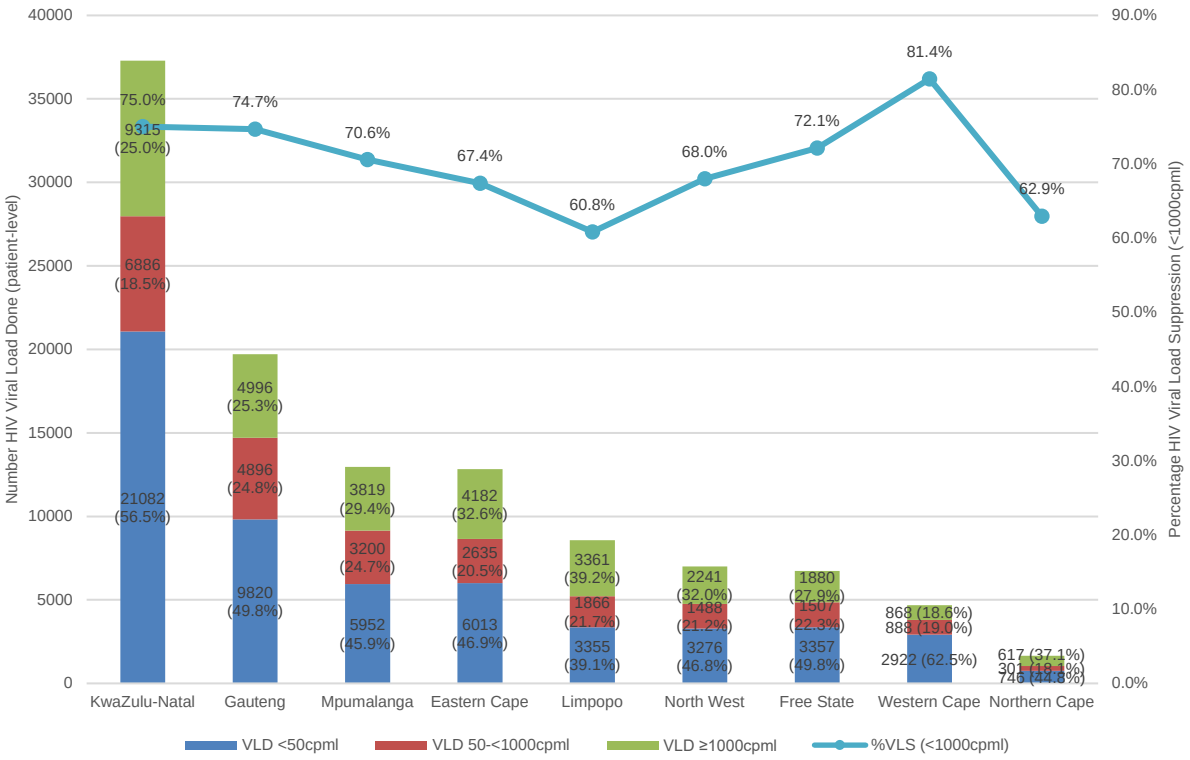

Figure 5. Provincial breakdown of HIV viral load (VLD) and viral load suppression (VLS) among patients 15-19 years of age, South Africa, July 2019–June 2020.

Differences in viral load suppression rates between males and females were apparent among all paediatric and adolescent age groups, with 51.8% of females compared with 46.8% of males aged 0-19 years suppressed between July 2019 and June 2020 (Figure 6). The biggest difference in the suppression rate between males and females was in the <1 year age group with 9.5% more females suppressed than males. Disaggregating HIV viral load data by age and sex, the group with the lowest suppression rate was males aged 1-4 years of whom only 33.4% had a viral load <50 RNA cps/ml.

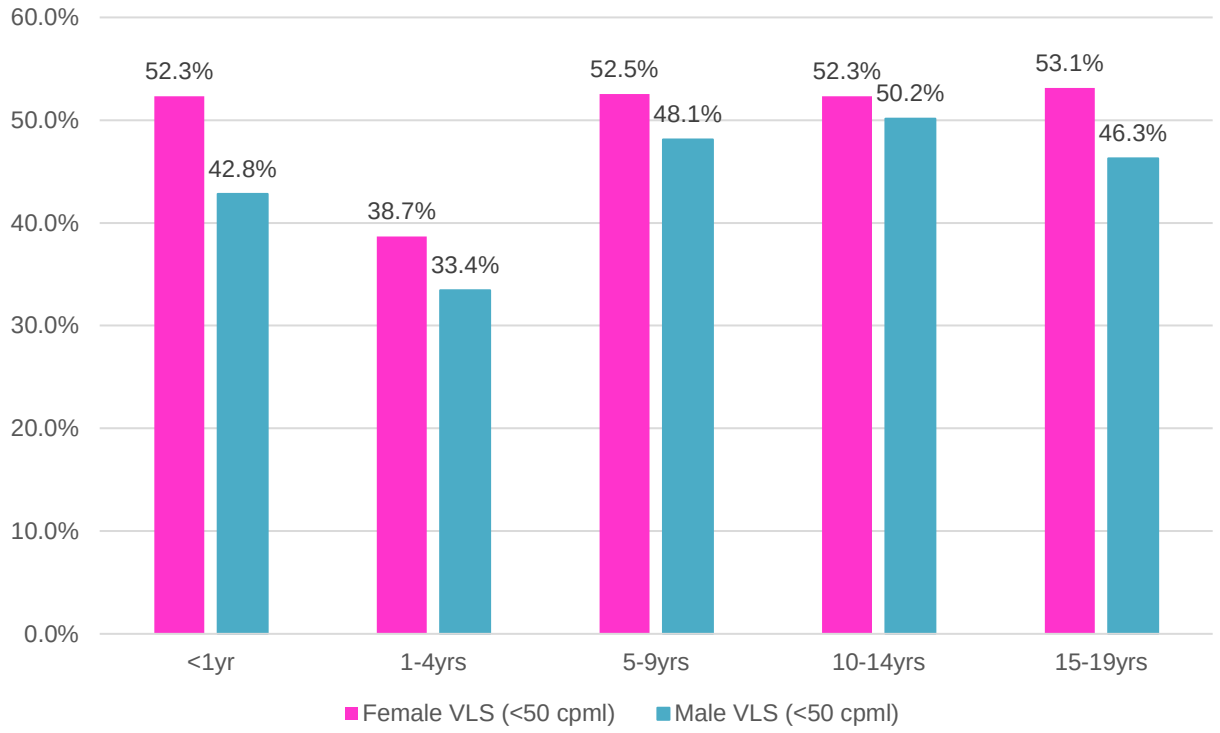

Figure 6. Differences in HIV viral load suppression (VLS) between males and females, South Africa, July 2019–June 2020.

Discussion

Although children and adolescents comprise only 5.5% of South Africa's total population living with HIV, they represent a critical group for monitoring and evaluation of the HIV treatment programme. Analysis of routine HIV viral load data, however, suggests that paediatric and adolescent populations are far from achieving the UNAIDS second and third 90 targets. Furthermore, data over the past six years demonstrates only marginal improvement towards reaching these goals from when they were initially set.

Nearly half of the HIV population aged 0-19 years have no evidence of viral load monitoring, which equates to approximately 140 000 and 89 000 children and adolescents aged <15 years and 15-19 years, respectively, who are presently not in care. Furthermore, viral suppression rates among children and adolescents with a viral load done remain extremely low with only 72% of patients having a viral load <1 000 RNA cps/ml and 50% having a viral load <50 RNA cps/ml. Although UNAIDS initially set viral suppression targets at <1 000 RNA cps/ml, subsequent evidence has demonstrated that low-level viraemia (i.e. 50-<1 000 RNA cps/ml) is clinically relevant.[7] Hence, targets aimed at ending the AIDS epidemic will require viral suppression to be redefined as <50 RNA cps/ml, highlighting considerable disparity between progress in the overall ART programme with that of children and adolescents.

Disaggregating HIV viral load data has revealed substantial variation in viral load testing coverage and suppression rates within the paediatric and adolescent population living with HIV. Of note is the markedly lower suppression rates among children 1-4 years of age, as well as reduced suppression rates among males

compared with females among all age groups - findings which warrant further investigation and analysis. Despite these variations in treatment outcomes within paediatric subpopulations, it is clear that as a whole children and adolescents living with HIV continue to represent a particularly vulnerable group within the overall ART programme.

Conclusions

Children and adolescents living with HIV in South Africa remain an especially vulnerable population who are far from achieving UNAIDS 90:90:90 targets. Major advances in paediatric HIV care, in particular retention in care and treatment adherence, will be required if South Africa is to achieve an end to the AIDS epidemic within the next 10 years.

Acknowledgements

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References

1. UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. Geneva: UNAIDS, 2014.
2. Sherman GG, Lilian RR, Bhardwaj S, et al. Laboratory information system data demonstrate successful implementation of the prevention of mother-to-child transmission programme in South Africa. *South African Medical Journal.* 2014;104(3 Suppl 1):235-238.
3. Johnson LF, May MT, Dorrington RE, et al. Estimating the impact of antiretroviral treatment on adult mortality trends in South Africa: a mathematical modelling study. *PLoS Medicine*. 2017;14(12): e1002468.
4. Woldesenbet SA, Kufa T, Lombard C, et al. The 2017 National Antenatal Sentinel HIV Survey, South Africa. Pretoria: National Department of Health, 2019.
5. Shisana O, Rehle T, Simbayi LC, et al. South African national HIV prevalence, incidence and behaviour survey, 2012. Cape Town: HSRC, 2014.
6. Davies MA, Pinto J. Targeting 90–90–90–don't leave children and adolescents behind. *J Int AIDS Soc.* 2015;18(Suppl 6):20745
7. Hermans LE, Moorhouse M, Carmona S, et al. Effect of HIV-1 low-level viraemia during antiretroviral therapy on treatment outcomes in WHO-guided South African treatment programmes: a multicentre cohort study. *The Lancet Infectious Diseases* 2018;18(2):188-97.

ACUTE FLACCID PARALYSIS SURVEILLANCE FOR POLIO, SOUTH AFRICA AND OTHER AFRICAN COUNTRIES, 2019

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Summary

The adequacy of acute flaccid paralysis (AFP) surveillance, the poliovirus surveillance system recommended by the World Health Organisation (WHO), is measured against international benchmarks. For January to December 2019, the South African national non-polio AFP detection rate was 3.5/100 000 children under 15 years, compared to 2.9/100 000 children under 15 years in 2018. The national average non-polio AFP detection rate exceeded the WHO's target of 2.0/100 000 population under 15 but did not reach the country's target of 4.0/100 000. Seven of the 52 districts in South Africa (SA) (13.5%) did not reach 2.0/100 000. Stool adequacy of less than 80% was reported in one of South Africa's nine provinces. Transport time between sample collection and receipt at the laboratory exceeded three days in 58% of samples. Therefore, AFP surveillance in SA has aspects still requiring strengthening.

Introduction

In 1988, when the Global Polio Eradication Initiative (GPEI) was established[1], there was an estimated 350 000 cases of wild poliovirus (WPV) types 1, 2 and 3 in more than 125 endemic countries. Since then, the global incidence has decreased to 175 reported cases of WPV type 1 in 2019 in the two endemic countries that remain affected. The last case of WPV type 2 was reported in 1999, leading to declaration of eradication of WPV type 2 in 2015. WPV type 3 has not been detected since November 2012 and was declared eradicated in October 2019. In South Africa, the last wild poliovirus case occurred in 1989.

Globally, two types of polio vaccines are used routinely, inactivated polio vaccine (IPV) to prevent symptomatic polio, and oral polio vaccine (OPV) to prevent both symptomatic polio and polio transmission. IPV is an injectable vaccine consisting of all three poliovirus serotypes. OPV is composed of live attenuated polioviruses and can be monovalent (mOPV, type specific) or bivalent (bOPV, types 1 and 3). The type 2 Sabin strain was globally withdrawn from OPV in April 2016. The polio vaccination schedule for South Africa comprises bivalent

OPV at birth and 6 weeks, and IPV as part of a hexavalent vaccine at 6, 10 and 14 weeks, followed by a booster at 18 months. Globally it has been shown that in geographic areas with low vaccination coverage, and therefore low herd immunity to polio transmission, Sabin strains can circulate in the environment for prolonged periods, resulting in mutation and circulation of vaccine-derived poliovirus (cVDPV) - posing a challenge to the GPEI.

The National Institute for Communicable Diseases (NICD) serves as the national polio reference laboratory for AFP surveillance in South Africa and other southern African countries, including Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, Seychelles and Swaziland. The NICD additionally serves as the regional reference centre for the polio laboratory network of the WHO African region, and conducts molecular characterization of poliovirus isolates from the national laboratories of the Democratic Republic of Congo (DRC), Ethiopia, Niger, Uganda, Cameroon, Central African Republic and Zambia.

There were 313 AFP cases caused by cVDPV2 within the WHO African region in 2019. These cases included samples analysed at NICD and reported here. These cVDPV2 cases were from Nigeria, DRC, Niger, Zambia, Chad, Angola, Benin, Ethiopia, Togo, Central African Republic, Burkina Faso and Ghana. Outside of the African region, China had 1 cVDPV2 case in 2019, and Myanmar and Malaysia reported outbreaks of cVDPV1, where Philippines had cases of cVDPV1 and cVDPV2. Somalia also reported 3 cases of cVDPV2 (www.polioeradication.org[1]).

Methods

Nationwide, case-based surveillance for AFP was conducted in South Africa in 2019. Surveillance comprises field and laboratory components.

Field Surveillance

Cases of AFP from all health facilities were notified to the Provincial and National Departments of Health with samples collected for investigation and case investigation forms forwarded to the NICD. An adequately investigated case requires the collection of two stool specimens from the AFP case within 14 days of onset of paralysis. The stool samples should be collected 24-48 hours apart, transported on ice and should arrive at the NICD laboratory within 72 hours of collection. Field surveillance, conducted through active case detection by retrospective record review targeting children under 15 years was conducted periodically throughout the year, targeting high priority sites. In 2019, the South African operational non-polio AFP target detection rate was 4.0/100 000, while the WHO target detection rate remained at 2.0/100 000. The National Polio Expert Committee (NPEC) met quarterly to determine the final classification of all inadequately investigated AFP cases (Table 1).

Laboratory methods

Viral Isolation was performed by inoculation of clarified faecal material into cell culture, followed by microscopic examination of the cells for cytopathic effect, which indicates the presence of suspected poliovirus. Intratypic differentiation (ITD) by polymerase chain reaction (PCR) was conducted on suspected poliovirus isolates.[2] Polioviruses were then sequenced to classify them as either WPV, Sabin or VDPV. Sequencing helps to monitor

poliovirus transmission pathways and transmission links. South African polioviruses were sequenced at the VP1 region and 5' untranslated region (UTR).

Table 1. Polio case classification system used by South Africa's National Polio Expert Committee (NPEC).

Status	Classification	Code	Reason
Final	Confirmed (wild-type)	A1	Wild-type poliovirus found in stool sample of case or one of the contacts
	Confirmed (vaccine-associated)	B1	Vaccine-type poliovirus found in stool sample of case, which has residual paralysis at 60-day follow-up; is confirmed clinically
	Compatible	C1	AFP[a] case lost to follow-up at 60 days
		C2	Death related to the illness within 60 days
		C3	Residual paralysis for which no other medical reason is evident
	Discarded	D1	No residual paralysis and no wild polio found in stool samples
		D2	Confirmed alternative diagnosis
		D3	Non-Polio Enterovirus isolated
		D4	No virological investigation and a clinical picture incompatible with polio
		D5	Two adequate negative stool specimens within 14 days of onset of paralysis
	Denotified	E1	Not an AFP[a] case
Pending	Inadequate information	F1	NPEC[b] is unable to make a decision due to the lack of information. The investigating team is given 30 days from the committee meeting to find further details. The final decision is taken at the next NPEC[b] meeting.
	60-day follow-up not yet done	F2	Final decision is referred to the next NPEC[b] meeting for final decision

[a]Acute Flaccid Paralysis
[b]National Polio Expert Committee

Results

South Africa

A total of 1268 samples was received from 636 cases with date of onset of paralysis between 1 January and 31 December 2019. No wild-type strains were detected. Sabin Poliovirus type 1 was detected in two cases, one each in Eastern Cape and Limpopo provinces, and Sabin Poliovirus type 3 was detected in two cases from Gauteng. Detection of Sabin virus from stool is usually a coincidental finding in countries using OPV; no case was classified by the NPEC as vaccine-associated paralytic poliomyelitis (VAPP). The 2019 NPEC final classification of 2019 AFP cases is listed in table 2.

Table 2. Final classifications of acute flaccid paralysis (AFP) cases in South Africa, 2019 (courtesy of the National Department of Health).

Classification	Number	Percentage of total cases
Compatible	2	0.3
Discarded	594	93.4
Denotified (not an AFP)	29	4.6
Pending	11	1.7
Total	636	100

Surveillance Indicators:

The NP AFP detection rate measures the sensitivity of the surveillance program and is calculated at a district, province and country level (Table 3). The 2019 AFP detection rate for South Africa was 3.5/100 000 children under the age of 15 years, compared to the 2018 rate of 2.9/100 000. While the rate was below the country's target of 4.0/100 000, it exceeded the WHO's target of 2.0/100 000. Free State, Limpopo, Northern Cape and Mpumalanga provinces exceeded the 4.0/100 000 country target; Eastern Cape, Gauteng, Kwazulu-Natal, North West and Western Cape provinces reached the WHO target but not the country target; no provinces had a detection rate below 2.0/100 000 and there were no silent districts.

The national stool adequacy rate was 88%, above the required target of 80% and an improvement from 59% in 2018.

Table 3. South African Acute Flaccid Paralysis (AFP) surveillance indicators for 2019 by province and health district.

AFP Summary-week 52 of 2019 (Updated)																	
			Key indicators												Additional indicators	
Province	District	Year	Total_ population	Under15 _years	Target_ AFP_ Case	Total_AFP_ Cases_ Under15	Denotified	Total_True_ AFP_Cases_ Under15	Adequately_ investigated _cases	Not_Adequately _investigated_ cases	NP_ Detection _Rate	Stool_ Adequacy	Compatible _Cases	Unclassified >90days	Average number days from onset to notification	% of samples arriving to the lab within 72 hrs from collection
Eastern Cape	A Nzo DM	2019	876,698	338,017	14	5	0	5	5	0	1.5	100.0	0	0	6	40.0
Eastern Cape	Amathole DM	2019	978,795	356,827	14	8	1	7	6	1	2.0	85.7	0	0	15	42.9
Eastern Cape	Buffalo City MM	2019	884,058	279,514	11	6	2	4	3	1	1.4	75.0	0	0	1	50.0
Eastern Cape	C Hani DM	2019	823,046	274,625	11	15	0	15	15	0	5.5	100.0	0	0	1	40.0
Eastern Cape	Joe Gqabi DM	2019	375,077	124,771	5	4	0	4	4	0	3.2	100.0	0	0	6	25.0
Eastern Cape	N Mandela Bay MM	2019	1,316,391	395,391	16	7	1	6	5	1	1.5	83.3	0	0	2	50.0
Eastern Cape	O Tambo DM	2019	1,508,419	571,203	23	25	0	25	21	4	4.4	84.0	1	0	5	16.0
Eastern Cape	Sarah Baartman DM	2019	530,252	164,541	7	4	0	4	4	0	2.4	100.0	0	0	0	25.0
Eastern Cape			**7,292,736**	**2,504,889**	**101**	**74**	**4**	**70**	**63**	**7**	**2.8**	**90.0**	**1**	**0**	**4**	**36.1**
Free State	Fezile Dabi DM	2019	506,856	138,314	6	23	9	14	10	4	10.1	71.4	0	0	1	28.6
Free State	Lejweleputswa DM	2019	673,104	185,516	7	17	0	17	14	3	9.2	82.4	0	0	3	23.5
Free State	Mangaung MM	2019	814,680	218,461	9	12	0	12	10	2	5.5	83.3	0	0	6	66.7
Free State	T Mofutsanyana DM	2019	795,927	239,641	10	11	0	11	8	3	4.6	72.7	0	0	5	36.4
Free State	Xhariep DM	2019	129,882	33,750	1	3	0	3	3	0	8.9	100.0	0	0	0	33.3
Free State			**2,920,449**	**815,682**	**33**	**66**	**9**	**57**	**45**	**12**	**7.0**	**78.9**	**0**	**0**	**3**	**38**
Gauteng	Ekurhuleni MM	2019	3,597,781	882,680	35	16	1	15	11	4	1.7	73.3	1	0	1	73.3
Gauteng	Johannesburg MM	2019	5,287,887	1,303,779	52	31	2	29	25	4	2.2	86.2	0	0	3	69.0
Gauteng	Sedibeng DM	2019	993,044	263,408	11	18	1	17	15	2	6.5	88.2	0	0	2	82.4
Gauteng	Tshwane MM	2019	3,531,230	904,748	36	27	2	25	22	3	2.8	88.0	0	0	1	52.0
Gauteng	West Rand DM	2019	888,265	230,502	9	11	1	10	10	0	4.3	100.0	0	0	3	90.0
Gauteng			**14,298,207**	**3,585,117**	**143**	**103**	**7**	**96**	**83**	**13**	**2.7**	**86.5**	**1**	**0**	**2**	**73**
KwaZulu-Natal	Amajuba DM	2019	585,389	218,295	9	6	0	6	5	1	2.7	83.3	0	0	2	0.0
KwaZulu-Natal	eThekwini MM	2019	3,804,794	1,112,677	45	29	0	29	24	5	2.6	82.8	0	0	2	24.1
KwaZulu-Natal	Harry Gwala DM	2019	520,188	204,447	8	7	0	7	5	2	3.4	71.4	0	0	3	14.3
KwaZulu-Natal	iLembe DM	2019	713,189	236,458	9	9	0	9	8	1	3.8	88.9	0	0	1	22.2
KwaZulu-Natal	King Cetshwayo DM	2019	1,005,822	395,129	16	8	0	8	8	0	2.0	100.0	0	0	4	0.0
KwaZulu-Natal	Ugu DM	2019	790,154	283,413	11	11	2	9	6	3	3.2	66.7	0	0	2	33.3
KwaZulu-Natal	uMgungundlovu DM	2019	1,172,768	384,930	15	11	0	11	8	3	2.9	72.7	0	0	5	36.4
KwaZulu-Natal	Umkhanyakude DM	2019	702,470	274,637	11	9	0	9	7	2	3.3	77.8	0	0	3	22.2
KwaZulu-Natal	Umzinyathi DM	2019	578,835	220,003	9	10	0	10	10	0	4.5	100.0	0	0	3	20.0
KwaZulu-Natal	Uthukela DM	2019	764,548	303,350	12	9	0	9	8	1	3.0	88.9	0	0	3	0.0
KwaZulu-Natal	Zululand DM	2019	890,722	332,577	13	11	0	11	11	0	3.3	100.0	0	0	5	9.1
KwaZulu-Natal			**11,528,879**	**3,965,916**	**158**	**120**	**2**	**118**	**100**	**18**	**3.0**	**84.7**	**0**	**0**	**3**	**17**
Limpopo	Capricorn DM	2019	1,347,201	416,213	17	17	0	17	16	1	4.1	94.1	0	0	1	52.9
Limpopo	Mopani DM	2019	1,235,297	391,114	16	24	0	24	24	0	6.1	100.0	0	0	2	20.8
Limpopo	Sekhukhune DM	2019	1,247,984	425,687	17	16	0	16	16	0	3.8	100.0	0	0	2	25.0
Limpopo	Vhembe DM	2019	1,472,489	498,451	20	20	2	18	17	1	3.6	94.4	0	0	4	50.0
Limpopo	Waterberg DM	2019	722,916	213,886	9	19	2	17	17	0	7.9	100.0	0	0	3	70.6
Limpopo			**6,025,887**	**1,945,351**	**78**	**96**	**4**	**92**	**90**	**2**	**4.7**	**97.8**	**0**	**0**	**2**	**44**
Mpumalanga	Ehlanzeni DM	2019	1,741,232	573,491	23	29	0	29	28	1	5.1	96.6	0	0	3	55.2
Mpumalanga	G Sibande DM	2019	1,210,593	346,526	14	23	1	22	22	0	6.3	100.0	0	0	2	54.5
Mpumalanga	Nkangala DM	2019	1,554,418	409,484	16	20	0	20	18	2	4.9	90.0	0	0	2	25.0
Mpumalanga			**4,506,243**	**1,329,501**	**53**	**72**	**1**	**71**	**68**	**3**	**5.3**	**95.8**	**0**	**0**	**3**	**45**
North West	Bojanala Platinum DM	2019	1,745,419	493,065	20	12	0	12	9	3	2.4	75.0	0	0	6	33.3
North West	Dr K Kaunda DM	2019	769,700	224,358	9	5	0	5	4	1	2.2	80.0	0	0	2	40.0
North West	Ngaka Modiri Molema DM	2019	965,968	295,060	12	11	0	11	11	0	3.7	100.0	0	0	2	27.3
North West	Ruth Segomotsi Mompati DM	2019	480,611	175,817	7	7	0	7	6	1	4.0	85.7	0	0	4	71.4
North West			**3,961,698**	**1,188,300**	**48**	**35**	**0**	**35**	**30**	**5**	**2.9**	**85.7**	**0**	**0**	**4**	**43**
Northern Cape	Frances Baard DM	2019	381,570	100,828	4	7	0	7	7	0	6.9	100.0	0	0	2	71.4
Northern Cape	J T Gaetsewe DM	2019	245,820	77,502	3	2	1	1	1	0	1.3	100.0	0	0	1	0.0
Northern Cape	Namakwa DM	2019	113,474	28,265	1	1	0	1	1	0	3.5	100.0	0	0	1	100.0
Northern Cape	Pixley ka Seme DM	2019	211,431	56,355	2	2	0	2	2	0	3.5	100.0	0	0	0	50.0
Northern Cape	ZF Mgcawu DM	2019	265,867	63,461	3	1	0	1	1	0	1.6	100.0	0	0	0	100.0
Northern Cape			**1,218,162**	**326,411**	**13**	**13**	**1**	**12**	**12**	**0**	**4.0**	**100.0**	**0**	**0**	**1**	**64**
Western Cape	Cape Town MM	2019	4,181,107	994,010	40	39	1	38	32	6	3.8	84.2	0	0	3	44.7
Western Cape	Cape Winelands DM	2019	929,218	240,760	10	8	0	8	6	2	3.3	75.0	0	0	2	37.5
Western Cape	Central Karoo DM	2019	77,411	21,431	1	1	0	1	1	0	4.7	100.0	0	0	1	100.0
Western Cape	Garden Route DM	2019	634,437	157,258	6	7	0	7	4	3	4.5	57.1	0	0	3	71.4
Western Cape	Overberg DM	2019	297,792	71,249	3	3	0	3	3	0	4.2	100.0	0	0	3	100.0
Western Cape	West Coast DM	2019	467,528	120,343	5	3	0	3	3	0	2.5	100.0	0	0	1	33.3
Western Cape			**6,587,493**	**1,605,051**	**65**	**61**	**1**	**60**	**49**	**11**	**3.7**	**81.7**	**0**	**0**	**2**	**64**
South Africa			**58,339,754**	**17,266,218**	**692**	**640**	**29**	**611**	**540**	**71**	**3.5**	**88.4**	**2**	**0**	**3**	**47**
Detection Rate					**0-1.99**	**2-3.99**	**4+**	**Silent**								
Stool Adequacy					**<80**	**80+**	**Silent**									
Proportion of samples arriving to the lab with 72 hrs from					**80+**	**50-79.99**	**<50**									

Laboratory Indicators

On arrival at the laboratory, 1304 of 1328 (98%) of samples were appropriately received on ice and 42% were received within three days of sample collection.

Laboratory surveillance indicators showed that 94% of samples were reported within 14 days of receipt, above the target of 80%. The Non-Polio Enterovirus (NPEV) isolation rate was 9%, below the target of 10% as stipulated by the WHO (https://apps.who.int/iris/handle/10665/68762[2]). The NPEV rate may be a useful indicator of laboratory performance, however, the rate can be influenced by a number of factors, including the season of the year, elevation, or population hygienic levels.

Southern African countries supported by NICD

A total of 3110 stool samples were received from other Southern African countries. Of these, 94% were received in good condition and 89% were processed within 14 days of receipt. The NPEV isolation rate was 17%. No WPV was detected. There were 8 cases of cVDPV2 detected from Mozambique, 2 cases of cVDPV2 from Malawi, and 129 cases of cVDPV2 from Angola from several outbreaks.

The broader African Region

A total of 548 samples from cases and contacts of cases in Central African Republic, Chad, Ethiopia, Niger, Democratic Republic of Congo (DRC), Zambia, Cameroon and South Sudan were received for molecular characterization. VDPV type 2 was detected in Central African Republic (21 cases), DRC (88 cases), Zambia (3 cases and 2 contacts), Chad (3 cases and 3 contacts), Ethiopia (3 cases and 10 contacts) and Niger (2 cases and 9 contacts). One case from South Sudan was Sabin 1. Sabin 2 was identified in 279 samples, with cases and contacts of cases from Cameroon, Chad, Ethiopia, Niger and DRC.

Environmental surveillance in South Africa

Environmental surveillance, a supplement to AFP surveillance, was initiated in South Africa in July 2019. A total of 32 samples was received from 3 sites in Gauteng Province. The NPEV isolation rate was 87% and Sabin-like virus was detected at 2 sites - an anticipated finding in a country using live oral polio vaccine.

Environmental surveillance for the African region

The NICD performed viral isolation on 98 samples from 9 sites in Angola, 76 samples from 4 sites in Mozambique and 253 samples from 10 sites in Zambia. The NPEV isolation rate was 44% in Angola, 41% in Mozambique and 29% in Zambia (Figure 1). Notably, cVDPV2 was detected in 7 of the 9 sites in Angola.

Molecular testing was conducted for environmental samples from Cameroon, Ethiopia, Cote d'Ivoire, Uganda and Madagascar. cVDPV2 was detected from environmental sites in Cameroon, Ethiopia and Cote d'Ivoire.

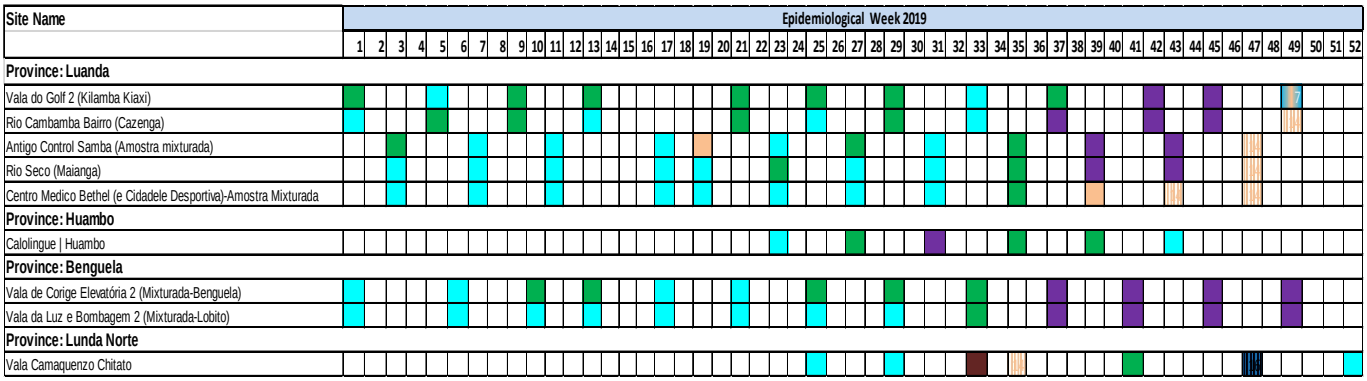

Figure 1a. Results from environmental sampling sites in Angola, 2019.

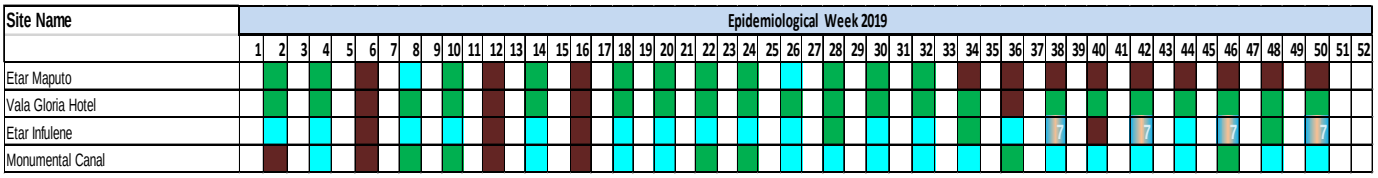

Figure 1b. Results from environmental sampling sites in Mozambique, 2019.

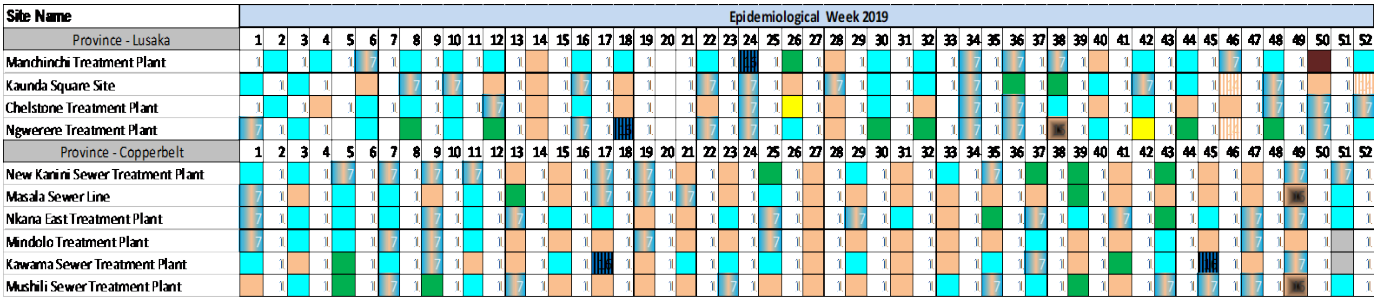

Figure 1c. Results from environmental sampling in Zambia, 2019.

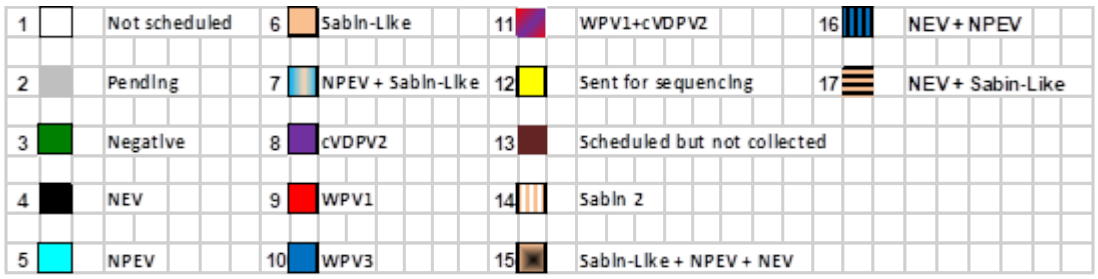

Figure 1. Matrices showing sampling frequency and viral isolation results of environmental samples processed at the National Institute for Communicable Diseases, South Africa, for Angola (figure 1a), Mozambique (figure 1b) and Zambia (figure 1c) in 2019.
NPEV = non polio enterovirus, NEV = non enterovirus.

Discussion

The global effort to eradicate polio is one of the largest health initiatives in history. The AFP surveillance network needs to be highly sensitive, enabling the immediate detection of polioviruses and ensuring that the polio eradication mission is successful. Although the last WPV case in South Africa occurred in 1989, deficiencies in the country's routine immunization coverage and surveillance systems resulted in South Africa's polio-free status being revoked by the African Regional Certification Commission in 2017. In response, a number of measures were put in place to address the identified weaknesses. The Department of Health set the target for South Africa to find four cases of AFP per 100 000 children and investigate them for polio. Following the African Regional Certification Commission's visit to South Africa and resubmission of certification documentation, the country was once again declared polio-free on 17 September 2019.

These data show that stool adequacy and AFP reporting rates have improved since 2018. However, the transport time for samples to reach the laboratory remains a challenge. Improvements are needed in terms of transport logistics to ensure samples reach the laboratory within the required timeframe. Continued training of healthcare workers is needed to ensure that the correct samples are collected, the correct test is requested, and samples are being sent to the laboratory without delay.

The NICD has supported the African region by molecular characterization of polioviruses of international public health concern. Additionally, the NICD implemented environmental polio surveillance in South Africa which has potential to supplement AFP surveillance as an early warning system, although its extent is limited by the need for labour-intensive viral culture prior to molecular confirmatory assays. The utility of environmental surveillance is demonstrated by detection of cVDPV strains through environmental surveillance for Angola.

The Sabin type 2 polioviruses detected in the African region were most likely due to mop-up campaigns using monovalent OPV type 2 to restrict VDPV type 2 circulation in those countries where it had been detected. Updated data is available on the GPEI website: www.polioeradication.org.[1]

The GPEI has developed a comprehensive new strategy to stop the spread of cVDPV2 outbreaks currently affecting mainly countries in Africa. The strategy aims to accelerate the development of a new vaccine-novel OPV2 (nOPV2) as a potential alternative for outbreak response and, ultimately, as a replacement for mOPV2. nOPV2 is a modification of the existing Sabin OPV type 2 and is specifically designed to improve the genetic stability of the vaccine. The nOPV2 has been given a WHO Emergency Use Listing (EUL) recommendation and should be available to address cVDPV2.[3]

Conclusion

The international spread of poliovirus remains a Public Health Emergency of International concern (PHEIC) as demonstrated by the widespread outbreaks of cVDPV2 in the African region. Countries need to strengthen their surveillance efforts and increase routine immunization efforts particularly with IPV to give protection against type 2 cVDPV.

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References

1. Polio Global Eradication Initiative, Polio Today, www.polioeradication.org. Access date 02 July 2020.
2. World Health Organization. (2004). Polio laboratory manual, 4th ed. World Health Organization. https://apps.who.int/iris/handle/10665/68762. Access date 06 October 2020.
3. http://polioeradication.org/wp-content/uploads/2020/07/cVDPV2-nOPV2-fact-sheet-July-2020.pdf. Access date 21 October 2020.

GERMS-SA ANNUAL SURVEILLANCE REPORT FOR LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL, *HAEMOPHILUS INFLUENZAE*, PNEUMOCOCCAL, GROUP A STREPTOCOCCAL AND GROUP B STREPTOCOCCAL INFECTIONS, SOUTH AFRICA, 2019

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Summary

The Centre for Respiratory Diseases and Meningitis (CRDM), of the National Institute for Communicable Diseases (NICD), through the GERMS-SA platform, performs national laboratory-based surveillance on five invasive bacterial diseases including: *Neisseria meningitidis, Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Streptococcus agalactiae.* The surveillance programme aims to describe the epidemiology of these invasive infections and monitor the impact of preventive measures, such as routine vaccination, over time. Diagnostic microbiology laboratories in South Africa are requested to submit isolates meeting the GERMS-SA surveillance case definition to the CRDM reference laboratory for further phenotypic and genotypic characterisation. Basic demographic data are collected from the patients' laboratory reports for all isolates detected. At selected enhanced surveillance hospital sites, trained surveillance officers interview the patients and review the medical records for all *Neisseria meningitidis, Haemophilus influenzae* and pneumococcal disease episodes. Invasive meningococcal disease incidence remained low in 2019 with serogroup B causing most disease in young infants, serogroup Y responsible for a peak in adolescents and serogroup W predominating through adulthood. In-hospital case fatality for IMD was 19%, with 20% of survivors suffering sequelae post-hospital discharge. Incidence of invasive *Haeomophilus influenzae* remained low with non-typeable *Haemophilus influenzae* causing most disease. Infants had the highest rates of *H. influenzae* type b and non-typeable (HNT) disease, with HNT incidence increasing into adulthood. In-hospital case fatality was 27% and long-term sequelae following meningitis occurred in 27% of survivors. Invasive pneumococcal disease (IPD) incidence has remained stable over the past 5 years across all age categories. Infants still have the highest disease incidence, with disease peaking again after age 25 years. Residual IPD in children aged <5 years is largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurs in children who have not received adequate doses of pneumococcal conjugate vaccine (PCV13). Serotypes causing IPD in those aged ≥5 years remain diverse including both vaccine and non-vaccine serotypes. Infants and the elderly experience the highest incidence of invasive Group A Streptococcal (GAS) infections in South Africa with the

majority of isolates being susceptible to first-line antibiotics. In 2020, clinical data will be collected from persons with invasive GAS infections admitted to our enhanced surveillance sites and molecular typing of all the 2019 and 2020 isolates will commence. Incidence of early and late onset invasive Group B Streptococcus (GBS) appears low, however this may be due to low specimen taking practices in many areas of South Africa. Most invasive GBS in infants was caused by serotypes III and Ia, although a range of serotypes was found to be causing invasive GBS in other age groups. This was the first year of active surveillance for invasive GBS and no clinical data were collected. Clinical laboratories are encouraged to send all isolates meeting the GERMS-SA case definition to the NICD so that further characterisation and serotyping can be done. In 2020, enhanced clinical surveillance will begin for both GAS and GBS at selected sites in order to report on risk factors predisposing to invasive infections and outcome following infection.

Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM), of the National Institute for Communicable Diseases (NICD), through the GERMS-SA platform, performs national laboratory-based surveillance on invasive bacterial diseases such as: *Neisseria meningitidis, Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Streptococcus agalactiae.* The surveillance aims to describe the epidemiology of these diseases and monitor the impact of routine pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. Surveillance has been ongoing since 2003, however this is the first year of *Streptococcus pyogenes* (Group A Streptococcus) and *Streptococcus agalactaie* (Group B Streptococcus) surveillance. This report summarises the findings for all pathogens in 2019.

Methods

Approximately 220 South African clinical microbiology laboratories participated in the GERMS-SA surveillance programme in 2019, including 31 enhanced surveillance hospital sites (ESS).[1]

The South African population under surveillance in 2019 was estimated at 58.8 million, with 954 532 births.[2,3] HIV-prevalence in South Africa is 13.5%, with 7.94 million persons living with HIV.[2]

The standard case definition for all five pathogens included the detection of the organism under surveillance from any normally sterile site. In addition, non-invasive isolates of *Streptococcus pyogenes* from skin or soft tissue were accepted if the accompanying diagnosis was necrotising fasciitis or septic shock syndrome. Diagnostic microbiology laboratories reported case patients to the NICD using laboratory case report forms and submitted available isolates from case patients on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. Only antimicrobial susceptibility testing was performed on *Streptococcus pyogenes* isolates in 2019. Genotypic characterisation of these isolates will be conducted at a later stage. Culture-negative cases with a positive supplementary test e.g. Gram stain and/or antigen detection were also reported, and samples were submitted for molecular detection of *Streptococcus pneumoniae, Haemophilus influenzae* or *Neisseria meningitidis*. Repeat isolates from the same patient were counted as a single case if they occurred within 21 days of the first culture.

At ESS surveillance officers completed clinical case report forms using the Mobenzi application on electronic tablets for patients with laboratory-confirmed invasive meningococcal, invasive *H. influenzae* and invasive pneumococcal disease, by case-patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status, and patient outcome. Case patients were followed up for the duration of the hospital admission. Data management was centralised at the NICD. Laboratory, clinical and demographic data from case-patients were recorded on a Microsoft Access database. A surveillance audit was performed for NHLS laboratories in all provinces using the NHLS Central Data Warehouse (CDW). The audit was designed to obtain basic demographic and laboratory data from additional case-patients with laboratory-confirmed disease not already reported to GERMS-SA by participating laboratories; these cases are included in this report. Incidence was calculated using mid-year population estimates for 2018 and 2019 from Statistics South Africa.[2] Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and from relevant university and provincial ethics committees for other enhanced surveillance sites.

Neisseria meningitidis

Results

In 2019, 111 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 43 (39%) viable isolates were received and 16 (14%) cases were detected on audit. The overall disease incidence remained low at 0.19 cases per 100 000 population, similar to that in 2018 (0.22/100 000). Incidence was highest in the Western Cape Province (0.56/100 000) followed by Gauteng (0.24/100 000) and Eastern Cape provinces (0.18/100 000) (Table 1). Most cases were sporadic, and disease peaked from winter through spring (May to October), with a further upsurge in December (Figure 1). Cerebrospinal fluid was the most common specimen from which meningococci were identified (70/111, 63%) (Table 2). Ninety-five percent (89/94) of IMD was caused by 3 serogroups - B (36/94, 38%), Y (27/94, 29%) and W (25/94, 27%) (Table 3). Incidence of IMD was highest in children <1 year (1.14/100 000) (Figure 2). Although the different serogroups occurred across most age-categories, serogroup B was most predominant in children aged <5 years, serogroup Y in persons aged 5-24 years and serogroup W in persons aged ≥25 years. (Figure 2) Of those with known sex, IMD occurred more frequently in males (59/109, 54%). Of the viable isolates tested for antimicrobial susceptibility, 26% (11/43) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) between 0.094µg/ml and 0.25µg/ml, and all were susceptible to 3rd generation cephalosporin and ciprofloxacin.

Table 1. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=236 (including audit cases).

Province	2018		2019	
	n	Incidence rate*	N	Incidence rate*
Eastern Cape	26	0.40	12	0.18
Free State	2	0.07	3	0.10
Gauteng	37	0.25	37	0.24
KwaZulu-Natal	8	0.07	13	0.12
Limpopo	4	0.07	2	0.03
Mpumalanga	2	0.04	1	0.02
Northern Cape	1	0.08	1	0.08
North West	6	0.15	4	0.10
Western Cape	39	0.59	38	0.56
South Africa	**125**	**0.22**	**111**	0.19

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

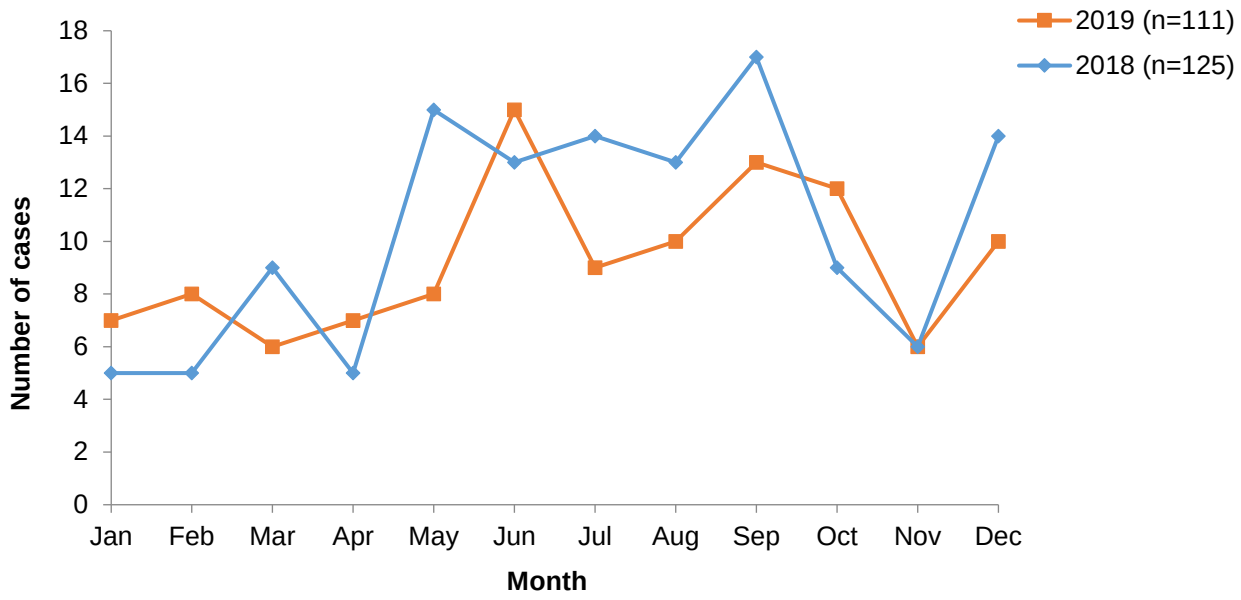

Figure 1. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2018-2019, n=236.

Table 2. Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=236**.**

Site of specimen	2018		2019	
	n	%	n	%
Cerebrospinal fluid	82	66	70	63
Blood	43	34	41	37
Other	0	0	0	0
Total	**125**		**111**	

Table 3. Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2019, n=111*.

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	E**	Total
Eastern Cape	1	0	2	0	1	8	0	0	12
Free State	0	0	0	0	2	1	0	0	3
Gauteng	7	0	10	2	12	6	0	0	37
KwaZulu-Natal	3	0	6	0	3	1	0	0	13
Limpopo	1	0	1	0	0	0	0	0	2
Mpumalanga	0	0	1	0	0	0	0	0	1
Northern Cape	0	0	0	0	0	1	0	0	1
North West	1	0	2	0	0	1	0	0	4
Western Cape	4	0	14	3	7	9	0	1	38
South Africa	**17**	**0**	**36**	**5**	**25**	**27**	**0**	**1**	**111**

*94 (85%) with viable isolates or specimens available for serogrouping/genogrouping; There were no Non-groupable meningococcal isolates causing invasive disease in 2019.

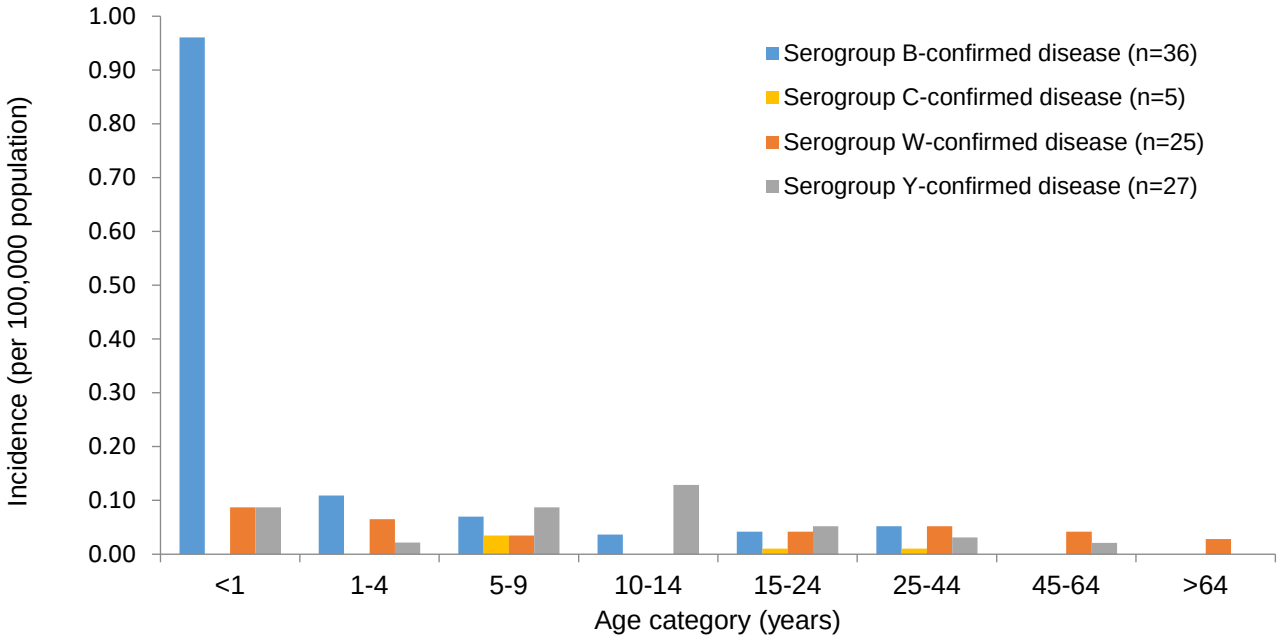

Figure 2. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2019, n=111** (**specimens or viable isolates unavailable for serogrouping n=17; one isolate serogroup E).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Thirty-eight (34%) IMD patients presented to the enhanced surveillance sites and 31/38 (82%) had additional clinical information available. The median time for admissions was 10 days (interquartile range 7-13 days). The case-fatality ratio was 19% (6/31); three patients died on the day of admission. Thirty-eight percent of patients with HIV status available were HIV-infected (9/24). For those who survived to discharge from hospital, 5/25 (20%) suffered sequelae following IMD. Two patients developed ongoing seizures, and one each had hearing loss, necrotic skin lesions and hydrocephalus.

Discussion

Incidence of IMD in South Africa remains low with a variety of serogroups (B, Y and W) causing disease in the different age-categories. Burden is highest in infants, particularly serogroup B disease, whilst serogroup Y disease has been responsible for a peak in 10-14 year olds. All IMD isolates were susceptible to third generation cephalosporins and an increase in penicillin non-susceptibility of the meningococci was noted. Third generation cephalosporins are frequently used as empiric therapy in patients presenting with meningitis/bacteraemias. Before switching over to high-dose penicillin once IMD is confirmed, clinicians should establish susceptibility of meningococcal isolates to penicillin. Provision of ciprofloxacin as chemoprophylaxis is recommended to all close contacts. Although uncommon, meningococcal disease in South Africa is a devastating illness affecting all age groups. In 2019, in-hospital case fatality was 19%, with 20% of survivors suffering sequelae post discharge from hospital.

Haemophilus influenzae

Results

There were 259 cases of invasive *Haemophilus influenzae* (HI) disease identified through the surveillance programme in 2019 - 41% (105) were detected on audit and 58% (149) had either viable isolates (109) or specimens (40) available for serotyping (Table 4). Eight cases were co-infected with invasive *Streptococcus pneumoniae*. Incidence of invasive HI disease was 0.44 per 100 000 population. Gauteng Province (88/259, 34%) had the highest number of cases reported, followed by Western Cape Province (78/259, 30%) (Table 4). Twenty-eight percent of cases (41/149) were serotype b (Hib) and non-typeable (HNT) disease was found in 55% (82/149) (Table 4). Most HI cases were isolated from blood (160/259, 62%), however Hib isolates were more likely than HNT isolates to be found in cerebrospinal fluid (CSF) (17/41, 41% versus 6/82, 7%, $p<0.001$) (Table 5). Although HI occurs in all ages, invasive disease is highest in infants followed by adults aged 25-44 years (Figure 3). Hib incidence is still highest in infants even though significant declines have been noted since 2010 (5.2 cases per 100 000 in 2010 to 1.2 cases per 100 000 in 2019 ($p<0.001$)) (Figure 4 and 5). Hib incidence has remained below 0.2 per 100 000 in 1-4 year olds since 2013 (Figure 5). HNT incidence is highest in infants (1.2 per 100 000) dropping substantially throughout the rest of childhood before increasing again in adulthood with a moderate peak from ages 25 years and older (Figure 4). Forty-one percent (12/29) of Hib isolates and 8% (5/60) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Twenty-five cases of Hib disease occurred in children <15 years of age and vaccine history was available for 32% (8/25). Three infants were <6 weeks and thus too young to receive Hib vaccine. Four children had received at least 3 doses of vaccine and were possible vaccine failures. One 3-month old child had only received one dose of Hib vaccine.

Table 4. Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2019, n=259*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	6	2	7	0	1	0	2	7	25
Free State	3	0	1	0	0	0	1	3	8
Gauteng	44	3	10	0	0	0	4	27	88
KwaZulu-Natal	28	0	5	0	0	0	1	8	42
Limpopo	2	0	1	0	0	0	0	2	5
Mpumalanga	0	0	4	0	0	0	2	0	6
Northern Cape	2	0	0	0	0	0	0	0	2
North West	3	0	1	1	0	0	0	0	5
Western Cape	22	3	12	1	0	0	5	35	78
South Africa	**110**	**8**	**41**	**2**	**1**	**0**	**15**	**82**	**259**

*149 (58%) with specimens or viable isolates available for serotyping.

Table 5. Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2019, n=259.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	19	17	17	41	9	35	6	7
Blood	60	55	21	51	17	65	62	76
Other	31	28	3	7	0	0	14	17
Total	**110**		**41**		**26**		**82**	

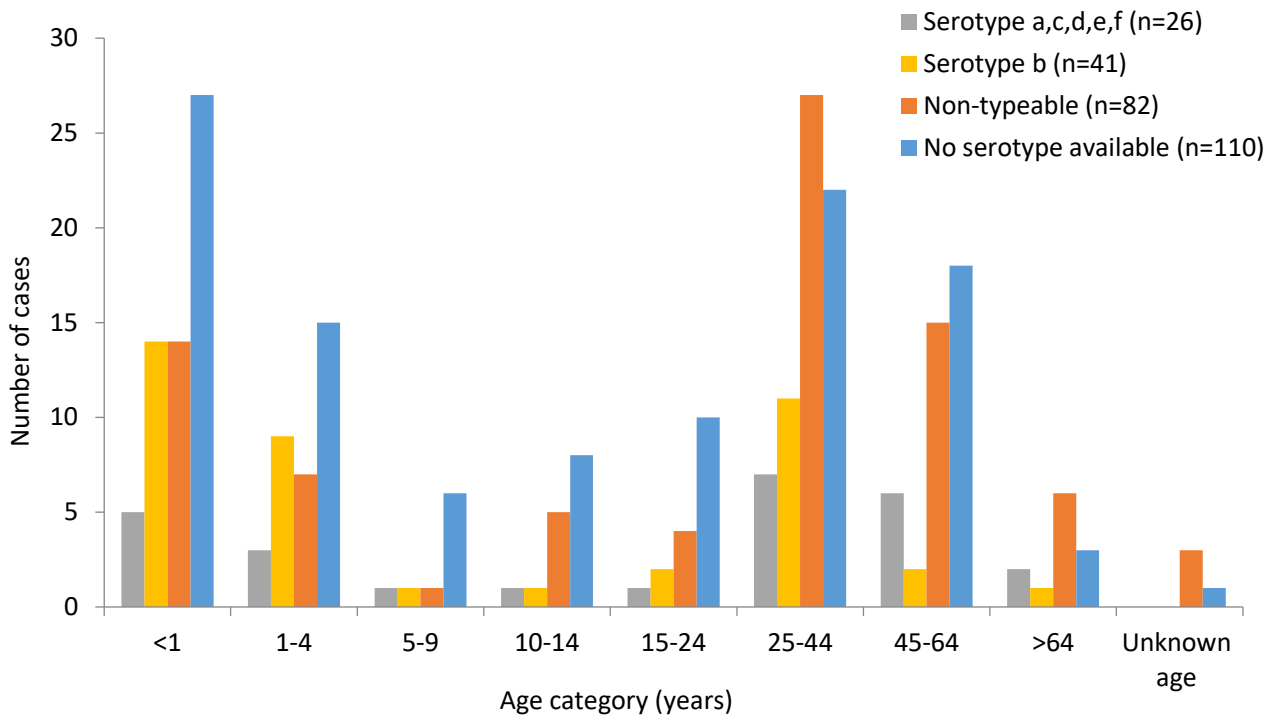

Figure 3. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2019, n=259 (age unknown for n=4; specimens or viable isolates unavailable for serotyping for n=110).

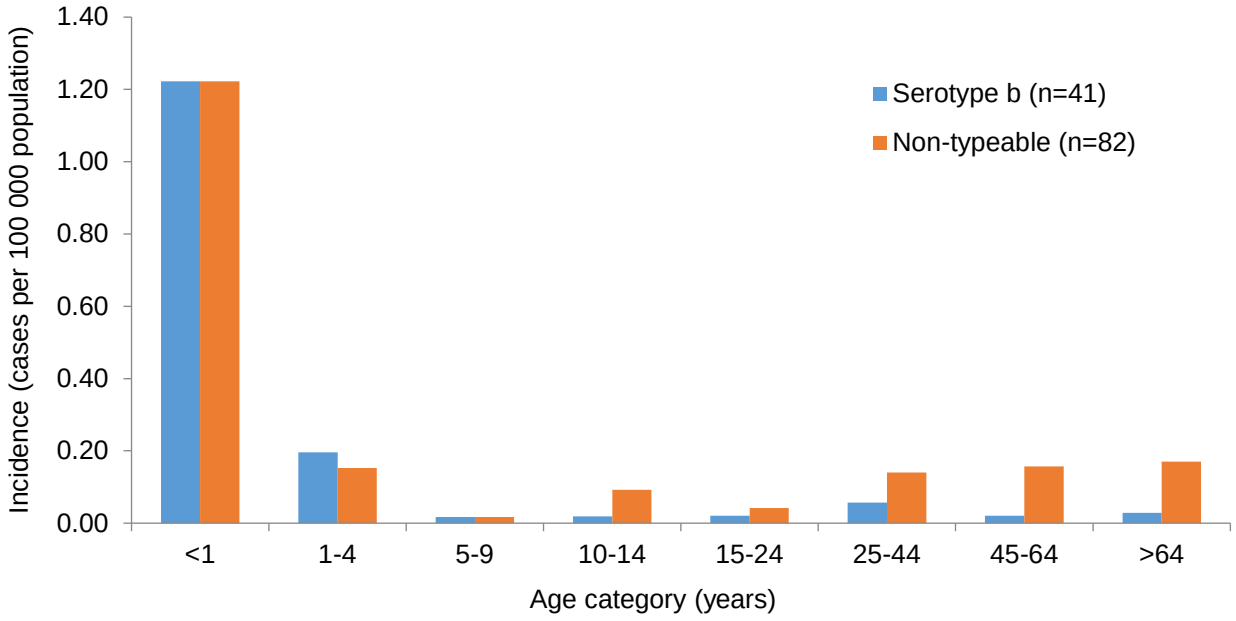

Figure 4. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2019, n=259 (age unknown, n=4; isolates unavailable for serotyping, n=110; other serotypes from cases with known age, n=26).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

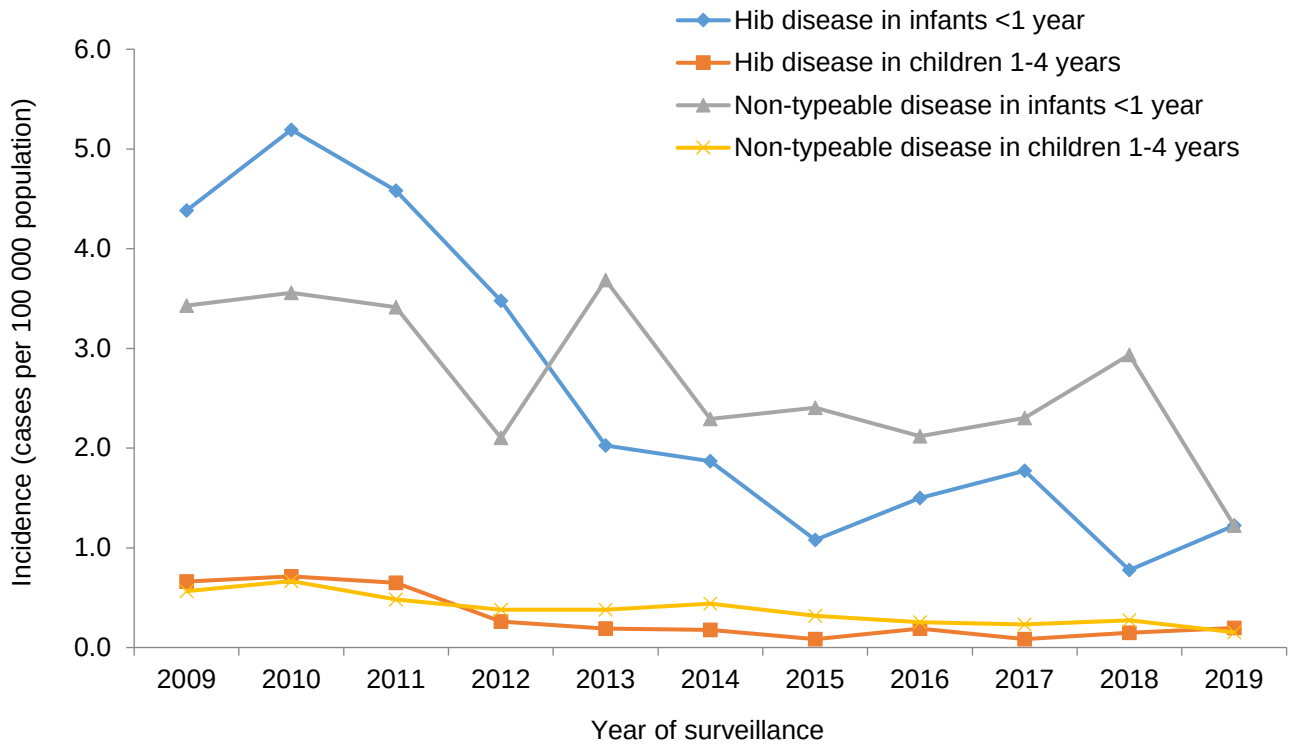

Figure 5. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2019.
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Clinical information was available for 85% (110/130) of cases presenting to the ESS. Patients were admitted for a median of 7 days (interquartile range (IQR) 3-16). Case fatality was 27% (36/110) and median time to death was within one day of admission (IQR 0-4). There was no statistically significant difference between case fatalities of those with Hib or HNT disease (25% (5/20) vs. 23% (11/47), p=0.5). Amongst those with known HIV status, 38% (33/86) were HIV-infected. Conditions other than HIV predisposing to HI disease were reported in 53/98 (54%) patients – the most common conditions included chronic lung disease (10), history of smoking (7), malignancy (7) and prematurity (6). Of the 19 patients at ESS with HI on CSF: eight patients died during their hospitalization, and 27% (3/11) of those who survived to discharge suffered sequelae – one developed ongoing seizures and two developed hydrocephalus.

Discussion

Overall incidence of HI remained low in 2019 and HNT accounted for the majority of cases. The highest rates of disease were seen in infants for both Hib and HNT, with HNT incidence increasing in adults. Many adults with invasive HI infection had an underlying chronic condition, such as chronic lung disease or malignancy. Case-fatality rates are high (27%) and long-term sequelae following meningitis occurred in 27% of survivors. Although many of the children with Hib disease had been fully vaccinated, only a few vaccine histories were obtainable.

Streptococcus pneumoniae

Results

Invasive pneumococcal disease (IPD) incidence for 2019 remained the same as 2018 at 4 per 100 000 population (Table 6). The highest incidence was seen in the Western Cape (9.3 per 100 000 population) followed by Northern Cape (7.1 per 100 000) and Gauteng provinces (5.1 per 100 000 population) (Table 6). Pneumococcal conjugate vaccine (PCV7) was introduced into the Expanded Programme on Immunisation (EPI) in 2009, and subsequently replaced by PCV13 in 2011. In 2019, peak IPD incidence occurred in infants (20 per 100 000 population), followed by adults (5-6 per 100 000 population in the 25 years and older age categories) (Figure 6). Eight patients with IPD were co-infected with invasive *Haemophilus influenzae* and one with *Neisseria meningitidis*. The majority of IPD cases were isolated from blood specimens (63%, 1490/2359) (Table 7). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 29% (413/1386) of IPD isolates and the highest proportion was in children 1-4 years of age (51%, 40/79) (Table 8 and Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 8% (110/1386) of isolates from all specimens including 8% (29/347) of IPD isolated from CSF. In 2019, serogroups 8, 12F, 19F, 7 and 14 were the most predominant serogroups causing 44% (80/180) of IPD in children <5 years-of-age, whilst serogroups 8, 12F, 3, 19A and 9N caused 43% (511/1194) of disease in persons >5 years (Figure 8A and 8B). Only 59% (1386/2359) of IPD isolates were sent to NICD, of which 1374 were serotyped (Figure 9). Of those serotyped, 22% (39/180) of isolates from children <5 years, and 30% (357/1194) of IPD isolates from person 5 years and older were PCV13-vaccine serotypes (Table 9 and 10).

Table 6. Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=4674 (including audit cases).

Province	2018		2019	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	259	3.96	274	4.08
Free State	106	3.59	84	2.91
Gauteng	757	5.14	776	5.11
KwaZulu-Natal	242	2.13	237	2.10
Limpopo	84	1.45	97	1.62
Mpumalanga	116	2.56	102	2.22
Northern Cape	52	4.24	90	7.12
North West	71	1.78	66	1.64
Western Cape	628	9.48	633	9.25
South Africa	**2315**	**4.01**	**2359**	**4.01**

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

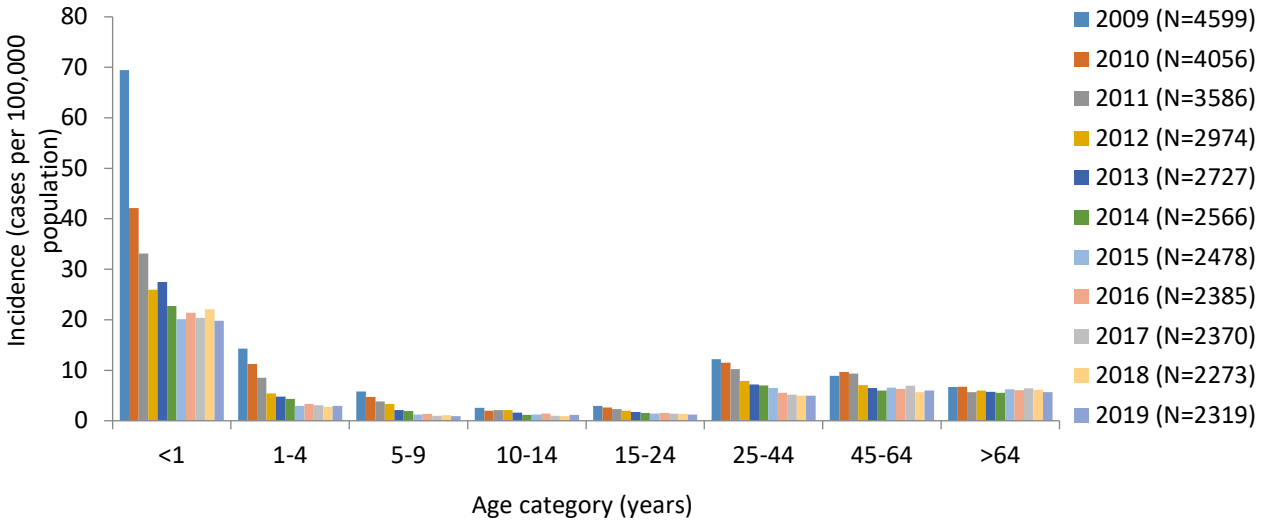

Figure 6. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2019, n=33,761.
2009: N=4,760 age unknown for n=161; 2010: N=4,197, age unknown for n=141; 2011: N=3,804, age unknown for n=218; 2012: N=3,222, age unknown for n=248; 2013: N=2,865, age unknown for n=138; 2014: N=2,731, age unknown for n=165; 2015: N=2,635, age unknown for n=157; 2016: N=2,433, age unknown for n=48; 2017: N=2,440, age unknown for n=70; 2018: N=2,315, age unknown for n=42; 2019: N=2359, age unknown for n=40
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Table 7. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=4674.

Site of specimen	2018		2019	
	n	%	n	%
Cerebrospinal fluid	795	34	700	30
Blood	1362	59	1490	63
Other	158	7	169	7
Total	**2315**		**2359**	

Table 8. Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2019, n=2359.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	99	119	68	44	25	12	7
Free State	38	34	74	7	15	5	11
Gauteng	364	297	72	78	19	37	9
KwaZulu-Natal	152	50	59	26	31	9	11
Limpopo	51	37	80	7	15	2	4
Mpumalanga	39	43	68	16	25	4	6
Northern Cape	36	38	70	11	20	5	9
North West	43	17	74	4	17	2	9
Western Cape	151	338	70	118	24	26	5
South Africa	**973**	**973**	**70**	**311**	**22**	**102**	**7**

*2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

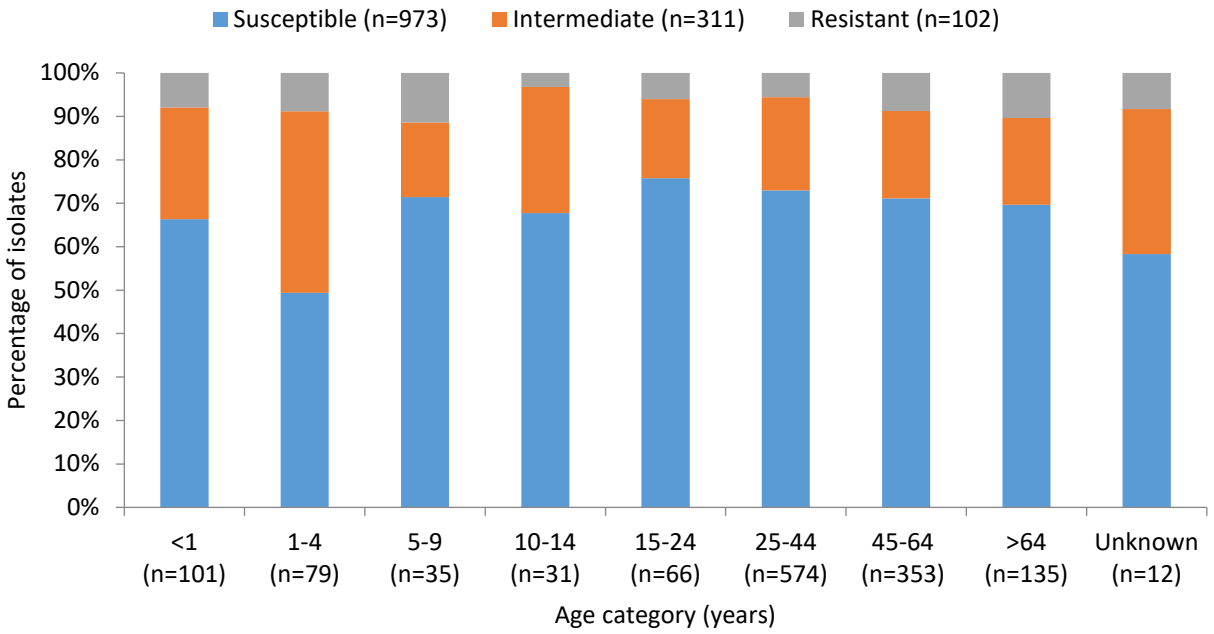

Figure 7. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2019, n=2359 (n=1386 with viable isolates).
2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

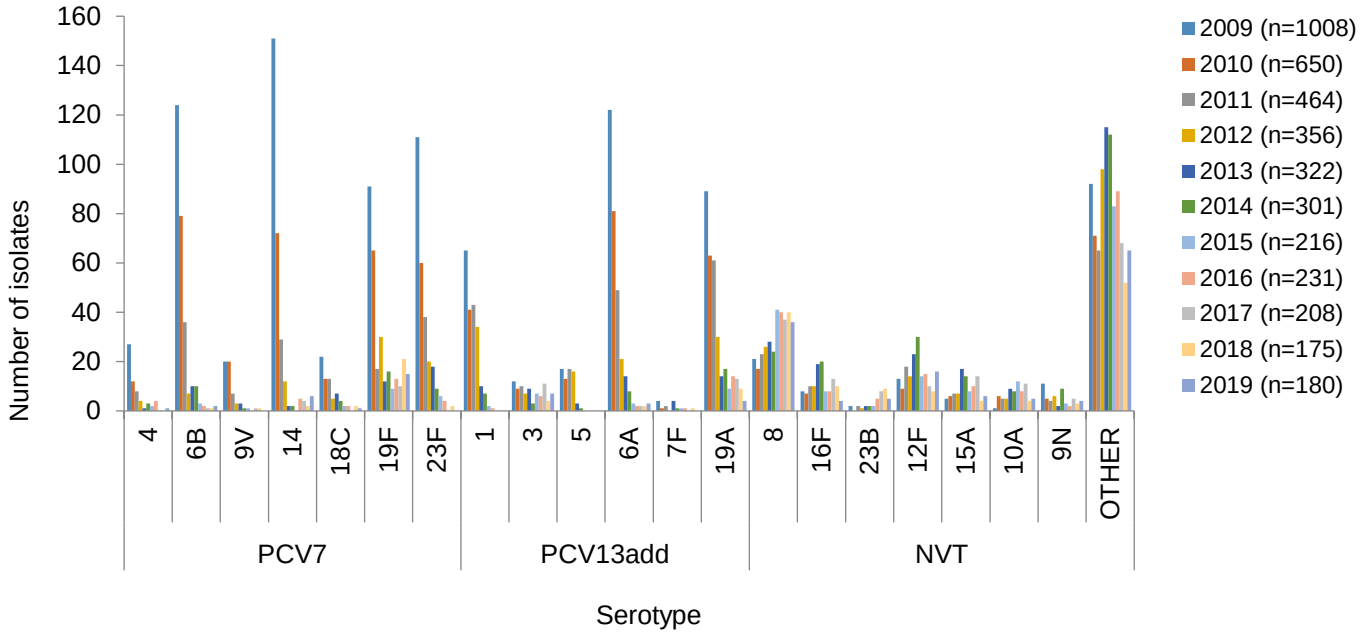

Figure 8a. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2019.
2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates; 2017: N=374, n=167 without viable isolates; 2018: N=386, n=211 without viable isolates; 2019: N=361, n=181 without viable isolates
Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

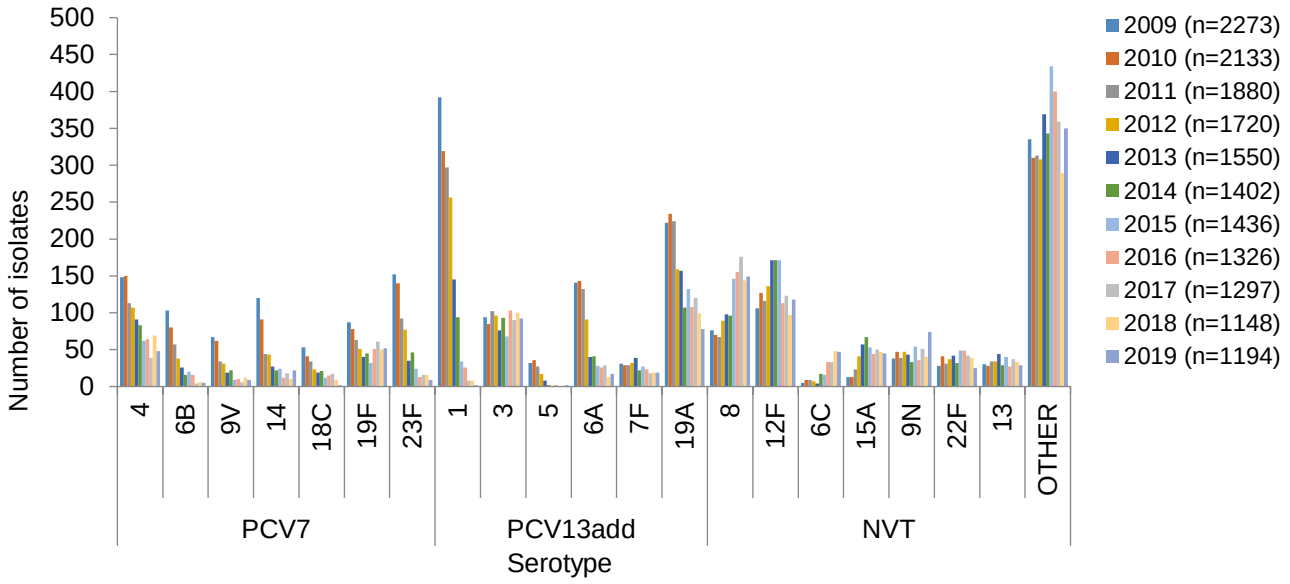

Figure 8b. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children ≥5 years, South Africa, 2009-2019.
2009: N=3264, n=991 without viable isolates; 2010: N=3146; n=1013 without viable isolates; 2011: N=2891, n=1011 without viable isolates; 2012: N=2462, n=742 without viable isolates; 2013: N=2229, n=679 without viable isolates; 2014: N=2101, n=699 without viable isolates; 2015: N=2097, n=661 without viable isolates; 2016: N=1986, n=660 without viable isolates; 2017: N=1996, n=699 without viable isolates; 2018: N=1871, n=723 without viable isolates; 2019: N=1998, n=804 without viable isolates.
Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

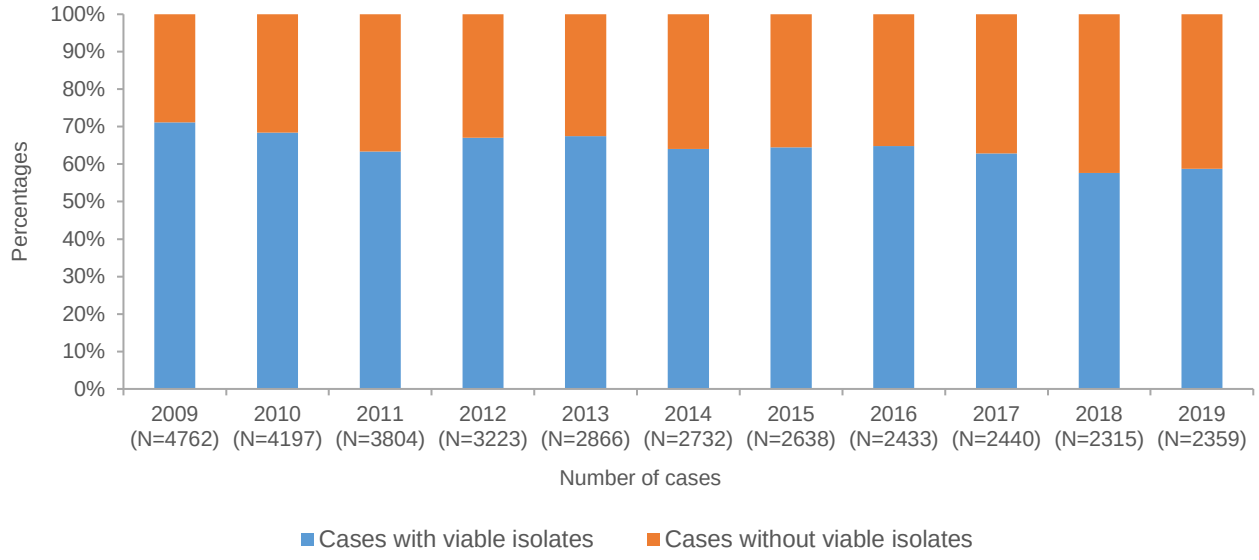

Figure 9. Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, South Africa, 2009-2019.

Table 9. Number and percentage of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2019, n=361 (n=180 with viable isolates).

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes**		13-valent serotypes***	
		n	%	n	%	n	%	n	%
Eastern Cape	17	2	12	0	0	2	12	3	18
Free State	7	1	14	0	0	1	14	1	14
Gauteng	68	8	12	1	1	8	12	12	18
KwaZulu-Natal	23	5	22	0	0	5	22	6	26
Limpopo	10	3	30	1	10	3	30	6	60
Mpumalanga	10	2	20	0	0	2	20	3	30
Northern Cape	1	1	100	0	0	1	100	1	100
North West	6	0	0	1	17	0	0	1	17
Western Cape	38	3	8	0	0	3	8	6	16
South Africa	**180**	**25**	**14**	**2**	**1**	**25**	**14**	**39**	**22**

All serotypes included in each of the categories: 7-valent serotypes*: 4, 6B, 9V, 14, 18C, 19F, 23F
10-valent serotypes**: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
13-valent serotypes***: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A
Cross-protection with 6B has been demonstrated

Table 10. Number and percentage of invasive pneumococcal cases reported amongst adults and children >5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2019, n=1998 (n=1194 with viable isolates).

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes**		13-valent serotypes***	
		n	%	n	%	n	%	n	%
Eastern Cape	158	20	13	1	1	26	16	45	28
Free State	39	7	18	0	0	7	18	12	31
Gauteng	335	45	13	8	2	50	15	94	28
KwaZulu-Natal	62	9	15	1	2	10	16	17	27
Limpopo	36	1	3	0	0	1	3	8	22
Mpumalanga	52	7	13	3	6	7	13	19	37
Northern Cape	53	8	15	0	0	10	19	22	42
North West	17	2	12	1	6	2	12	6	35
Western Cape	442	48	11	3	1	57	13	134	30
South Africa	**1194**	**147**	**12**	**17**	**1**	**170**	**14**	**357**	**30**

All serotypes included in each of the categories: 7-valent serotypes*: 4, 6B, 9V, 14, 18C, 19F, 23F
10-valent serotypes**: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
13-valent serotypes***: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A
Cross-protection with 6B has been demonstrated

Eighty-three percent (745/893) of IPD patients presenting to ESS had clinical information available. Patients were admitted for a median hospital stay of 7 days (interquartile range (IQR) 3-13) and most deaths occurred within 2 days of admission (IQR 1-6). Overall case fatality was 33% (246/744). HIV-infection was present in 66% (407/616) of IPD patients; and 47% (27/58) of infants with maternal HIV-status available were HIV-exposed

(10 HIV-infected, 14 HIV-uninfected and 3 HIV-status unknown). Forty-three percent (327/744) of patients had a condition/risk factor (excluding HIV-infection) predisposing them to IPD. The top three factors included: history of smoking (102 patients), diabetes (41 patients) and chronic lung disease (38 patients).

Of 180 patients at ESS with pneumococcus on CSF, 41% (73/180) died during their hospitalization, and 30% (32/107) who survived to discharge suffered at least one sequelae – these included new onset seizures (11), limb weakness/paralysis (9), hydrocephalus (4), hearing loss (4), visual loss (3) and necrotic skin lesions (1). Eighteen episodes of IPD caused by serotypes present in the PCV13 vaccine occurred in children <10 years-of-age at ESS. Vaccine history was available for 67% (12/18) of these children. Seventeen percent (2/12) were too young to receive vaccine; 25% (3/12) of children eligible to receive vaccine had not received any PCV doses; 25% (3/12) had received all 3 doses of PCV; one child had received two doses; and 25% (3/12) had only received one dose of PCV at 6 weeks of age. The serotypes responsible for disease in those who had received any PCV13 included serotypes 19F (3 episodes), 6A (2 episodes), 14 and 6B (one each).

Discussion

IPD incidence has remained stable over the past 5 years across all age categories. Infants still have the highest disease incidence, with disease peaking again after age 25 years. Penicillin and ceftriaxone susceptibility of IPD isolates remained unchanged from 2018. HIV-infection, infant HIV-exposure and history of smoking remained important risk factors for IPD. Pneumococcal disease has a high mortality and high rate of sequelae following infection. Residual disease in children aged <5 years is largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurs in children who have not received adequate doses of PCV13. Serotypes causing IPD in those aged >5 years remain diverse including both vaccine and non-vaccine serotypes. Clinicians should ensure that all children (and adults with risk factors for IPD) receive adequate PCV doses to protect them from this serious illness.

Group A *Streptococcus* (*Streptococcus pyogenes*)

Results

Thirty-four percent (363/1060) of isolates meeting the GERMS-SA case definition for laboratory confirmed invasive Group A Streptococcus (GAS) were sent to the reference laboratory for further characterisation – these cases included isolates from skin and soft tissue infections thought to be causing systemic illness. Incidence of invasive GAS was highest in infants (6.4 per 100 000) with a second peak in those aged >64 years (3 per 100 000) (Figure 10). Most cases were reported from the Western Cape Province (n=466, 44%), followed by Gauteng (208, 20%), KwaZulu Natal (173, 16%) and Eastern Cape (159, 15%) provinces. More invasive GAS disease occurred in males (551/1041, 52%) than females. Forty-six percent (478/1045) of cases were identified on blood culture, followed by 41% (426/1045) from skin and soft tissue specimens (Table 11). Of those isolates available for antimicrobial susceptibility testing, 97% (338/348) were susceptible to penicillin (MIC<0.06µg/ml) and 95% (331/348) were susceptible to erythromycin (MIC<0.25µg/ml) (Table 12).

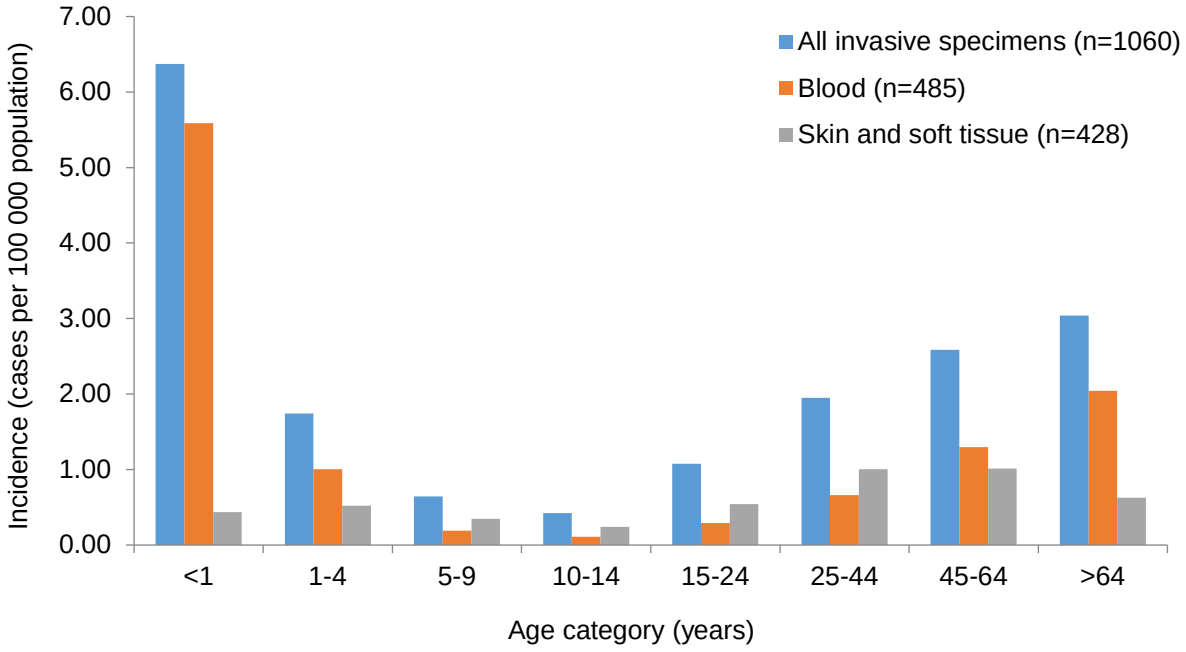

Figure 10. Age-specific incidence rates* for laboratory-confirmed, invasive Group A Streptococcal disease, reported to GERMS-SA, South Africa, 2019, n=1060.
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Table 11. Number and percentage of cases of invasive Group A Streptococcal disease reported to GERMS-SA by specimen type and age category, South Africa, 2019, n=1060 (age unknown for n=15).

Site of specimen	Age <5 years		Age ≥5 years	
	n	%	n	%
Cerebrospinal fluid/brain	7	5	8	1
Blood	110	72	368	41
Skin and soft tissue	29	19	397	45
Bone	4	3	72	8
Other*	3	2	47	5
Total	**153**		**892**	

*Other includes invasive specimens from respiratory, genitourinary and gastrointestinal tracts

Table 12. Number and percentage of penicillin and erythromycin susceptible and non-susceptible isolates from invasive Group A Streptococcal disease case reported to GERMS-SA, South Africa, 2019, n=1060.

Antimicrobial agent	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Penicillin	712	338	97	8	2	2	1
Erythromycin	712	331	95	1	0	16	5

*2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Discussion

Infants and the elderly experience the highest incidence of invasive GAS infections in South Africa. Of the isolates characterized, the majority were highly susceptible to the first line antimicrobial agents, penicillin and erythromycin. This was the first year of active surveillance for invasive GAS and clinical laboratories are encouraged to send all invasive GAS isolates meeting the case definition to the NICD so that further phenotypic and genotypic characterisation can be performed. In 2020, clinical data will be collected from persons with invasive GAS infections admitted to our enhanced surveillance sites and molecular typing of all the 2019 and 2020 isolates will commence.

Group B *Streptococcus* (*Streptococcus agalactiae*)

Results

One thousand and thirty-four cases of invasive Group B streptococcal infections (GBS) were reported through the GERMS-SA surveillance network, of which 347 (34%) isolates were received for further characterisation. Incidence for early onset GBS (<7days) was 0.34 per 1000 live births and 0.24 per 1000 live births for late onset (7-90 days) invasive disease (Table 13). Gauteng Province reported the highest incidence of early and late onset GBS (0.65 and 0.47 per 1000 live births), followed by the Western Cape Province (0.46 and 0.36 per 1000 live births) (Table 13). In infants, invasive GBS incidence was 60 per 100 000 population and decreased rapidly by month of age (Figure 11a). Whilst in persons >1 year of age, overall incidence of invasive GBS was 0.74 per 100 000, peaking in those >64 years of age (Figure 11b). In infants, most cases were isolated from blood (472/574, 82%) or cerebrospinal fluid (91/574, 16%) (Table 14). However, in persons >1 year of age blood (168/426, 39%) and soft tissue (162/426, 38%) specimens were most frequent (Table 14). Disease occurred more frequently in females (569/995, 56%) than males. Of the specimens available for serotyping, serotype III was the most predominant (166/321, 52%), followed by serotype Ia (78, 24%) (Table 15). Serotypes III and Ia were the most predominant serotypes causing invasive disease in early and late onset GBS (Figure 12). In persons >90 days of age, invasive GBS was caused by serotypes III, Ia, II and V (Figure 12). Ninety percent (283/316) of invasive GBS isolates were susceptible to penicillin (MIC<0.12mg/l) and 95% (296/313) were susceptible to gentamycin.

Table 13. Number of cases and incidence rates of invasive Group B Streptococcal disease reported to GERMS-SA by province and age category*, South Africa, 2019, n=1034**.

Province	Early onset (<7 days)		Late onset (7-90 days)		Age category ≥1 year	
	n	Incidence (per 1000 live births)	n	Incidence (per 1000 live births)	n	Incidence (per 100 000 population)
Eastern Cape	17	0.15	13	0.12	31	0.47
Free State	11	0.23	6	0.13	9	0.32
Gauteng	137	0.65	99	0.47	186	1.24
KwaZulu-Natal	74	0.37	43	0.21	78	0.70
Limpopo	12	0.09	11	0.09	12	0.20
Mpumalanga	17	0.21	12	0.15	8	0.18
Northern Cape	1	0.04	2	0.08	4	0.32
North West	5	0.09	5	0.09	2	0.05
Western Cape	46	0.46	36	0.36	96	1.42
South Africa	**320**	**0.34**	**227**	**0.24**	**426**	**0.74**

*N=27 cases in infants >90 days and less than one year excluded from above. **Age unknown for n=34.

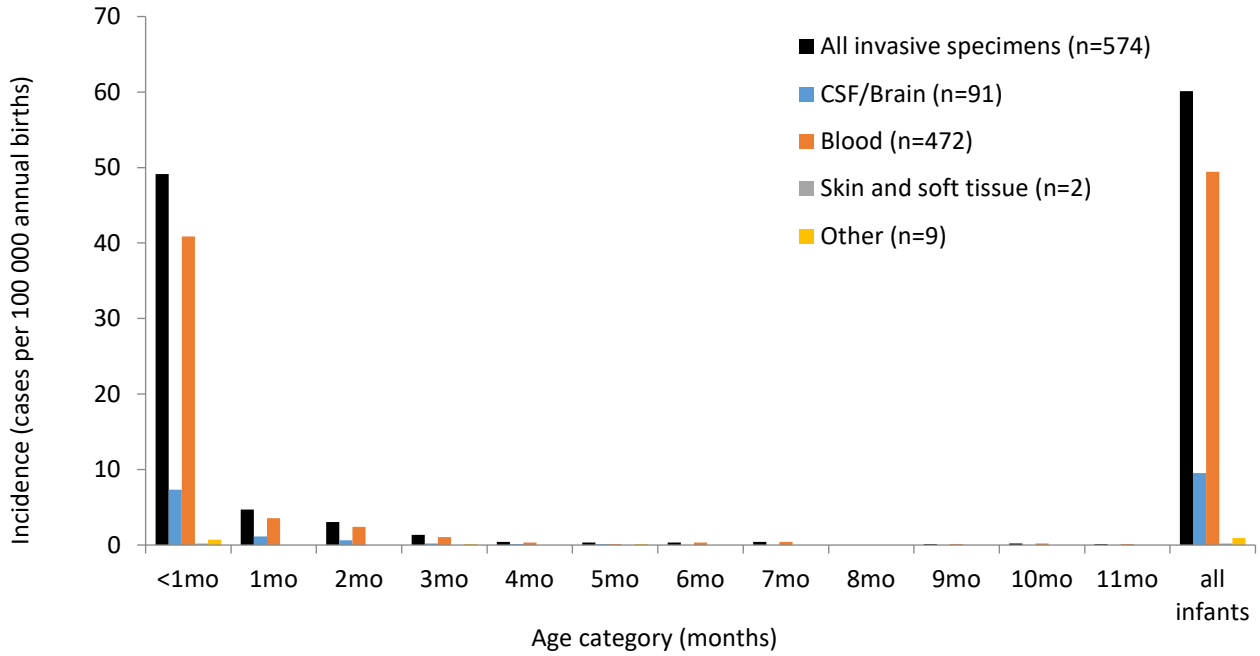

Figure 11a. Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in children <1 year of age, reported to GERMS-SA, South Africa, 2019, n=1034 (n=574 in children <1 year, age unknown for n=34).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

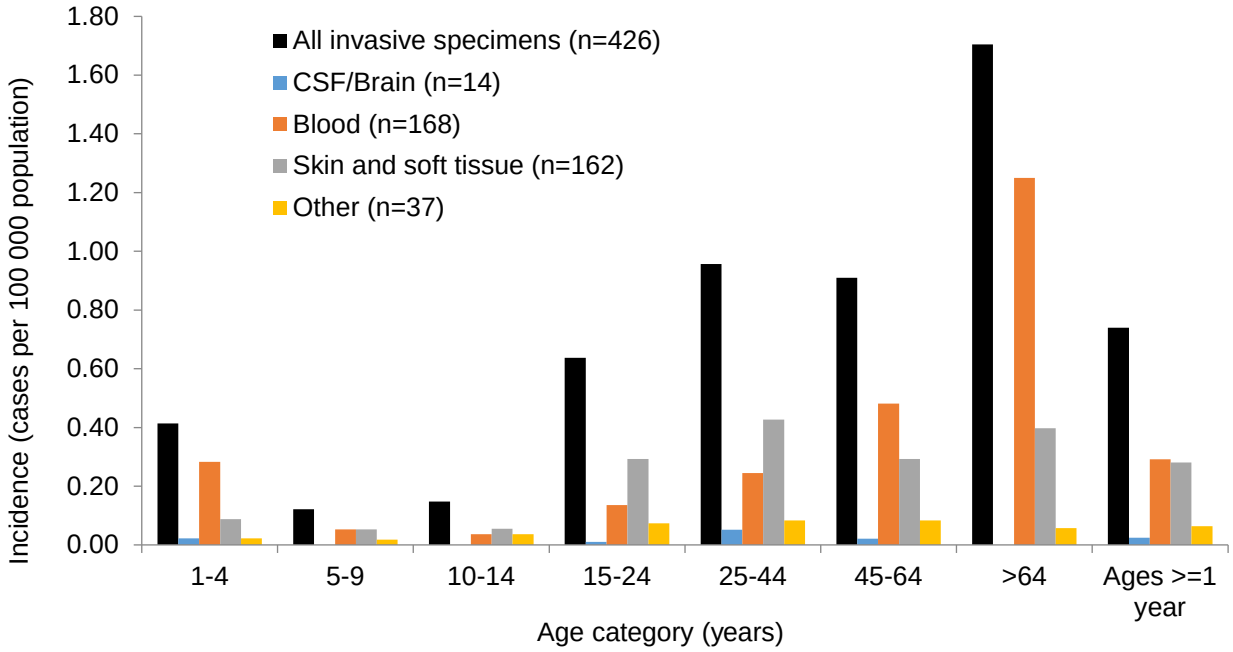

Figure 11b. Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in persons ≥1 year of age, reported to GERMS-SA, South Africa, 2019, n=1034 (n=426 in persons ≥1 year, age unknown for n=34).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Table 14. Number and percentage of cases of invasive Group B Streptococcal disease reported to GERMS-SA by specimen type and age category*, South Africa, 2019, n=1034.

Site of specimen	Age <1 year		Age ≥1 years	
	n	%	n	%
Cerebrospinal fluid/brain	91	16	14	3
Blood	472	82	168	39
Skin and soft tissue	9	2	162	38
Genitourinary	0	0	45	11
Other**	2	0	37	9
Total	**574**		**426**	

*Age unknown for n=34. **Other includes invasive specimens from bone, respiratory and gastrointestinal tracts.

Table 15. Serotype distribution of invasive Group B Streptococcal disease reported to GERMS-SA by province, South Africa, 2019, n=1034 (all ages).

Province	Total isolates available for serotyping	Ia		Ib		II		III		V	
		n	%	n	%	n	%	n	%	n	%
Eastern Cape	21	3	14	0	0	3	14	9	43	4	19
Free State	7	0	0	0	0	1	14	4	57	0	0
Gauteng	140	31	22	3	2	13	9	68	49	11	8
KwaZulu-Natal	34	12	35	1	3	1	3	16	47	2	6
Limpopo	16	0	0	1	6	2	13	11	69	0	0
Mpumalanga	12	2	17	0	0	2	17	7	58	1	8
Northern Cape	1	0	0	0	0	1	100	0	0	0	0
North West	2	0	0	0	0	0	0	0	0	1	50
Western Cape	111	30	27	7	6	9	8	51	46	9	8
South Africa	**321**	**78**	**24**	**12**	**4**	**32**	**10**	**166**	**52**	**28**	**9**

In addition, there was one mixed III/Ia isolate from Free State, one mixed III/V from Western Cape, and three non-typeable (one from Gauteng and two from KwaZulu Natal).

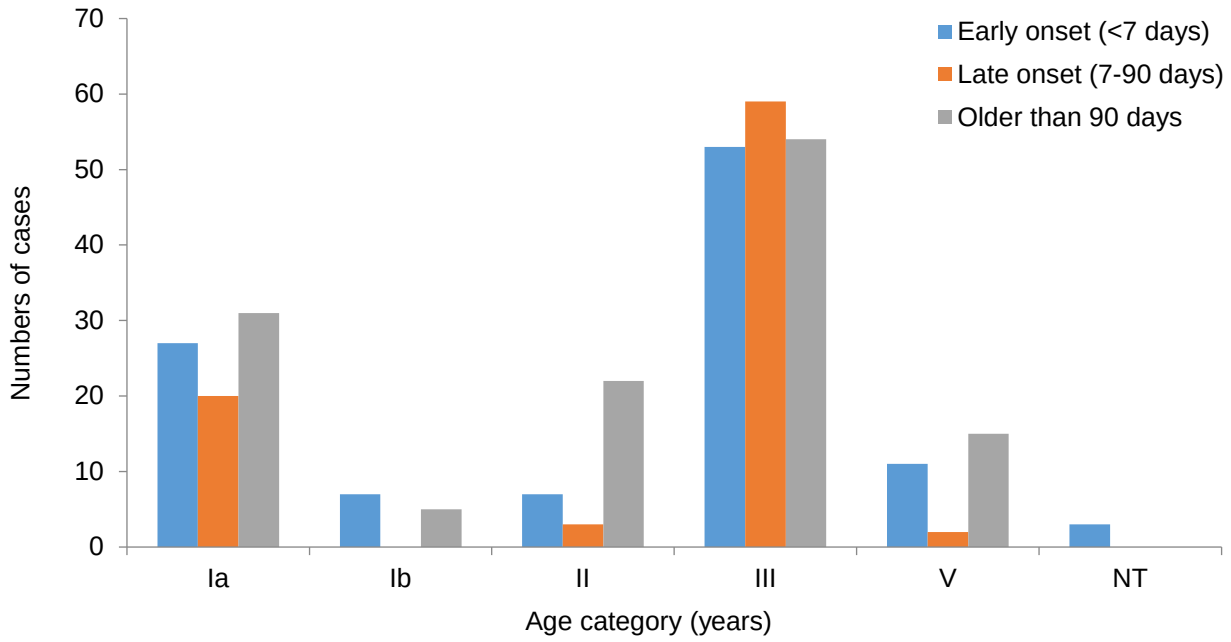

Figure 12. Numbers of cases of laboratory-confirmed, invasive Group B Streptococcal disease by serotype, reported to GERMS-SA, South Africa, 2019, n=1034 (isolates unavailable for 690 cases).

Discussion

Incidence of early and late onset invasive GBS appears low, however this may be due to decreased case ascertainment in many areas of South Africa. Most invasive GBS in infants was caused by serotypes III and Ia, although a range of serotypes was found to be causing invasive GBS in other age groups. This was the first year of active surveillance for invasive GBS and no clinical data was collected. Clinical laboratories are encouraged to send all GBS isolates meeting the GERMS case definition to the NICD so that further characterisation and serotyping can be done. In 2020, enhanced clinical surveillance will begin at selected sites in order to report on risk factors predisposing to invasive GBS and outcome following infection.

Conclusions

Incidence of invasive meningococcal and *Haemophilus influenzae* disease remained low for 2019, with rates of invasive pneumococcal disease being stable over the past 5 years. Infants have the highest rates of invasive meningococcal, *Haemophilus influenzae*, pneumococcal, GAS and GBS infections, despite routine vaccination programmes targeting pneumococcal and *Haemophilus influenzae* type b disease prevention in young children. There was a wide diversity of serogroups/serotypes of the different organisms circulating in South Africa, making targeting of residual disease difficult to achieve through limited vaccination options. Despite the low incidence of disease, in-hospital case-fatality remains high for invasive meningococcal, *Haemophilus influenzae* and pneumococcal disease, with high rates of sequelae amongst survivors. This highlights the importance of continued active surveillance of these infections and others such as Group A and B streptococcus in order to understand the disease burden and monitor serotype/serogroup diversity for future vaccine targets.

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References

1. GERMS-SA. GERMS-SA Annual Report, 2018. 2019; Available at: https://www.nicd.ac.za/wp-content/uploads/2019/11/GERMS-SA-AR-2018-Final.pdf.
2. Statistics South Africa. Midyear Population Estimate 2019. 2019. Available at: https://www.statssa.gov.za/publications/P0302/P03022019.pdf.
3. Statistics South Africa . Statistical Release: Recorded Live Births: South Africa 2019. 2019. Available at: https://www.statssa.gov.za/publications/P0305/P03052019.pdf.

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