ANNUAL MEASLES, RUBELLA AND CONGENITAL RUBELLA SURVEILLANCE REVIEW, SOUTH AFRICA, 2019

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Summary

In 2019, 4,608 febrile rash cases were recorded via active national surveillance systems. Of those tested for measles and rubella IgM antibodies, 65 (1.4%) were laboratory-confirmed measles cases, 1,496 (33.2%) were laboratory-confirmed rubella cases, and 44 (1.0%) were dual measles and rubella cases. There were four laboratory confirmed congenital rubella cases.

Overall, the national measles incidence rate was comparable to that of 2018. Use of serology for case determination has limitations in South Africa, where rubella is endemic and rubella vaccine is not in use in public health programmes. Future use of throat swabs in addition to serology is therefore recommended.

Using a narrow case definition (excluding cases dual positive for measles and rubella IgM), South Africa met the pre-elimination target of less than one case per million (0.4 per million population). There is therefore optimism that measles elimination can be achieved in South Africa. To achieve elimination, a target date will need to be set and significant improvements in surveillance and vaccine coverage will be necessary to prevent sporadic cases or outbreaks.

Background

Measles is a highly infectious viral disease.¹ Infants and young children are at greatest risk from measles infections, with potential complications including pneumonia and encephalitis, as well as lifelong disabilities such as permanent brain damage, blindness or hearing loss.² In 2011, the World Health Organisation (WHO) African Region set a measles elimination goal for 2020. However, despite effective vaccination that resulted in a global drop in measles deaths between 2000 and 2011³, recent measles outbreaks have occurred worldwide, particularly in the Democratic Republic of the Congo, Liberia, Madagascar, and Somalia. In 2018, more than 140,000 people died from measles. The WHO estimated that 52,600 of these deaths occurred in Africa.²

Measles elimination is defined as the absence of endemic measles virus transmission in a region or other defined geographical area for more than 12 months in the presence of a wellperforming surveillance system.⁴ To meet this goal, vaccine coverage needs to be 95% or higher, with two doses administered per person. However, over the past decade completion of the primary series of infant vaccines in sub-Saharan Africa has stalled at approximately 72%⁵, exposing populations to vaccine-preventable diseases and outbreaks. In South Africa, vaccination coverage also plateaued. Immunisation coverage of children under 1 year averaged 71.7%, whilst measles 2nd dose coverage averaged 68.8% over the period 2012 to 2017.⁶ In 2018, the national measles 2nd dose coverage was 76.4%, and at the provincial level only two of nine provinces (Mpumalanga and Northern Cape) exceeded the coverage target of 87% for measles 2nd dose coverage.⁶ South Africa has consistently experienced several measles outbreaks over the last decade.^{7,8}

In South Africa, the measles vaccine is available in single (Measbio[®]) or in combination format i.e. measles-mumps-rubella (MMR, Trimovax[®] or Priorix[®]) or measles-mumps-rubella-varicella (MMRV, Priorix Tetra[®]). Currently, the South African Expanded Programme on Immunization (SA-EPI) offers the MeasBio[®] vaccine to infants within the public health sector at 6 months and again at 12 months of age. A rubella containing vaccine (RCV) is not yet part of the SA-EPI, but can be obtained within the private health sector as MMR administered at 6 months and again at 12 months.

Rubella is generally a mild infection caused by the rubella virus.⁹ Complications of rubella are rare and generally occur more often in adults than in children. The most serious complication of rubella infection is congenital rubella syndrome (CRS), which occurs when the virus is transmitted transplacentally during pregnancy.^{10,11} Infection within the first trimester is teratogenic and can lead to miscarriage, foetal death, stillbirth, or serious birth defects. Historically, the omission of a rubella vaccine from the SA-EPI was based on the understanding that that natural rubella infection during childhood should render most women of childbearing age immune, thereby preventing CRS. Under conditions of imperfect vaccine coverage, the addition of a RCV could increase the susceptibility of adult women by slowing, not interrupting, rubella transmission.¹² This paradoxical increase has been attributed to the overall decrease in childhood rubella such that the age of primary rubella infection shifts to adolescence or adulthood, thus increasing the number of CRS cases.¹²⁻¹⁵

This report summarises the results of the South African measles and rubella surveillance programme for the period 1 January to 31 December 2019. We review the measles incidence in terms of reaching the African 2020 measles elimination goal of less than one measles confirmed case per million population.

Methods

Measles is a category 1 notifiable medical condition (NMC) in South Africa and, as such, health care workers in the public and private health sectors are required to report any suspected measles case to the National Department of Health (NDoH) within 24 hours. Additionally, suspected cases must have a blood sample taken for confirmatory testing at the Centre for Vaccines and Immunology, National Institute for Communicable Diseases (NICD). Private laboratories that test for measles are therefore requested to send all positive measles samples to the NICD for confirmatory testing and inclusion in the national database.

Unlike measles, rubella is a category 3 NMC, to be notified through a written or electronic notification to the NDoH within 7 days of diagnosis by private and public health laboratories. Rubella does not require confirmatory testing at the NICD. The rubella surveillance data presented here are from samples tested at the NICD only.

Sample collection and laboratory testing

Serum samples were tested using commercial enzyme-linked immunosorbent assay (ELISA) kits for anti-measles and anti-rubella IgM antibodies (Euroimmun, Luebeck, Germany) according to the manufacturer's instructions. A second sample was requested for repeat testing on all those with measles IgM equivocal results. Sera that tested positive and/or equivocal for measles IgM were assayed for the presence of measles virus by real-time reverse transcription (RT)-PCR amplification and, where possible, selected for genotyping. Of note, sera are suboptimal samples for measles detection by RT-PCR. Throat swabs are ideal but are not routine.

Based on the measles serology and/or PCR result, each suspected case was provisionally classified as measles IgM positive, measles PCR positive, measles compatible or epidemiologically linked. Each case was thereafter classified as either discarded, compatible or confirmed (Table 1) on review of case information. The definition of a measles outbreak is considered as three confirmed cases within one district within one month.

Final measles	Comment						
classification							
1. Discarded	Case did not meet the clinical or laboratory definition						
I. Distalueu	(IgM negative, vaccine associated, or had vaccine strain present)						
	Case met the clinical case definition, was not epidemiologically						
2. Compatible	linked, but no blood specimen was received, or blood specimen						
	was equivocal						
	Case was laboratory-confirmed (IgM positive and/or PCR						
	positive and/or epidemiologically-linked)						
3. Confirmed	- Narrow case definition: excludes those with rubella IgM						
	positive result						
	 Wide case definition: regardless of rubella IgM result 						

Table 1. Final classifications for laboratory-confirmed measles cases in South Africa.

IgM: Immunoglobulin M; PCR: polymerase chain reaction)

Congenital rubella syndrome surveillance

Congenital rubella syndrome sentinel-site surveillance was established in 2015 at 28 clinical sites and 6 laboratories.¹⁶ Paediatricians, neonatologists, paediatric infectious disease specialists and the virology departments of the National Health Laboratory Service (NHLS) were

requested to share information on any laboratory-confirmed CRS cases on a monthly basis. The CRS case definition included any positive rubella result in patients aged \leq 12 months who presented with cataract, congenital glaucoma, congenital heart disease, hearing impairment, pigmentary retinopathy, purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, or radiolucent bone disease.¹⁶

Notifiable medical conditions system

In 2017, a web- and mobile-based NMC notification (app) system was launched to provide for the collection, collation, analysis, interpretation and dissemination of health/disease surveillance information in South Africa. For this report NMC cases received over the period 1 January to 31 December 2019 were included in the analysis, with specific attention paid to suspected cases without samples for confirmatory testing.

Data analysis

Descriptive analyses were performed using Excel 2016. Results were reported as frequencies for categorical variables or as median values with ranges for continuous variables. Where date of rash onset was not available, date of sample collection was used.

Results

A total of 4,608 febrile rash-based samples was received between 1 January and 31 December 2019 (Figure 1). A total of 4,500 (97.7%) samples was tested for measles and rubella IgM antibodies, whilst the remaining 108 (2.3%) were rejected either due to insufficient sample volume or inappropriate sample type. For measles, 69 (2.5%) were IgM positive, 4,308 (95.9%) were IgM negative and 114 (2.5%) were IgM equivocal. For rubella, 1,496 (33.2%) were IgM positive, 2,643 (58.7%) were IgM negative and 361 (8.0%) were IgM equivocal. Of note, 44 (0.98%) samples were dual positive for measles and rubella IgM antibodies. Of the samples tested, 95.4% of results were reported within seven days of receipt in the laboratory, exceeding the target of 80% within 7 days.

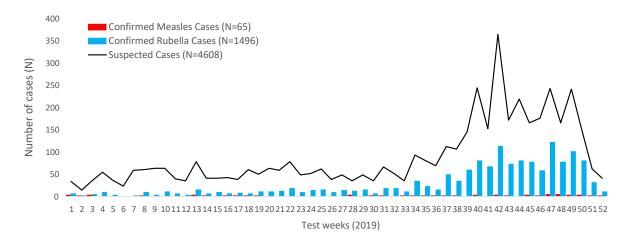


Figure 1. The number of suspected cases (N=4,608) from febrile rash surveillance in South Africa, with corresponding laboratory-confirmed measles (N=65) and rubella cases (N=1,496) for the period 1 January to 31 December, 2019.

Circulating measles

Of those that were measles IgM positive and/or PCR-positive, 65 cases were classified as confirmed, two were denotified, nine were discarded and one was left pending receipt of case investigation reports by the end of 31 January 2020. Of the discarded cases, six (66.7%) were classified as vaccine-associated after epidemiological investigation, and the remaining cases failed to meet the clinically compatible measles case definition. Of the confirmed measles cases, 64.6% (42 of 65) had dual rubella positive IgM results. Although rubella was the more likely diagnosis based on higher incidence, we did not use the rubella IgM result to discard measles IgM positive cases as dual infection is not impossible. For the purposes of this report, we refer to confirmed measles cases as either single positive measles samples (narrow case definition) or single and dual positive rubella samples (wide case definition).

Using the wide case definition, there were 65 laboratory-confirmed measles cases which occurred throughout the year, and were detected in eight of nine provinces (Figure 2), of which the Western Cape (N=14, 21.5%) and Gauteng (N=13, 20.0%) provinces had the highest disease burden. Measles case numbers were higher in females compared to males (60.3% vs. 39.7%, respectively). Measles cases occurred predominantly in the 1 - 4 year old age group, accounting for 30.8% of the total measles cases (Figure 3A). However, when comparing age distribution of laboratory-confirmed measles cases without rubella infection (Figure 3B), both the 1 - 4 and 20 - 44 year old age groups were equally affected (21.7%). When stratifying according to age

group and population figures as defined by Statistics South Africa¹⁷, the 0 - 4 year old age group had the highest measles incidence rate compared to the other age groups (Table 2).

Of the measles IgM-equivocal cases (N=114), five (4.4%) tested positive for measles RNA and were classified as confirmed measles cases, 33 (28.9%) met the clinical case definition and were classified as compatible, and the remaining 76 (52.8%) did not meet the clinical case definition and were discarded. Compatible measles cases were mostly identified in the Western Cape (N=12, 36.4%) and KwaZulu-Natal (N=9, 27.3%) provinces, and were predominant in the 5 - 9 year old age group (N=16, 48.5%). Of note, 19 (57.6%) of the compatible measles cases were also positive for rubella, suggesting that despite best efforts to classify the measles equivocal cases, a proportion were likely not true measles, although that possibility cannot be excluded. Other concomitant rash illnesses may cause elevated IgM antibody levels leading to false positive measles serology.

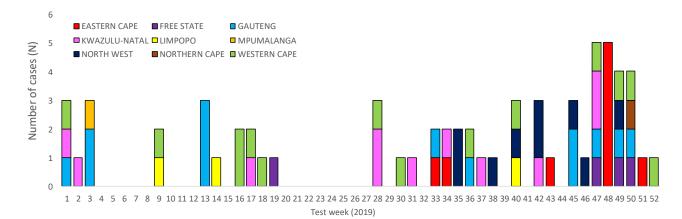


Figure 2. Provincial distribution of laboratory-confirmed measles cases in South Africa for the period 1 January to 31 December 2019 (N=65).

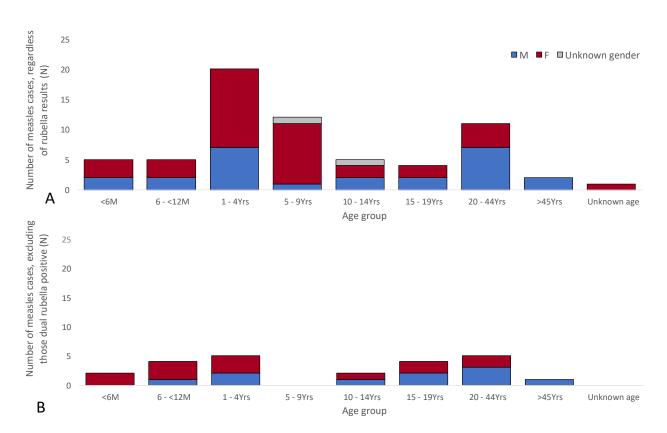


Figure 3A. Age and gender distribution of laboratory-confirmed measles cases, including samples dual-positive for rubella (wide case definition, males N=25; females N=38; unknown gender N=2). **B**. Age and gender distribution of laboratory-confirmed measles cases after the exclusion of dual-positive rubella cases (narrow case definition; males N=10; females N=13) in South Africa for the period 1 January to 31 December 2019.

Age group (years)	Confirmed Measles cases (wide case definition)	Confirmed Measles cases (narrow case definition)	Confirmed rubella cases	Total population	Confirmed Measles cases (wide case definition) per 1,000,000	Confirmed Measles cases (narrow case definition) per 1,000,000	Confirmed rubella case incidence per 1,000,000
0-4	30	11	594	5,733,946	5.23	1.92	103.59
5 – 9	12	0	718	5,737,439	2.09	0.00	125.14
10 - 14	5	2	102	5,427,902	0.92	0.37	18.79
15 – 19	4	4	15	4,660,002	0.86	0.86	3.22
20 – 44	11	5	39	24,137,303	0.46	0.21	1.62
> 45	2	1	6	13,078,429	0.15	0.08	0.46
unknown	1	0	22	-	-	-	-
Total	65	23	1,496	58,775,021	1.11	0.39	25.45

Table 2. Measles and rubella incidence rate per million by age group in South Africa for the period 1 January to 31 December 2019.

Total population figures by age group are 2019 mid-year population estimates supplied by Statistics South Africa¹⁷

Measles cases notified through the NMC system

A total of 882 cases was notified through the national NMC system. Of the 796 (90.2%) cases with blood samples that were received for testing at the NICD, 86 (9.8%) were without a blood sample and classified as compatible based on signs and symptoms (N=22, 25.6%), or discarded due to incomplete case information (N=64, 74.4%).

Measles/rubella clusters

Three measles clusters were investigated in 2019. However, on subsequent review two of these were reclassified as rubella clusters, highlighting the complexities of serological measles surveillance in an area with high rubella prevalence.

The first cluster was reported in April in the City of Cape Town, Western Cape Province. Four cases were unvaccinated siblings aged 12, 14, 17 and 19 years who had recently travelled to Georgia. Three tested positive for measles IgM (one also tested measles PCR positive) and one was IgM negative, likely in the incubation period. Outbreak response measures were implemented and contacts were vaccinated. As these cases were related and no additional cases were found in the district, it is likely that these cases were imported.

The second cluster was detected in October in the Bojanala Platinum district, Rustenburg, North West Province (Figure 5). Four cases tested IgM positive for measles infection. The North West Provincial Department of Health initiated localised vaccination response activities. Of note, all four had dual rubella infection, 2 (50%) had received the two doses of measles vaccine, and none had any travel history. On review, this cluster was considered to be due to rubella.

The third cluster occurred in November in the Sarah Baartman district, Eastern Cape Province. Seven cases with febrile rash were investigated for suspected measles infection, of which three tested dual positive for measles and rubella IgM. Two of the three cases were up-to-date with their measles vaccination, and one had unknown vaccination status. The cases were investigated and contacts vaccinated for measles. A local mass vaccination campaign was conducted with 731 children aged <5 years old being vaccinated. On review by the National Advisory Group on Immunisation, this cluster was determined as likely due to rubella.

Circulating rubella

Of 4,500 samples tested for rubella, 1,496 (33.2%) were laboratory-confirmed rubella cases, with North West (N=332, 22.2%) and Western Cape (N=278, 18.6%) provinces having the highest burden of disease (Figure 4A). Rubella was similarly distributed amongst males (N=695, 47.9%) and females (N=757, 52.1%) and was predominant in the 1 - 4 and 5 - 9 year old age groups (Figure 4B). Of females with rubella, 4.2% (32 of 757) were aged between 15 - 44 years old, comparable to the figures reported in 2018 (4.1%, 24 of 579). As rubella vaccination is not part of the expanded programme on immunisation in South Africa, rubella circulates widely and rubella clusters are not routinely investigated unless occurring within a particular institution.

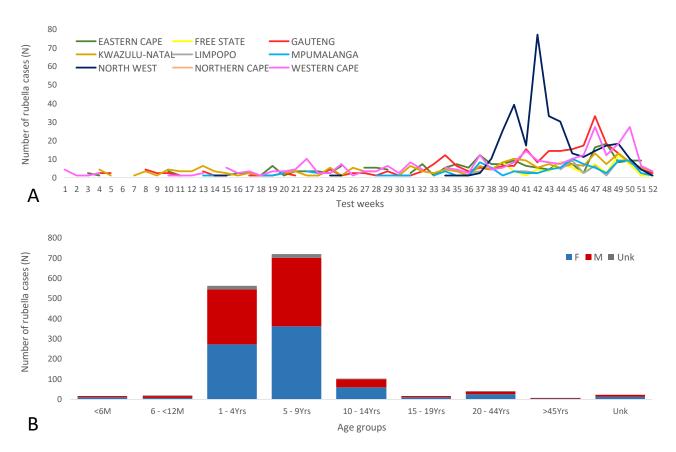


Figure 4. Provincial distribution (**A**), age and gender distribution (**B**) of laboratory-confirmed rubella cases in South Africa for the period 1 January to 31 December 2019 (N=1,496; males, N=695; females, N=757; unknown, N=44).

Notably in the North West Province, and specifically in the Bojanala Platinum district (Figure 5A), an outbreak of rubella was detected, beginning at the end September (weeks 39 to week 44). Rubella incidence was highest in the 5 - 9 year old age group, amounting to 56% of the total rubella infections (Figure 5B). There were more females than males with rubella (54% vs. 46%, respectively), and of the females with rubella, 1.2% (2 of 165) were aged between 15 - 44 years old. Moreover, due to investigation of a possible measles outbreak at the time, there was enhanced case-finding that may have contributed to the higher rubella numbers.

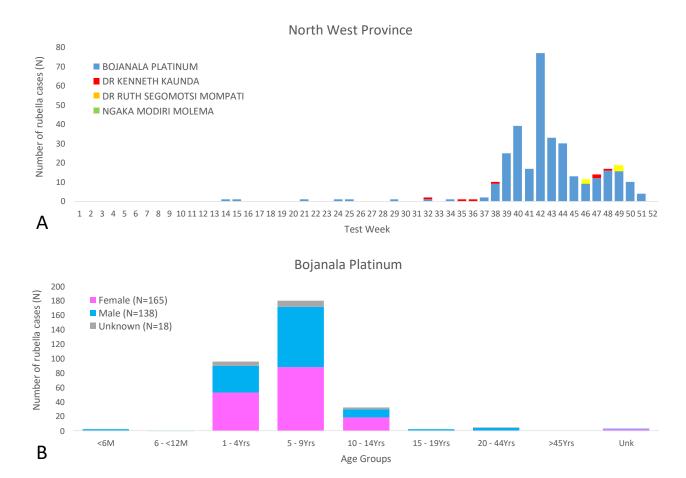


Figure 5A: Epidemic curve showing rubella distribution in the North West Province, South Africa, by district for the period 1 January to 31 December 2019 (N=332). **Figure 5B**. Age and gender distribution of rubella cases in the Bojanala Platinum district (N=321; males, N=139; females, N=165; unknown, N=18).

More than half of all measles and rubella cases had a case investigation form as well as a unique epidemiological (EPID) number (Table 3). In approximately half of measles cases, vaccination status was not recorded. Using the narrow case definition (measles positive serology only), 8.7% (2 of 23) were too young to have received their first measles vaccine (i.e. <6 months of age). Using the narrow case definition, 18 of 23 (78.3%) had not been vaccinated or had unknown vaccine status compared to 21 of 42 (50.0%) using the wide case definition (dual positive serology), suggesting that many of the dual positive cases likely did not have measles.

Measles genotyping and cluster detection

A total of 165 specimens (eight throat swab, one urine, one CSF and 155 sera) were tested for measles RNA using RT-PCR. Fourteen (8.54%) were positive for the presence of measles virus, three of which had the D8 genotype. The remainder had insufficient material for genotyping. Of these three cases, two had a European travel history (one travelled to Georgia and the other to Germany, Italy and France), and the third refused to meet with the outbreak response team, thus travel history could not be obtained.

Congenital rubella syndrome (CRS) surveillance

In 2019, responses to monthly e-mails sent to clinicians at study sentinel sites varied from 11% to 30%. Overall, there were four laboratory-confirmed CRS cases reported, two via the NMC system and two from sentinel site surveillance. This was less than the number reported in 2018 (N=5). Clinical information regarding infant's birthplace, gender, signs and symptoms as well as maternal information remains unknown.

Field and laboratory surveillance indicators for suspected rash cases

In 2019, the national detection rate for non-measles and non-rubella febrile rash illness was 4.41 per 100,000 population (Table 4). Eight of nine provinces exceeded the WHO target of detecting at least two non-measles, non-rubella febrile rash cases per 100,000 population. The detection rate in Limpopo province was 1.6 per 100,000. Overall, the surveillance system was sensitive to detect, notify and investigate suspected measles cases. Regarding the incidence rate for confirmed measles cases, using the wide case definition, the national target of less than one measles case per million population was not met. Specifically, four provinces (Eastern Cape, Free State, North West and Western Cape) had a measles incidence rate above 1 case per million population. However, a review of the measles cases using the narrow case definition (excluding those with concomitant rubella infection), shows that the measles incidence rate was less than 0.4 per million population.

Category	Measles single positive (narrow case definition) N=23	Measles dual positive (wide case definition) N=42	Rubella positive N=1,496	Discarded cases (non- measles, non- rubella N=2,591	Total laboratory cases N=4,608
Case investigation form (CIE)	12	26	862	1293	2397
Case investigation form (CIF)	(52.2%)	(61.9%)	(57.6%)	(49.9%)	(52.0%)
Epidemiological (EPID) number	19	28	1185	2155	3721
	(82.6%)	(66.7%)	(79.2%)	(83.2%)	(80.8%)
Cases with a CIF & EPID number	9	21	790	1200	2207
	(39.1%)	(50.0%)	(52.8%)	(46.3%)	(47.9%)
Measles vaccination status					
Too young (<6months)	2	3	15	87	112
	(8.7%)	(7.1%)	(1.0%)	(3.4%)	(2.4%)
Blank	13	18	831	1729	2882
DIGIIK	(56.5%)	(42.9%)	(55.5%)	(66.7%)	(62.5%)
No	3	0	9	31	50
NO	(13.0%)	-	(0.6%)	(1.2%)	(1.1%)
Yes	5	21	641	744	1564
165	(21.7%)	(50.0%)	(42.8%)	(28.7%)	(33.9%)
Measles vaccine doses					
1	1	2	33	111	162
1	(20.0%)	(9.5%)	(5.1%)	(14.9%)	(10.4%)
2 or more	4	18	519	611	1361
	(80.0%)	(85.7%)	(92.2%)	(82.1%)	(87.0%)
Docado unknown	0	1	17	22	41
Dosage unknown	-	(4.8%)	(2.7%)	(3.0%)	(2.6%)

Table 3. Surveillance indicators for laboratory-confirmed measles, rubella and discarded casesin South Africa for the period 1 January to 31 December 2019.

Province	Measles single positive cases	Measles dual positive cases	Total measles cases	Non- measles non- rubella cases	Total population	Measles single positive cases	Measles dual positive cases	Total measles cases	Non- measles non-rubella cases
						II 1 00	Illness rate per 100 000 population		
ECP	0	9	9	227	6,712,277	0,00	1,34	1,34	3.38
FSP	1	3	4	104	2,887,466	0,35	1,04	1,39	3.60
GP	6	7	13	569	15,176,115	0,40	0,46	0,86	3.75
KZP	2	9	11	300	11,289,083	0,18	0,80	0,97	2.66
LPP	2	1	3	96	5,982,583	0,33	0,17	0,50	1.60
MP	1		1	213	4,592,185	0,22	0,00	0,22	4.64
NCP	0	1	1	94	1,263,874	0,00	0,79	0,79	7.44
NWP	2	7	9	664	4,027,160	0,50	1,74	2,23	16.49
WCP	9	5	14	324	6,844,272	1,31	0,73	2,05	4.73
South Africa	23	42	65	2591	58,775,015	0,39	0,71	1,11	4.41

 Table 4. Field surveillance adequacy by provinces, South Africa, January - December 2019.

Population estimates obtained from Statistics South Africa mid-year population estimates, 2019.¹⁷ For confirmed measles cases, green shading indicates good performance meeting the pre-elimination goal of less than 1 case per 1 000 000 population, and red indicates poor performance. For non-measles, non-rubella illness rate per 100 000, green shading indicates good performance meeting the WHO surveillance target of non-measles febrile rash illness rate of more than 2 per 100 000 population, and red indicates poor performance i.e. not meeting the surveillance target. ECP = Eastern Cape Province, FSP = Free State Province, GP = Gauteng Province, KZP = KwaZulu-Natal Province, LPP = Limpopo Province, MP = Mpumalanga Province, NCP = Northern Cape Province, NWP = North West Province, WCP = Western Cape Province.

Discussion

There were 65 confirmed measles cases in South Africa in 2019. However, 23 were single positive and 42 were dual positive cases, indicating the complexities of measles serological testing in areas of high concurrent rubella. Although two measles cases required hospital admission no complications or deaths were reported. Overall, despite the 2020 measles elimination goal for South Africa, sporadic cases of measles as well as clusters still occurred. Using the wide case definition (all measles positive by serology), the pre-elimination target of less than one case per million was not achieved. However, when reviewing the measles incidence rate using the narrow case definition (exclusion of cases with dual rubella positive serology) (Table 2), the incidence rate was less than 0.4 per million population, suggesting that the South African measles elimination goal may be achievable within the next few years. Moreover, given that confirmed and suspected measles clusters were promptly identified, the National Surveillance System performed well and provincial health workers were able to respond rapidly with investigation and vaccination.

Measles cases occurred largely in the 1 - 4 year old age group (34.0%), similar to cases reported in 2018 (44.9%). However, the second highest proportion in 2019 was amongst the 20 - 44 year old age group (16.0%), indicating pockets of young adults who remain susceptible to measles infection. When comparing the 2019 provincial distribution of measles single positive cases, Western Cape Province had the highest burden of 1.31 per million population. This is due to the confirmed measles cluster with a recent travel history.

Incorporation of the NMC measles cases into the annual measles review is a recent strength. The fact that 86 cases were reported to the NMC system without a laboratory specimen having been received for testing highlights logistic difficulties, emphasizing the need to improve sample transportation.

The rubella incidence rate increased from 21.3 per million in 2017 to 25.5 per million in 2019. Rubella was predominant in children aged less than 10 years old. Of female cases, 4.2% were of reproductive age, highlighting a significant rubella immunity gap in females of reproductive age, indicative of the growing need to implement a RCV into the SA-EPI. In addition, there were four laboratory CRS cases. Thus, RCV introduction needs to be carefully planned, coordinated and maintained with high coverage in order to avoid increasing rubella incidence in females of childbearing age.

Many areas of surveillance still require improvement. These include CIF completion, EPID number allocation and follow-up investigation reports. For example, on average, less than half of the suspected cases had a CIF and EPID number. From a review of the discarded cases, many did not have information on vaccination history. More than 80% of those with vaccination history reported receiving two vaccine doses, giving an indication of vaccine coverage in South Africa. Confirmation of coverage figures awaits results from the ongoing national vaccine coverage survey.¹⁸

Conclusion

In South Africa in 2019, there was one imported cluster of four measles cases and no outbreaks. Two clusters of febrile rash illness, in which more than three individuals had dual positive measles and rubella serology, highlighted the complexities of serological surveillance in an area with endemic rubella but low measles incidence. Using the narrow case definition (exclusion of dual positive rubella cases), the measles incidence was below the pre-elimination target of less than one case per million. While the African measles elimination goal of 2020 has lapsed, there is hope that measles elimination can be achieved in South Africa. Future inclusion of throat swabs for expansion of molecular testing for febrile rash surveillance is recommended. Four laboratory confirmed CRS cases emphasizes the need for introduction of rubella vaccination in the expanded programme on immunization, subject to sufficiently high vaccination coverage.

Acknowledgements

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References

- 1. Moss WJ. Measles. *Lancet* (London, England). 2017;390(10111):2490-502.
- WHO Joint News Release. More than 140,000 die from measles as cases surge worldwide. 2019. Available at: <u>https://www.who.int/news-room/detail/05-12-2019-</u> more-than-140-000-die-from-measles-as-cases-surge-worldwide
- 3. Progress in global control and regional elimination of measles, 2000-2011. Wkly Epidemiol Rec. 2013;88(3):29-36.
- 4. Masresha B, Luce R, Shibeshi M, Katsande R, Fall A, Okeibunor J, et al. Status of measles elimination in eleven countries with high routine immunisation coverage in the WHO African Region. *J Immunol Sci.* 2018;Suppl:140-4.
- Madhi SA, Rees H. Special focus on challenges and opportunities for the development and use of vaccines in Africa. *Human Vaccines & Immunotherapeutics*. 2018;14(10):2335-9.
- WHO Africa. Experts caution against stagnation of immunization coverage in Africa.
 2019. Availble at: <u>https://www.afro.who.int/news/experts-caution-against-stagnation-immunization-coverage-africa</u>
- Massyn N, Pillay Y, Padarath A, editors. District Health Barometer 2017/18. Durban: Health Systems Trust; 2019. Available at: <u>https://www.hst.org.za/publications/District%20Health%20Barometers/DHB+2017-18+Web+8+Apr+2019.pdf</u>
- Hong HA, Makhathini L, Mashele M, Malfeld S, Motsamai T, Sikhosana L, et al. Annual measles and rubella surveillance review, South Africa, 2017. Available at: <u>http://wwwnicdacza/wp-content/uploads/2018/09/Annual-measles-and-rubella-</u> <u>surveillance-review-South-Africa-2017pdf</u> 2018.

- 9. Ntshoe GM, McAnerney JM, Archer BN, Smit SB, Harris BN, Tempia S, et al. Measles outbreak in South Africa: epidemiology of laboratory-confirmed measles cases and assessment of intervention, 2009-2011. *PLoS One*. 2013;8(2):e55682.
- 10. Lambert N, Strebel P, Orenstein W, Icenogle J, Poland GA. Rubella. *Lancet* (London, England). 2015;385(9984):2297-307.
- Grant GB, Desai S, Dumolard L, Kretsinger K, Reef SE. Progress toward rubella and congenital rubella syndrome control and elimination - Worldwide, 2000-2018. MMWR Morb Mortal Wkly Rep. 2019;68(39):855-9.
- 12. Lee JY, Bowden DS. Rubella virus replication and links to teratogenicity. *Clin Microbiol Rev.* 2000;13(4):571-87.
- Panagiotopoulos T, Antoniadou I, Valassi-Adam E. Increase in congenital rubella occurrence after immunisation in Greece: retrospective survey and systematic review. *BMJ*. 1999;319(7223):1462-7.
- 14. Metcalf CJ, Cohen C, Lessler J, McAnerney JM, Ntshoe GM, Puren A, et al. Implications of spatially heterogeneous vaccination coverage for the risk of congenital rubella syndrome in South Africa. *J R Soc Interface*. 2013;10(78):20120756.
- 15. Cameron NA. When, and how, should we introduce a combination measles-mumpsrubella (MMR) vaccine into the national childhood expanded immunization programme in South Africa? *Vaccine*. 2012;30 Suppl 3:C58-60.
- 16. Schoub BD, Harris BN, McAnerney J, Blumberg L. Rubella in South Africa: An impending greek tragedy? *South African Med J.* 2009;99(7):515-9.
- 17. Motaze NV, Manamela J, Smit S, Rabie H, Harper K, duPlessis N, et al. Congenital rubella syndrome surveillance in South Africa using a sentinel site approach: a cross-sectional study. *Clin Infect Dis*. 2018.
- 18. Mid-year population estimates, 2019. Department of Statitics South Africa Stastistcal Release, P0302.
- 19. R J Burnett, Dlamini NR, Meyer JC, Mutevedzi P, Kibuuka DK, Mphahlele MJ, et al. South Africa's first national vaccination coverage survey since 1994. *South African Medical Journal*. 2019;109(5):289.