

SECOND EDITION COVID-19 COUNTRY REPORT

DRAFT CHAPTER NOVEMBER 2022

CHAPTER 5.1 HEALTH

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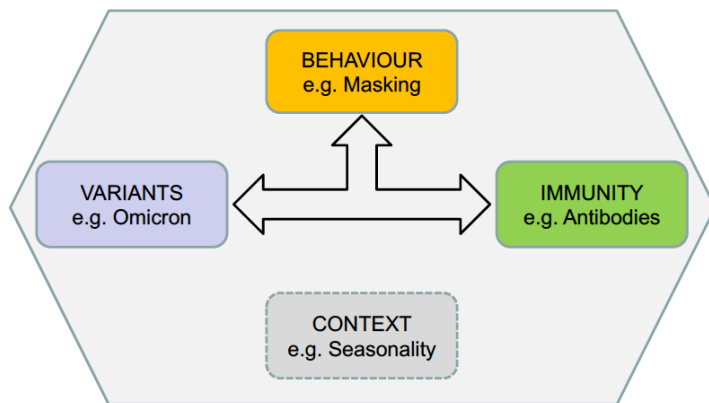
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Introduction

In this edition of the South African Covid-19 Report, the section on the health sector response to the Covid-19 pandemic extends on the work previously reported in the first edition of the Country Report, to now include developments beyond the second (Beta) wave of the Covid-19 Pandemic in South Africa. In this regard, we focus on Stage 8 of the South African response framework to Covid-19, Ongoing Vigilance (refer to previous edition). The 8th and final stage of the framework places emphasis on surveillance of new cases/waves, antibody levels and vaccine actions, and we include in this report surveillance of new variants, disease severity and socio-behavioural aspects of vaccine acceptance and hesitancy. The emergence of new variants in the reporting period for this edition imposed the most significant impact on the country's experience of the Covid-19 pandemic, particularly during the third (Delta) wave, and to some extent during the fourth (Omicron) wave. Vaccines for Covid-19 were by all accounts the most important intervention since their introduction by the health sector at the tail end of the second (Beta) wave of the pandemic. There was also recognition that increasing antibody levels in the population, from vaccine and/or infection immunity, contributed immensely to the reduction in the negative impact of Covid-19 in South Africa, observed increasingly from the fourth (Omicron) wave onwards. However, the role of socio-behaviour was also observed to greatly influence the response to the pandemic, mediated largely through masking, vaccine hesitancy, misinformation/disinformation and mandatory vaccination. Therefore, we can convey in this report that in a particular context, environment or period, we found that the severity of the subsequent

waves in South Africa were influenced predominantly by variants, immunity and behaviour, as shown below in Figure 1, and these aspects will emerge as common running themes in the rest of this chapter.



Surveillance

Testing and case-based surveillance

In March 2020, the National Institute for Communicable Diseases (NICD) established a surveillance system of SARS-CoV-2 tests and cases (Sila SAMJ 2022). They report daily and weekly on the numbers of SARS-CoV-2 tests conducted and percentage testing positive (NICD testing reports), and positive SARS-CoV-2 cases in South Africa (NICD weekly epidemiological reports), and were able to monitor trends in resurgences and the emergence of the five COVID-19 waves.

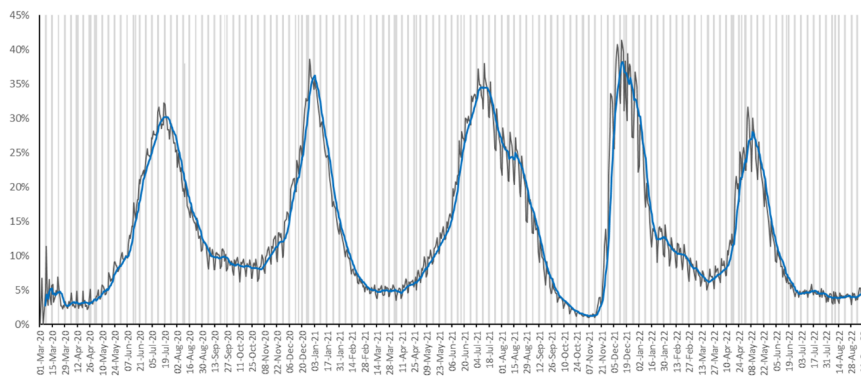


Figure 1: Percentage of PCR tests positive for SARS-CoV-2 by date of specimen collection, South Africa, 5 March 2020-17 September 2022

Blue line shows the 7-day moving average of the percentage testing positive.

Grey bars highlight weekend days and public holidays.

Modelling

The NICD and the DSI-NRF Centre of Excellence in Epidemiological Modelling and Analysis (SACEMA) analysed data on rT-PCR-confirmed COVID-19 cases, hospital admissions, and deaths to estimate the effective reproductive number (R) of SARS-CoV-2 over time in South Africa at the national and provincial levels (NICD/SACEMA reports). R is the average number of secondary cases per infectious case in a population composed of both susceptible and non-susceptible hosts (once the infectious agent is circulating). If $R > 1$, the number of new cases per time unit will increase, such as at the start of an epidemic. Where $R = 1$, the number of new cases is stable over time, and where $R < 1$, there will be a decline in the number of new cases per time unit.

The South African COVID-19 Modelling Consortium was established to project the spread of the disease to support policy and planning in South Africa. They produced reports on modelling the emergence of new waves (SACMC reports). They also reported on trends in re-infection (NICD re-infections reports, Pulliam 2021).

Genomic surveillance

The Network for Genomics Surveillance in South Africa (NGS-SA), which includes the National Institute for Communicable Diseases (NICD), KRISP at the University of KwaZulu-Natal (UKZN), University of Cape Town (UCT), Stellenbosch University (SUN), the University of the Free State (UFS), the University of Pretoria, the University of the Witwatersrand (WITS) and the National Health Laboratory Service (NHLS), continued to monitor and assess the evolution of SARS-CoV-2. They conducted sequencing of a sample of positive cases, reporting on the variants of concern that circulated in South Africa throughout the pandemic (NGS reports). The NGS reported on the emergence of the Beta and Omicron variants in South Africa.

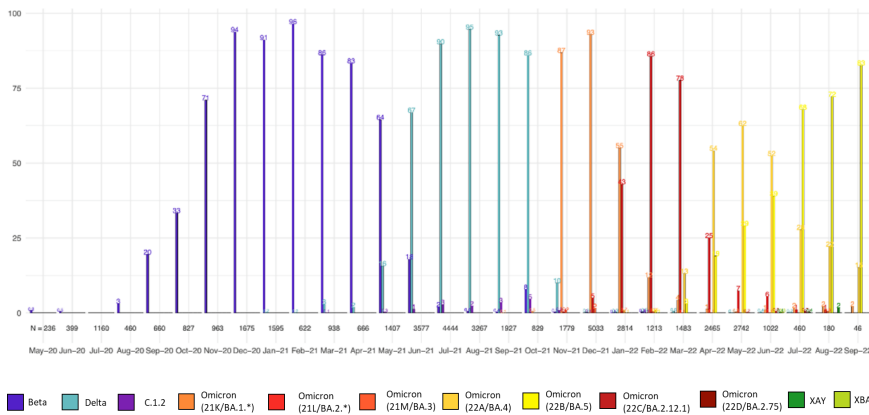


Figure 2: Detection rates of variants of concern being monitored, South Africa, May 2020-10 September 2022

Bars represent percentage prevalence of variant for the month; total number sequences collected for the month are given below the bar

Wastewater surveillance

SARS-CoV-2 is shed from symptomatic and asymptomatic persons and can be monitored in wastewater. A consortium of partners including the NICD Centre for Vaccines and Immunology, collected and interpreted findings from detection and quantification of SARS-CoV-2 levels by in influent (untreated) wastewater in 18 wastewater treatment plants (WWTP) across five provinces tested by the NICD, and 24 additional plants tested by SACCESS partners including the National Institute for Occupational Health, Lumegen Laboratories, Green Hill Laboratories and Precaution to cover all provinces. Levels of SARS-CoV-2 in wastewater correlated with population levels of SARS-CoV-2 over time and indicated the geographic distribution of disease (NICD Centre for Vaccines and Immunology reports). Variants of SARS-CoV-2 identified in wastewater through detection of single-nucleotide polymorphisms (SNPs) that are specific to each variant, were shown to correspond to variants prevalent in clinical cases, across time and place.

Hospital surveillance

The NICD established DATCOV, a hospital surveillance system for COVID-19 in March 2020. DATCOV was adopted by the National Department of Health (NDoH) as a national hospital surveillance system and by August 2022, received data from 408 public and 262 private hospitals in all nine provinces of

South Africa (NICD weekly hospitalisation reports). Analysis of DATCOV data revealed risk factors for in-hospital COVID-19 mortality included older age, male sex, Black, Coloured and Indian race, admission in the public sector and in certain provinces, as well as pre-existing comorbidities including hypertension, diabetes, chronic cardiac and renal disease, malignancy, HIV and TB (Jassat Lancet HIV 2021). Other DATCOV publications also reported increased mortality in the Beta-dominated second wave (Jassat Lancet Global Health 2021); decreased severity in the Omicron BA.1 dominated fourth wave (Jassat Lancet Global Health 2022); and decreased mortality in the Omicron BA.4/BA.5 dominated fifth wave (Jassat medrxiv 2022). Further analyses of DATCOV data revealed disparities related to race and socio-economic status in COVID-19 treatment and outcomes (Jassat SAJS 2022).

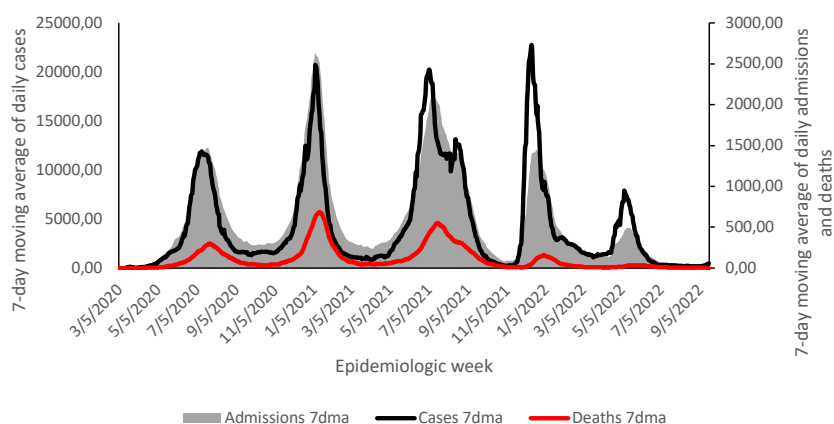


Figure 3: 7 day moving average (DMA) of SARS-CoV-2 cases, COVID-19 admissions and in-hospital deaths, South Africa, 5 March 2020-17 September 2022

Excess mortality

The South African Medical Research Council (SAMRC) reported on excess mortality during the COVID-19 pandemic. In the context of the emerging COVID-19 pandemic, it became essential to track the weekly number of deaths that occurred. Deaths recorded on the National Population Register were provided to the SAMRC on a weekly basis. The estimated numbers were compared with the number that would be expected based on the historical data from 2014-2019. While official reports placed the COVID-19 deaths by 5 September 2022 at just over 104,000, the MRC reported excess deaths of

328,506 during the same period, suggesting that the true toll of COVID-19 deaths was significantly higher than the reported deaths (SAMRC excess death reports).

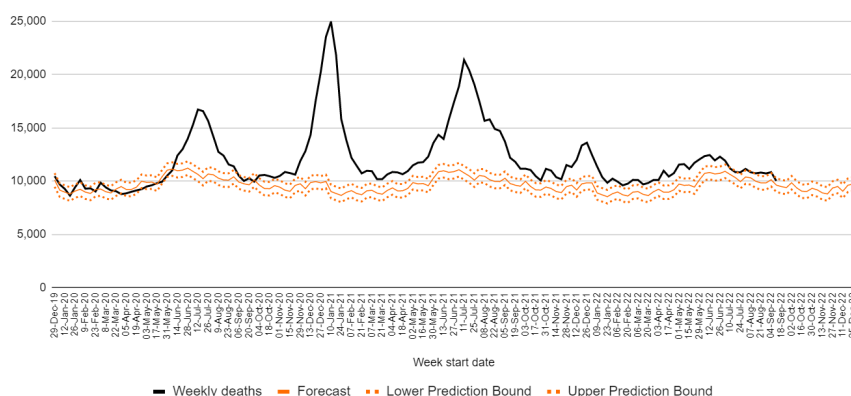


Figure 4: Number of weekly deaths from all causes, South Africa, 29 December 2019-17 September 2022

Serosurveys

A number of studies reported on seroprevalence of SARS-CoV-2 using antibody surveys in different communities at different timepoints in the pandemic. These sero-surveys suggested increasing population immunity with each successive wave, reaching over 90% after the Omicron BA.1 dominated fourth wave. The reduced mortality in the Omicron waves were presumed to be related to the high prevalence of humoral and cell-mediated immunity in South Africa, from prior infection and vaccination.

After the second (Beta) wave, SARS-CoV-2 antibody sero-prevalence estimates were 47% in blood donors in South Africa (SANBS, 2021). After the third (Delta) wave, seroprevalence was estimated at 71% in blood donors (Cable, 2021) and 73% in Gauteng (Madhi, 2022). After the fourth (Omicron BA.1/BA.2) wave, seroprevalence was estimated at 97% in blood donors (Bingham, 2022) and 91% in Gauteng (Madhi medrxiv, 2022). The latter serosurvey indicated that 61% of individuals had serological evidence of SARS-CoV-2 infection during the Omicron BA.1/BA.2 wave in South Africa (Madhi medrxiv, 2022).

A South African study demonstrated that prior infection whether symptomatic or not, provided durable protection against reinfection beyond a year and resulted in a complex immune landscape (Sun medrxiv, 2022).

Household cohort studies

The prospective household cohort study of SARS-CoV-2, influenza, and respiratory syncytial virus community burden, transmission dynamics, and viral interaction in South Africa (PHIRST-C) included households in Agincourt, Mpumalanga province (rural site) and Klerksdorp, North West province (urban site) from July, 2020 to August, 2021. They reported a high rate of SARS-CoV-2 infection, with most infections being asymptomatic in individuals of all ages (Cohen, 2022). Asymptomatic individuals transmitted SARS-CoV-2 at similar levels to symptomatic individuals, suggesting that interventions targeting symptomatic individuals such as symptom-based testing and contact tracing of individuals tested because they report symptoms might have limited effects as control measures. Increased household transmission of beta and delta variants was likely to have contributed to recurrent waves of SARS-CoV-2 infection, with more than 60% of individuals infected by the end of follow-up. Increased attack rates, reinfection, and acquisition in adolescents and prolonged SARS-CoV-2 shedding in people living with HIV who were not virally suppressed suggests that prioritised vaccination of individuals in these groups could affect community transmission.

Variant Consortium

A consortium was established in early 2021 to facilitate sharing of information and collaboration between South African researchers around the emergence and characteristics of new variants of concern (VOC). Chaired by AHRI, meetings are held weekly, or bi-weekly, attended by NICD, MRC, KRISP, Netcare, research and academic organisations. With the following working groups: (1) = Clinical/epi/modelling; (2) Diagnostics; (3) Virology; (4) Vaccines.

SARS-CoV-2 variants

Since the identification of the first mutations in the spike protein (S) of SARS-CoV-2 (the main target of vaccines against COVID-19) several variants of concern emerged. According to the World Health Organisation (WHO, 2022a) a SARS-CoV-2 strain is considered to be a variant of concern if it has at least one of the following changes: 1) Increase in transmissibility or detrimental change in COVID-19 epidemiology, 2) Increase in virulence or change in clinical disease presentation, and 3) Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics

These variants of concern are named according to their genetic lineages, but in order to facilitate public discussions of variants, an expert group convened by WHO has recommended using letters of the Greek alphabet as a more practical naming system. In the previous report the variants now designated as Alpha (B.1.1.7), Beta (B.1.351) and Gamma (P.1) were discussed. This report will therefore focus on variants Delta (B.1.617.2) and Omicron (B.1.1.529).

Delta (B.1.617.2)

During October 2020 a new variant (now named Delta) was identified in the state of Maharashtra, India. From there it quickly spread throughout the world, outcompeting existing circulating variants (Mlcochova et al., 2021). In South Africa, genomic data indicated that the occurrence of Delta increased from 14% in May 2021 to 49% in June 2021 (NICD 2021). During this time Gauteng had the highest incidence of this variant in South Africa.

Sequencing revealed that Delta has 23 new mutations compared to Alpha (Mohammadi et al. 2021). These mutations have been linked to the increased ability of Delta to bind to the ACE2 receptor (Starr et al., 2021), causing higher replication efficiency in host cells (Mlcochova et al., 2021). This variant also proved to be more transmissible than the Alpha variant, which could be attributed to its higher replication efficiency resulting in a decrease in the generation time of this variant (Hart et al., 2022). In addition, the mutations that allowed Delta to escape from immune cells (Shiehzadegan et al., 2021). This variant is also significantly less sensitive to neutralising antibodies from both previously infected individuals as well as from vaccination. However, the NICD still found that vaccines remained effective in preventing severe disease.

Omicron (B.1.1.529)

The B.1.1.529 variant (now named Omicron), with more than 50 mutations compared to the original SARS-CoV-2 virus isolated in Wuhan, China, was first reported to the World Health Organisation (WHO) from South Africa on 24 November 2021, from a specimen collected on 9 November 2021 (WHO, 2021). However, retrospective testing found earlier samples from individuals in England on 1 and 3 November, and in South Africa, Nigeria and the United States on 2 November (Mallapaty, 2022). By December 2022, this variant had spread around the world faster than any previous variant. It also replaced the Delta variant in South Africa from November 2021 (NGS-SA, 2022).

The replacement of the original Omicron variant could be explained by the ability of BA.4 and BA.5 to evade neutralizing antibodies generated by both prior infections by BA.1 (7.5-7.6 fold lower antibody

levels) as well as vaccination (2.6-3.6 fold lower antibody levels) as found in a preliminary study by Khan and co-workers (2022).

Severity of disease caused by Omicron in South Africa

One of the important aspects regarding Omicron in the light of its highly infectious nature and ability to evade the immune response, is the severity of disease it causes as this will contribute to the clinical outcome of infections. This is important in planning a public health response, including the allocation of resources and guiding clinical management.

Initial data suggested that, although Omicron is more transmissible than Delta, it may cause less severe disease (Ledford, 2021; Wolter et al., 2022; Wang et al. 2022). It was also found that Omicron preferentially infects the upper respiratory tract and therefore causes less infection and damage to the lungs (Hui et al. 2022).

In a study by the WHO (WHO, 2022), comparing 17 693 South African patients from the “Omicron period” and 16 749 patients from the “Delta period”, it was found that a lower percentage of Omicron patients had severe or critical disease, compared to Delta patients. Omicron also caused significantly fewer deaths among hospitalised patients than Delta. It must be noted that a confounding factor may be the statistically significant difference in the media age of the two patient groups (41 years for Omicron patients vs 52 years for Delta patients). However, the results of the multivariable regression model for severity of disease by variant adjusted for age (ordinal variable), sex, vaccination status (vaccinated/unknown or unvaccinated), public or private sector, comorbidities (none/one or more), ethnicity (nominal) and reinfection, clearly showed that Omicron was associated with a lower likelihood of developing severe or critical disease as well as in-hospital mortality than Delta.

In their report the WHO cautions that this data should not be seen as supporting the narrative that Omicron is a mild variant as significant numbers of patients still developed severe disease and died. All variants of concern continue to contribute to substantial morbidity and mortality, especially among vulnerable populations.

Continued emergence of new variants

As stated in the previous report, it is important to remember that new variants continue to emerge as mutations are still occurring. Examples of these are a new Omicron subvariant (BA.5.2.1) identified in Shanghai, China on 8 July 2022 (Reuters, 2022) and BA.2.75, which was found many countries,

including India, Australia, Germany, the United Kingdom, Canada and the United States of America (Ungar and Goshal, 2022). Although it is still too early to know how these variants will impact the course of the pandemic, this ongoing emergence of new variants again emphasizes the importance of genomic surveillance in order to monitor and respond effectively to the pandemic.

The national COVID-19 Vaccine Programme

South Africa first rolled out COVID-19 vaccination among health care workers in February 2021, using Ad26.COV2.S under the Sisonke programme. In May 2021, vaccination using BNT162b or Ad26.COV2.S was introduced for individuals older than 60 years, then expanding to those aged 35-50 years in July 2021, 18-35 years in August 2021, and 12-18 years in October 2021. In December 2021, booster doses were introduced. By August 2022, 49% of adult South Africans had received at least one vaccine dose, although the uptake of COVID-19 booster doses was low, with less than 5% of people having received a booster (sacoronavirus, 2022).

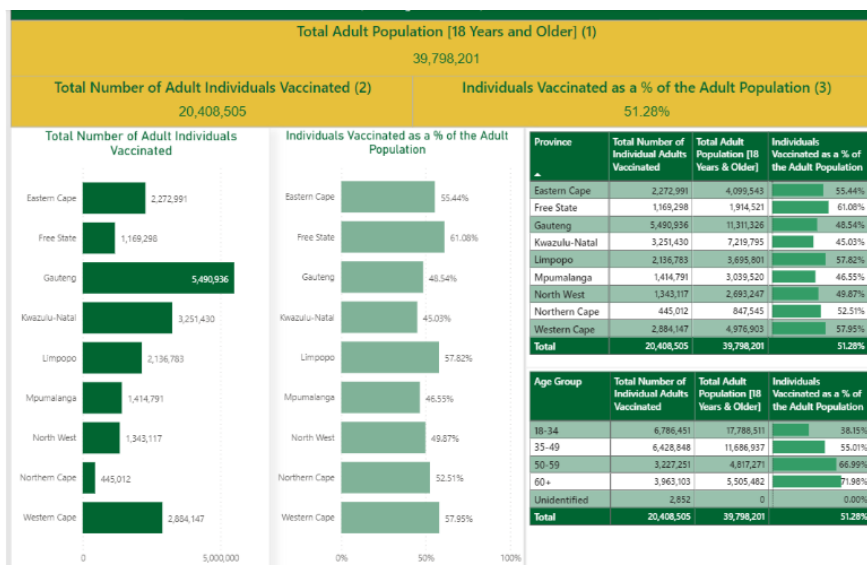


Figure 5: Number and coverage of COVID-19 vaccination by province and age group, South Africa, 23 September 2022

Electronic Vaccine Data System (EVDS)



The NDoH launched the Electronic Vaccine Data System (EVDS) system in April 2021 (NDoH EVDS). EVDS is a complete vaccination health information system from registration to certification, to ensure facilities are accredited, co-ordinate the supply of vaccines, enable a pre-booking and vaccination system, and record who is and isn't vaccinated. The EVDS self-registration portal is an online application that can be accessed via cellphone or via a computer with an Internet connection. It captures basic information to be able to assign date of vaccination and vaccination site. Information submitted during registration will be used to: Identify eligible vaccination beneficiaries; Plan supply of vaccines and ancillary items; Allocate beneficiaries to their nearest available service point; Communicate with enrolled individuals about the vaccination program, including but not limited to eligibility, when and where they will be vaccinated, follow-up vaccination appointments.

Vaccine adverse events reporting

The National Immunisation Safety Expert Committee (NISEC), appointed by the Minister of Health, determine the role of vaccines causing adverse events. Experts on the committee include pharmacists, pharmacovigilance experts, infectious disease specialists, paediatricians, EPI programme experts, immunologists, microbiologists, pathologists, public health specialists. Allocated persons from province and district are responsible for investigating adverse events following vaccination and completing a 'case investigation form'. Questions on the form include vaccination details and procedures, immunisation practices at the place where the vaccine was administered, cold chain and vaccine transport, community investigations (to identify clusters of cases), patient medical history, clinical examination and results of investigations. These reports are submitted to NISEC. The NISEC committee reports findings to the Minister of Health, the National Department of Health and the Provincial Departments of Health and to the South African Health Products Regulatory Authority (SAHPRA). SAHPRA has reported two deaths from Guillaine Barre Syndrome related to Janssen vaccine. xxx

Vaccine coverage surveys

PHIRST: Vaccination uptake was low in the rural site and urban site, with 57 (4.8%) of 1200 individuals fully vaccinated by August 2021 (Cohen, 2022).

The South African government reports vaccination doses administered on the sacoronavirus website. The uptake of vaccine increased with each group offered vaccine in mid to late 2021, then decreased until the new group was eligible, until vaccine for the last eligible group 12-17 years was introduced. From December 2021 when additional doses for immunocompromised and booster doses were

introduced, weekly number of individuals vaccinated has remained low and decreased throughout 2022.

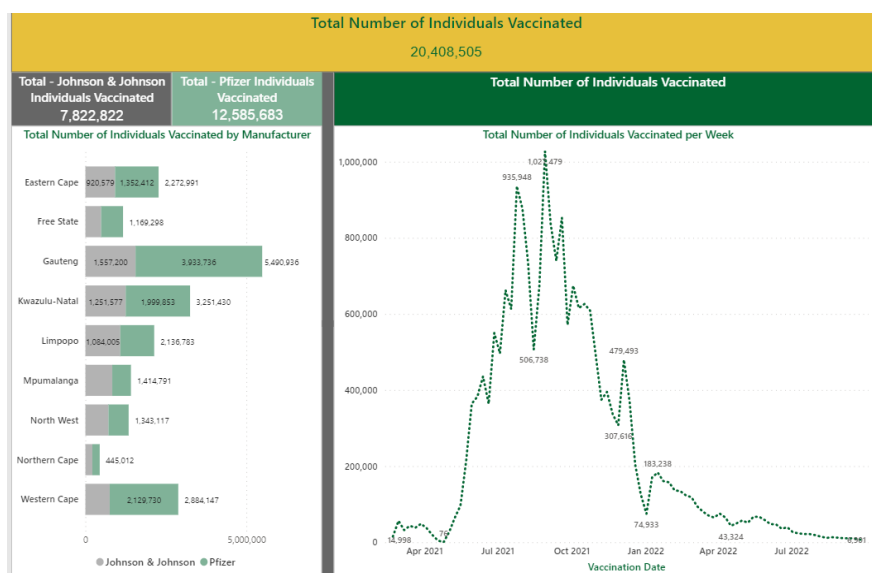


Figure 6: Number of individuals vaccinated per week, South Africa, 1 April 2021-23 September 2022

The programme was announced with highly ambitious targets of vaccinating about 70% of the South African adult population by the end of December 2021. Despite COVID-19 vaccines becoming widely available over time and being freely provided in South Africa, by end of August 2022 only about 51% (20.4 million individuals) of the adult population had received at least one vaccination dose, while 47% (18.6 million) of adults were fully vaccinated. A further 3.7 million booster vaccines have been administered. Among 12- to 17-year-olds, 2.7 million vaccines doses have been administered, of which 1.9 million were first doses and 0.8 million second doses, (see table 1)¹.

Table 1: Vaccination status among adults 18 years and older, South Africa September 2022

Commented [WJ1]: Maybe say something about vaccine procurement, SAHPRA approvals, when and which vaccines. The arrival of astrazeneca, evidence of effectiveness against Beta variant, decision to not use at a time that it could have prevented deaths in the devastating Delta wave

Sex	Total Adult Population [18 Years & Older]	Total Number of Individual Adults Vaccinated	Individuals Vaccinated as a % of the Adult Population
Female	20,719,946	11,444,227	55.23%
Male	19,078,255	8,925,005	46.78%
Unknown	0		
Total	39,798,201	20,369,232	51.18%

Age Group	Total Adult Population [18 Years & Older]	Total Number of Individual Adults Vaccinated	Individuals Vaccinated as a % of the Adult Population
18-34 Years	17,788,511	6,778,626	38.11%
35-49 Years	11,686,937	6,417,326	54.91%
50-59 Years	4,817,271	3,220,505	66.85%
60+ Years	5,505,482	3,949,907	71.74%
Unidentified	0	2,868	0.00%
Total	39,798,201	20,369,232	51.18%

Covid-19 treatment in South Africa

The Covid-19 oral antiviral Molnupiravir received approval from SAHPRA in February 2022 under Section 21 of the Medicines and Related Substances Act for compassionate use, to treat of mild to moderate disease, and has to be taken with five days of symptom onset. Although approved by SAHPRA and recommended by the WHO, the Ministry of Health did not commit to procurement of the drug in the public sector. Table below shows other drugs that are recommended by the WHO (Karim and Devnarain, NEJM 2022). The WHO has a recommendation against the use of Ivermectin, but its use was prevalent in South Africa. When SAHPRA observed excessive use of Ivermectin in South Africa, the regulator released guidelines on the use of Ivermectin. The guidelines were released in spite of the lack of evidence to support the use of Ivermectin. In fact, the WHO prohibits the use of Ivermectin and Fluvoxamine, although the use of the drugs is reportedly quite high, often prescribed by General Practitioners. Certain lobby groups advocated greatly for the use of this drug, to an extend of lodging cases with the courts in South Africa. SAHPRA relented after reports of increased illegal smuggling of Ivermectin into the country, often from India, as well as increased reports of toxicity from the use of Ivermectin. The aim of SAHPRA was not necessarily to authorise the use of Ivermectin for Covid-19, but rather to regulate the use in order to protect citizens. This step by SAHPRA was often misinterpreted by the lobby groups as authorisation to use Ivermectin. A coincidental authorisation of topical ivermectin for human use by SAHPRA also added to the public confusion, which was seen

by lobby groups as a loophole to advocate for use of Ivermectin for Covid-19. Other drugs that were used clinically to treat Covid-19 in South Africa include Remdesivir and corticosteroids.

Time to stop using ineffective Covid-19 drugs

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Supplementary online Table 1: World Health Organisation recommendations on which medications should or should not be used to treat Covid-19 (adapted from the WHO living guidelines for therapeutics and Covid-19, 14 July 2022)^g

	Strong recommendation against	Recommendation against	No recommendation for or against	Recommendation for	Strong recommendation for
Non-severe disease	- Convalescent plasma - Hydroxychloroquine - Lopinavir-ritonavir - Colchicine	- Corticosteroids^a - Ivermectin^b - Fluvoxamine^b - Nirmatrelvir and ritonavir^{a,c}	- Heparin - Metformin	- Molnupiravir^{a,d} - Sotrovimab^{a,d,e} - Remdesivir^{a,d} - Casirivimab and imdevimab^{a,d,f}	Nirmatrelvir and ritonavir^d
Severe disease	- Hydroxychloroquine - Lopinavir-ritonavir	- Ruxolitinib and tofacitinib^a - Ivermectin^b - Convalescent plasma^b		Casirivimab and imdevimab^{a,f}	- Corticosteroids - IL-6 receptor blockers or Baricitinib

Note: Severe disease is defined as oxygen saturation <90% on room air, pneumonia or respiratory distress

^a Conditional recommendation

^b Only recommended for use within the context of a clinical trial

^c In non-severe patients at low risk of hospitalization

^d In non-severe patients at highest risk of hospitalization

^e Excluding pregnant or breastfeeding women, and children

^f If seronegative for SARS-CoV-2 antibodies (note: evidence of limited efficacy for omicron BA.1 variant)

^g Agarwal A, Rochewig B, Lamontagne F, Siemieniuk RA, Agoritsas T, Askie L, et al. A living WHO guideline on drugs for covid-19. BMJ. 2020;370:m3379.

SAHPRA Approval (include WHO drug list in use of Ivermectin in South Africa)

Impact of Covid-19 on the Health System

When the third (Delta) wave began in South Africa, there was much fear and concern about its potential impact on the health system and health outcomes after the world witnessed the collapse of the health systems in much of Asia, particularly in India. The images that were shared globally by the media sent a wave of shock throughout the world, and South Africans were also fearful of what the impact will be when the variant arrived in the country. At the time, the country was still in its infant stages of the vaccine rollout, and most recipients were health workers and some of the elderly citizens, translating into relatively low levels of population immunity. As a result, the Delta variant caused very high levels of infection, disease and hospitalisation in the country, the highest levels the country had seen up to that point. The province that was most affected was Gauteng, after the province was largely spared from the devastation of the previous second (Beta) wave over the holiday season. The health system in Gauteng encountered so much strain that the country lockdown levels were increased from Alert level 3 to Alert Level 4 at the height of the increased case load. As the third wave was receding, the country Alert Level was reduced to Level 3, which contributed to increased infection through increased mobility and a prolonged tail of a high case load. Although the health system in Gauteng

was severely affected and strained, there was no evidence to suggest collapse of the health system at the time of the pandemic. The dysfunction of hospitals such as Charlotte Maxeke, which suffered damage from fire, did not help as the capacity for care was greatly reduced. However, the coordinated efforts between private and public sector assisted in absorbing the burden of care throughout the province, together with the referral of severely ill patients to other provinces in the country when acute care was at full capacity.

When the fourth (Omicron) wave began in South Africa in October and November of 2021, the levels of population immunity were estimated at about 83% (Madhi et al.), attributed to both vaccine coverage and infection immunity largely from the third (Delta) wave. Omicron was identified in Botswana and South Africa, resulting in much of the world banning travellers from South Africa from entering their countries, particularly in the Global North (Mendelson et al 2021 lancet commentary paper). However, the burden on the health system was limited, and as a result, South Africa stayed on Alert Level 3 throughout the fourth wave, even reducing some of the restrictions such as mask restrictions in outdoor spaces. Although early evidence from Tshwane suggested a milder form of illness than expected given the nature of the mutations, the questions around severity of disease remained inconclusive for a while, even when the Omicron variant was increasingly spreading globally. Ultimately, the variant still had potential to cause severe disease in vulnerable individuals, but at a broader population level, the data showed a less severe form of illness compared to previous variants. The lack of strain on the health system was cautiously taken a sign that the pandemic may be releasing its hold on the country. The evidence of this was seen in what can be considered the fifth (Omicron) wave of the pandemic in South Africa, which was not officially declared by Ministry of health although all the thresholds of a wave were met. There was such little impact on the health system that most of the restrictions were relaxed, and emphasis was placed on the importance of ventilation. At this point, the national vaccination programme had also slowed significantly.

(include burden on the Gauteng's health system, hospitalisation – Data from the dat.cov database)

Long COVID or Post COVID-19 Condition

Post COVID-19 Condition (PCC) as defined by the World Health Organization (WHO), “occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis” (Soriano, 2022). It is estimated that 30% people who have been infected with SARS-CoV-2 may go on to develop PCC (Fernandez-de-Las-Penas, 2021). One study reported that as many as 60% of COVID-19 survivors will experience PCC at least during the first year (Han, 2022).

Longitudinal studies have reported persistent symptoms up to two years after acute COVID-19 (Huang, 2022).

PCC displays a wide spectrum of clinical manifestation. Over 60 physical and psychological sequelae have been described (Michelen, 2021). The most common symptoms reported include fatigue, shortness of breath, joint/muscle pain and weakness, headache, cough, chest pain, sleep disturbance, depression/anxiety, and cognitive deficits ('brain fog') including loss of memory and difficulty concentrating (Aiyegbusi, 2021; Crook, 2021; Parums, 2021; Nguyen, 2022; Han, 2022; Alkodaymi, 2022; van Kessel, 2022). Systematic reviews have reported impaired functional status and reduced quality of life among adults with PCC (Aiyegbusi, 2021; Michelen, 2021; Amdal, 2021; Pizarro-Pennarolli, 2021; Ceban, 2022).

Risk factors identified for PCC include age, sex, ethnicity/race, comorbidities, number of acute COVID-19 symptoms, and severity of COVID-19 disease requiring hospitalisation, ICU or invasive mechanical ventilation (Aiyegbusi, 2021; Parums, 2021; Chen, 2022; Crook, 2021; Sudre, 2021). Recent studies have suggested that the prevalence of PCC among people infected during the Omicron-dominant wave was lower than those infected in previous waves dominated by Delta and Alpha (Chen, 2022; Wise, 2022; Antonelli, 2022; Morioka, 2022). Some studies have also suggested that COVID-19 vaccination may reduce the risk of developing PCC or improve PCC symptoms (Kuodi, 2022; Venkatesan, 2022; Ayoubkhani, 2022).

Theories regarding mechanisms for the development of PCC include sequelae of COVID-19 organ involvement during acute infection, pathological prolonged hyperinflammation from viral persistence, immune dysregulation, and cross-reactivity of SARS-CoV-2 specific antibodies with host proteins resulting in autoimmunity (Yong, 2021); autonomic nervous system damage, endothelial dysfunction (Castenaras, 2022); alterations in microbiome leading to long-term health consequences of COVID-19 (Alkodaymi, 2022); microvascular changes (Strain, 2022); and a pro-coagulant state induced by SARS-CoV-2 infection (Nalbandian, 2021). Post-COVID fatigue may be attributed to lung dysfunction (Maltezou, 2021). In addition, the sequelae of critical illness including social isolation and trauma may be a factor (Premraj, 2022; Nalbandian, 2021).

A Western cape retrospective cross-sectional study included adults diagnosed with mild COVID-19 who were called two months post-diagnosis. It was found that 60% of patients with mild COVID-19 had ≥ 1 long COVID symptom, while 35% had ≥ 3 ongoing symptoms for two months (Mendelsohn, 2022). Dyspnoea and fatigue were the most common symptoms. The findings revealed that 52% of employed patients missed work and 25% of patients self-reported non-recovery from their COVID-19.

Moreover, 24% of patients consulted a clinician for long COVID, but only 7% of patients received long COVID care in the public sector.

The Department of Physiological Sciences at Stellenbosch University (SU) established an online registry for Long COVID. The study showed that plasma samples from Long COVID/PASC still contain large anomalous (amyloid) deposits (microclots) and that these microclots in both acute COVID-19 and Long COVID/PASC plasma samples were resistant to fibrinolysis (compared to plasma from controls and T2DM), even after trypsinisation (Pretorius, 2021). Various inflammatory molecules were substantially increased in samples from individuals with acute COVID-19 and Long COVID/PASC.

The NICD established a Post COVID-19 Condition (PCC) longitudinal cohort study to report prevalence of and risk factors for PCC. Participants who were SARS-CoV-2 were recruited including, (a) 1074 individuals who were not hospitalised, identified through the national case line list (NMC-SS), and (b) 2626 individuals who were hospitalised in public and private hospitals from all provinces of South Africa, identified through the DATCOV national hospital surveillance. At 3 months of follow-up, 1249 (66.7%) of 1873 participants reported new or persistent COVID-19-related symptoms, compared with 1978 (82.1%) of 2410 at 1 month after hospital discharge (Dryden, 2022). The most common symptoms reported at 3 months were fatigue (50.3%), shortness of breath (23.4%), confusion or lack of concentration (17.5%), headaches (13.8%), and problems seeing or blurred vision (10.1%). On multivariable analysis, the factors associated with persistent symptoms after acute COVID-19 were being female (adjusted incident rate ratio 1.20, 95% CI 1.04–1.38) and admission to an intensive care unit (1.17, 1.01–1.37).

The longitudinal observational cohort study by the National Institute for Communicable Diseases (NICD) recruited hospitalised and non-hospitalised participants, infected during the periods that Beta, Delta and Omicron BA.1 variants dominated in South Africa. Participants aged 18 years or older were randomly selected to undergo telephone assessment at 1, 3, 6 and 12 months after hospital discharge or laboratory-confirmed SARS-CoV-2 infection. Participants were assessed using a standardised questionnaire for evaluation of symptoms and health-related quality of life.

The study reported a high prevalence of PCC at 6 months following SARS-CoV-2 infection in a cohort of 3,700 hospitalised and non-hospitalised participants. Overall, 46.7% of hospitalised participants and 18.5% of non-hospitalised participants experienced persistent symptoms at 6 months. This differed by the variant period (lower prevalence of PCC among those infected during the Omicron period), and also the severity of acute COVID-19 (higher prevalence of PCC with more severe acute COVID-19). The

study also demonstrated the impact of PCC on quality of life, with participants still reporting fatigue (38%), disability (24%), and pain/discomfort (16%) at 6 months.

Risk factors for PCC in the study included older age, female sex, non-black race, the presence of a comorbidity, greater number of acute COVID-19 symptoms, and hospitalisation/ COVID-19 severity. The study reported a lower risk of persistent symptoms among participants infected in the Omicron wave. Participants who were vaccinated had no statistically significant difference in persistent symptoms compared to those who were unvaccinated.

The prevalence of persistent symptoms in this cohort declined with successive follow-up periods, from 82% at 1 month to 53% at 3 months and 47% at 6 months for hospitalised participants, and from 32% at 3 months to 19% at 6 months for non-hospitalised participants. However, the proportion of participants that remained symptomatic at 6-months, represents a substantial potential burden on individuals and the health system. Extrapolating the prevalence of PCC to the total hospitalised COVID-19 patients (from hospital surveillance) and likely total infected individuals (from serosurveys), it is possible that over 250,000 hospitalised and 6.3 million non-hospitalised individuals have persistent symptoms at 6 months after SARS-CoV-2 infection in South Africa.

Socio-behavioural response to COVID-19

(include changes in the regulations over time; perhaps also airborne disease emphasis)

In the early stages of the pandemic, the Minister of Health set up the COVID-19 Ministerial Advisory Committee (MAC) in March 2020. Despite the common understanding that the COVID-19 pandemic was largely driven by human behaviour, the original MAC predominantly consisted of people who were not social and behavioural sciences experts and therefore could not provide much insight on how to deal with socio-behavioral issues (SAMJ, 2020). There were calls for the Minister of Health to relook at the composition of the MAC, as it was dominated by clinical experts, by bringing on board members who were more experienced in socio-behavioural interventions. Eventually this process led to the reconfiguration of the MAC, and inclusion of two additional teams on socio-behavioural and vaccine-related aspects, in order to provide the Minister and the Department of Health with more comprehensive and holistic advice on how the country should be handling the COVID-19 pandemic.

The socio-behavioural MAC was a critical structure that could potentially provide valuable advice and guidance as the country was gradually moving towards less restrictions and reduction in lockdown levels, but its impact remain unclear. Furthermore, with the introduction of COVID-19 vaccines in the country, the success or failure of the roll-out was highly dependent on people's behavior such as

acceptance, perceptions as well as addressing the multitude of misinformation that was being peddled about the safety of the vaccines.

Vaccination behavior, acceptance and uptake

The acceptance and uptake of new innovations such as the COVID-19 is driven by complex factors both at the individual and social level, influencing how people make the decision to either adopt or reject the new innovation, regardless of the claimed benefits. The stages of change theory outline various stages within which individuals or communities can be categorized in the process of adopting new innovations which are, Pre-contemplation, Contemplation, Preparation, Action and then Maintenance (). Within this broad spectrum there are various levels of vaccine acceptance as well as vaccine hesitancy in varying degrees. Vaccine hesitancy is generally defined as the reluctance and delay in acceptance or refusal of vaccination despite availability of vaccination services (Machingaidze & Wiysonge C 2021; Macdonald, 2015). Several surveys were conducted in South Africa aimed at measuring vaccine hesitancy in the general population. The data showed that vaccine hesitancy was reported by about a third of respondents. The UJ/HSRC Democracy surveys reported vaccine hesitancy of between 28 % and 33% measured over a series of survey waves during 2021 (Runciman et al, 2021). Additional data from the HSRC COVID-19 “one year later surveys” reported that about 27% were hesitant (Sewpaul, et al, 2021) and findings from the VaxScenes study reported hesitancy in about 32% of the people who responded to the survey (Katoto et al, 2022). Data from the National Income Dynamics Study — Coronavirus Rapid Mobile Survey (NIDS/CRAM) reported vaccine hesitancy constantly below 30% amongst respondents, while acceptance increased over time (Spaull et al, 2021). Some of the key determinants cited for vaccine hesitancy in the various studies included misinformation, fear of needles, distrust of the government, beliefs in conspiracy theories and religious reasons. In almost all the surveys young people were the most hesitant sub-population and this is clearly evident in the vaccination statistics for South Africa.

In the South African context vaccine hesitancy has been described as “a complex social phenomena” that’s driven by various constructs such as fear, doubt, indecision and even mistrust of the vaccine (Cooper, et al 2022). Vaccination hesitancy in South African indigenous communities especially may have been strongly driven by the cultural context and social spaces that people occupy grounded in their Socio-economic situation cultural and religious beliefs, as well as the historical inequalities and disparities. Addressing long term hesitancy and improved acceptance and uptake of the COVID-19 vaccine will require that all strategies take stronger cognizance of the “context” and the non-

homogenous nature of the so called ‘vaccine hesitant’ as we continue to live with the virus in its endemic phase (Sifunda et al, 2022).

Vaccine mandates

The South African government never adopted the strategy and policies of mandatory vaccinations which had been adopted in many countries in Europe such as Austria, Germany, Italy and several states in the United States of America. Mandatory vaccination was a controversial policy that received a lot of resistance both in South Africa and across the world. However, in the course of 2021 as part of the vaccine roll-out and COVID-19 mitigation, many institutions and organizations introduced mandatory vaccinations and only vaccinated individuals could be allowed into work places and campuses. The decision to implement vaccine mandate policies was left at the discretion of the companies and campuses. Though controversial, several employers and universities did require people to be fully vaccinated before they could be allowed to return to work or campuses. Some strong supporters of vaccine mandates have provided various arguments on why vaccine mandates can be positive in the fight against COVID-19 such as improving vaccine uptake, protecting the rights of others, especially people who are already immunocompromised.

Commented [WJ2]: Perhaps include the occupational health regulations on mandatory vaccine policies

Commented [CPA3]: Should we also include anything on court cases to challenge these mandates?

COVID-19 vaccination communication

Science communication was arguably at the core of a successful fight against the outbreak of COVID-19 right from the beginning of the pandemic. Earlier on the rapport between the government and the public was perceived as positive based on goodwill, and most surveys showed that civil society accepted most of the decisions that were being implemented in the national COVID-19 response (CRAM/NIDS Survey, Reddy et al, 2020, UJ/HSRC Survey 2020). Eventually, increasingly poor communication and draconian decisions probably led to a significant “trust deficit” between the government and local communities. The emergence of reports on rampant corruption in personal protective equipment (PPE) tenders, mostly driven by politically connected individuals and government officials, led to even further erosion of trust in the government. However, the straw that broke the camel’s back was the emergence of the scandal around the NDOH COVID-19 communications contract with a dubious company called Digital Vibes. This scandal almost explained why the country’s communications programme fell apart, and unfortunately also involved the then Minister of Health, his associates and his family members as per allegations. The corruption laden communication strategy may have had a strong impact on the COVID-19 vaccination roll-out in the country which has been less than optimal, with South Africa having lower vaccination rates, compared to neighboring countries such as Botswana, Mozambique and Namibia.

Conclusions

(to be added)

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