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FOREWORD

The second wave of the COVID-19 pandemic has arrived with greater intensity than the first, and may be driven by a new variant of the SARSCov2 virus that is even more infectious. South Africa is currently in the grip of this second wave that threatens to overwhelm the public and private health sectors. In order to monitor and describe trends of COVID-19 hospitalisations and the epidemiology of hospitalised patients in South Africa, the National Institute for Communicable Diseases (NICD) established a hospital surveillance system, DATCOV, in 2020. Using DATCOV data from three districts in South Africa, this important report describes the critical features of the second COVID-19 wave in comparison to the first.

Prof Basil Brooke, Editor

MULTIVARIABLE ANALYSIS COMPARING IN-HOSPITAL MORTALITY IN THE FIRST AND SECOND WAVE OF COVID-19 IN THREE DISTRICTS OF SOUTH AFRICA

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Summary

- In the metros of Nelson Mandela Bay, City of Cape Town and eThekwini, South Africa, weekly COVID-19 cases, admissions and in-hospital deaths in the second wave have exceeded the numbers in the first wave. There has additionally been a faster increase of weekly incidence risk for COVID-19 admissions in the second wave.

- There was a 40-80% increased risk for mortality in those weeks with very high levels of weekly admissions in the three districts. The increase in mortality of hospitalized patients at the peaks of the first and second waves reflects increasing pressure on the health system.

- On multivariable analysis, when adjusting for weekly COVID-19 district hospital admissions, there was no difference in in-hospital mortality between the first and second wave in Nelson Mandela Bay Metro, City of Cape Town Metro and eThekwini Metro.

- In the second wave in all three districts, individuals having comorbidities and being of Black race were less likely to be admitted to hospital in comparison to the first wave. In one district admissions were generally younger during the second wave but age distribution was similar in the other two districts. The lower proportion of reported comorbidities in the second wave, even accounting for age distribution, could reflect differences in clinician practice, survival bias, variation in reporting of comorbidities or changing manifestation in individuals without underlying illness.

- A major limitation of this analysis is possible residual confounding as we could not adjust for several factors including burden of non-COVID-19 admissions, changes in treatment administration, the impact of national restrictions and change in individual preventive behaviour. We also did not have data on the lineage type infecting individuals included in the analysis.

- While data on SARS-CoV-2 lineage was not available for the individuals included in this analysis, preliminary reports suggest that the majority of infections during the second wave in the included districts may have been caused by the lineage 501Y.V2. The second wave appears to be associated with higher incidence and faster increases in cases and hospitalizations. It is however not associated with increased in-hospital mortality in the three large metropolitan districts surveyed, but this possibility cannot be completely excluded.

Background

SARSCov2 cases peaked in South Africa during the first wave in late July 2020, and then began to increase again in October in the Eastern Cape and Western Cape Provinces, in early November in KwaZulu-Natal Province, followed by all provinces by late November 2020.[1]

A new lineage of SARS-CoV-2 has been detected in the Eastern Cape (21 September), Western Cape (5 October) and KwaZulu-Natal (5 October) provinces. This lineage, named 501Y.V2, contains several mutations that were not previously identified in SARS-Cov-2 viruses from South Africa prior to September 2020 (from now on referred to as old lineages).[2] Eight of these mutations are in the spike protein coding region and could potentially lead to enhanced binding to the human ACE2 receptor or reduced virus sensitivity to antibodies. This lineage had been detected in 251 specimens of 2801 South African sequences by 28 December 2020, and made up more than 50% of initially-tested samples in each of the Eastern Cape, Western Cape and KwaZulu-Natal provinces during the second wave. Sequencing of additional samples is ongoing. Preliminary data suggest that the new lineage viruses may be more transmissible than other lineages.[3] There are currently limited data on the severity of the new lineage.

In light of the emergence of the new lineage 501Y.V2, the resurgence of COVID-19 in all provinces and the increase in the numbers of in-hospital deaths, the aim of this report is to describe and compare epidemiologic characteristics of cases and in-hospital mortality between the first and second waves of COVID-19 in three districts in South Africa: Nelson Mandela Bay Metro (Eastern Cape Province), City of Cape Town Metro (Western Cape Province) and eThekwini Metro (KwaZulu-Natal Province).

Methods

Data

Secondary data analysis was conducted of the DATCOV database, an active hospital surveillance system for COVID-19 admissions. As of 9 January 2021, a total of 627 facilities submitted data on hospitalised COVID-19 cases, 377 from the public sector and 250 from the private sector. A COVID-19 case was defined as a person with a positive reverse transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 who was admitted to hospital. Case-fatality risk (CFR) was calculated for all closed cases, *i.e.* COVID-19 deaths divided by COVID-19 deaths plus COVID-19 discharges, excluding individuals who are still admitted in hospital. For the calculation of incidence risks, StatsSA mid-year population estimates for 2020 were utilised.

Selection of districts

We first describe national trends in order to characterise the resurgence of COVID-19 cases and in-hospital mortality in the country. We then focused the analysis of epidemiologic characteristics of cases and in-hospital mortality in the first and second wave to three districts, Nelson Mandela Bay Metro (Eastern Cape Province), City of Cape Town Metro (Western Cape Province) and eThekwini Metro (KwaZulu-Natal Province), as these districts have had a sustained second wave for many weeks, with weekly incidence surpassing 250 cases per 100,000 population. Restriction of this analysis to the district level allows better adjustment for burden of COVID-19 cases on the healthcare system.

Selection of time period for analysis

The periods of analysis were estimated using hospital admission data in the three districts. Since the second wave is ongoing in all three districts, the analysis of epidemiologic characteristics in the first and second waves included only the first part (period of increasing incidence) of each wave. The time period for each starts when the district recorded an incidence risk of 5 admissions per 100,000 population, and ends when the district reached the peak of admissions (Table 1). For the analysis of factors associated with in-hospital mortality the COVID-19 outbreak was divided into four periods, pre-wave 1, early wave 1, late wave 1 and early wave 2 (Table 1). It is unclear whether City of Cape Town Metro and eThekwini Metro have reached their peaks in hospitalisations, due to possible data lags and the fact that the trends in COVID-19 admission are still evolving.

Table 1. Time periods for analysis of the first and second waves of the COVID-19 epidemic by Metro, South Africa, 2020-2021.

	Pre-wave 1	Early wave 1	Late wave 1	Early wave 2
Nelson Mandela Bay Metro	5 March-16 May	17 May-18 July	19 July-3 October	4 October-21 November
City of Cape Town Metro	5 March-25 April	26 April-27 June	28 June-14 November	15 November-2 January
eThekwini Metro	5 March-13 June	14 June-25 July	26 July-21 November	22 November-26 December

Outcomes and covariates

We conducted two multivariable analyses of data from each of the three selected districts. The first analysis compared the characteristics of hospitalised COVID-19 cases in early wave 1 and early wave 2, and the second assessed risk factors for in-hospital mortality accounting for wave period. For the multivariable model comparing early wave 1 and early wave 2 as outcomes, covariates included were age, sex, race, health sector, presence of comorbidity and in-hospital mortality, also adjusting for weekly district COVID-19 admissions. The analysis included only data from early wave 1 and early wave 2, and not the other wave periods.

For the multivariable model assessing risk factors for mortality, covariates included were age, sex, race, health sector, presence of comorbidity, including wave period, and adjusting for weekly district COVID-19 admissions. In the mortality model, we included all four wave periods, *i.e.* pre-wave 1, early wave 1, late wave 1, and early wave 2.

Weekly COVID-19 admission categories as a proxy of burden of COVID-19 cases on the healthcare system were based on the weekly numbers of admissions in each district throughout the epidemic (Table 2).

Table 2. Categories of weekly district hospital admission numbers for COVID-19 by metro, South Africa.

	Low admissions	Medium admissions	High admissions	Very high admissions
Nelson Mandela Bay Metro	<200	200-399	400-599	>600
City of Cape Town Metro	<600	600-1199	1200-1799	>1800
eThekwini Metro	<500	500-899	900-1299	>1300

There is still potential for residual confounding that is not possible to account for, including the following:

- We adjusted for COVID-19 admissions but were not able to adjust for weekly hospital admission volumes for persons under investigation (PUIs) and non-COVID-19 admissions.
- We are not able to adjust for differences between the first and second wave related to the level of national restrictions/lockdowns, and to individual preventive behaviours.
- The analysis includes only in-hospital deaths. Any differences between the two waves in the proportions of patients who did not or could not access care and those that died outside of hospital are not accounted for in the analysis.
- There have been changes in treatment protocols with better COVID-19 treatment regimens including steroid use and high flow oxygen. These have likely decreased mortality rates as the epidemic progresses.
- The numbers of hospitals reporting to DATCOV increased in October 2020 and while all hospitals were required to back-capture historic admissions, they may not have done this completely, leading to reporting bias with possible underreporting in the first wave.
- The characteristics of those patients who died in the first wave (such as old age, comorbidities, obesity etc) may have differed from the survivors and those who escaped infection. Therefore, the characteristics of those patients admitted to hospital in the second wave may be different compared to those of the first wave as a result of survival bias.

Results

National trend in COVID-19 cases and admissions

From 5 March 2020 to 9 January 2021, a total of 1,231,596 SARS-CoV-2 cases and 161,350 COVID-19 hospitalisations were reported in South Africa. Following the first wave peak in cases in epidemiologic week 28, there was a resurgence beginning in the Eastern Cape Province from week 40, followed by all other provinces subsequently. The weekly numbers of cases, admissions and in-hospital deaths surpassed the numbers recorded during the peak of the first wave (Figure 1). Decreases in the most recent week may reflect delays in data submission.

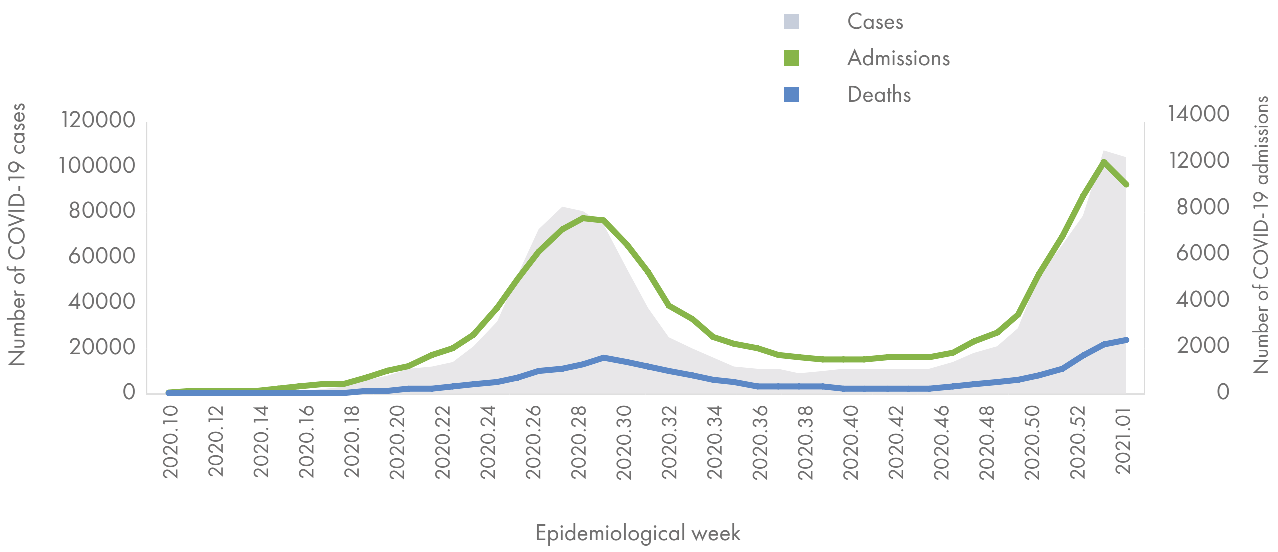

Figure 1. Numbers of reported SARS-Cov-2 cases including COVID-19 admissions and in-hospital deaths by epidemiologic week of diagnosis, South Africa, 5 March 2020-9 January 2021.

The majority of admissions were recorded in four provinces: Gauteng, Western Cape, Eastern Cape and KwaZulu-Natal. Admissions increased in Eastern Cape Province from week 40, Western Cape from week 43, KwaZulu-Natal from week 46, Gauteng from week 48, Limpopo from week 50 and all other provinces from week 48 or 49 (Figure 2). The weekly numbers of admissions in Eastern Cape, Western Cape, KwaZulu-Natal and Limpopo provinces surpassed the numbers during the peak of the first wave.

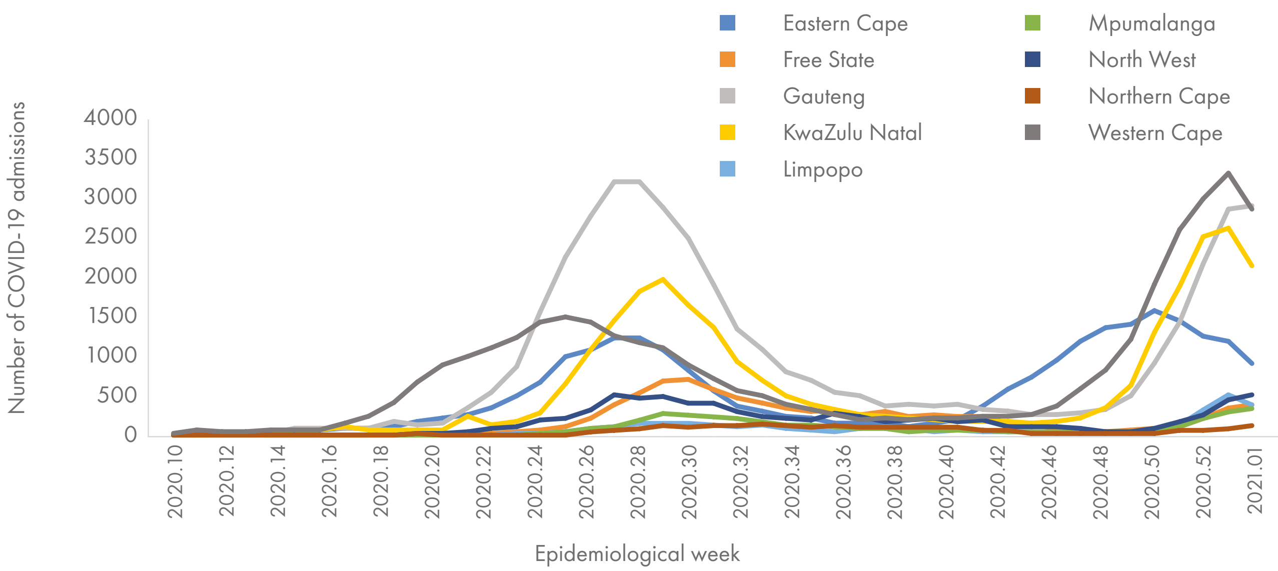

Figure 2. Numbers of reported COVID-19 admissions, by province and epidemiologic week of diagnosis, South Africa, 5 March 2020-9 January 2021, n=161,350.

National trends in mortality

Of the 143,293 COVID-19 patients nationally with a recorded in-hospital outcome (died or discharged), 29,783 died and the case fatality rate (CFR) was 20.1%. The CFR increased in June (19.8%) and July (19.8%) at the peak of the first wave and in December (23.7%) toward the peak of the second wave (Table 3). The peak monthly CFR observed in the second wave was higher than in the first wave.

Table 3. COVID-19 in-hospital case fatality ratio reported by month, South Africa, 5 March 2020-9 January 2021.

Month	Died	Total outcomes	CFR (%)
March	9	248	3,6
April	110	980	11,2
May	711	3985	17,8
June	2625	13271	19,8
July	6888	34773	19,8
August	4681	24470	19,1
September	1625	10663	15,2
October	1087	8289	13,1
November	1818	9243	19,7
December	6543	27639	23,7
January	4256	14503	29,3

The weekly CFR was higher in the public sector, and exceeded the peak of the first wave in both sectors. In the public sector, the weekly CFR increased towards the peak of each wave. In the private sector, while there was not much variation in CFR in the first wave, there was an increase in CFR in the second wave in the last four weeks (Figure 3).

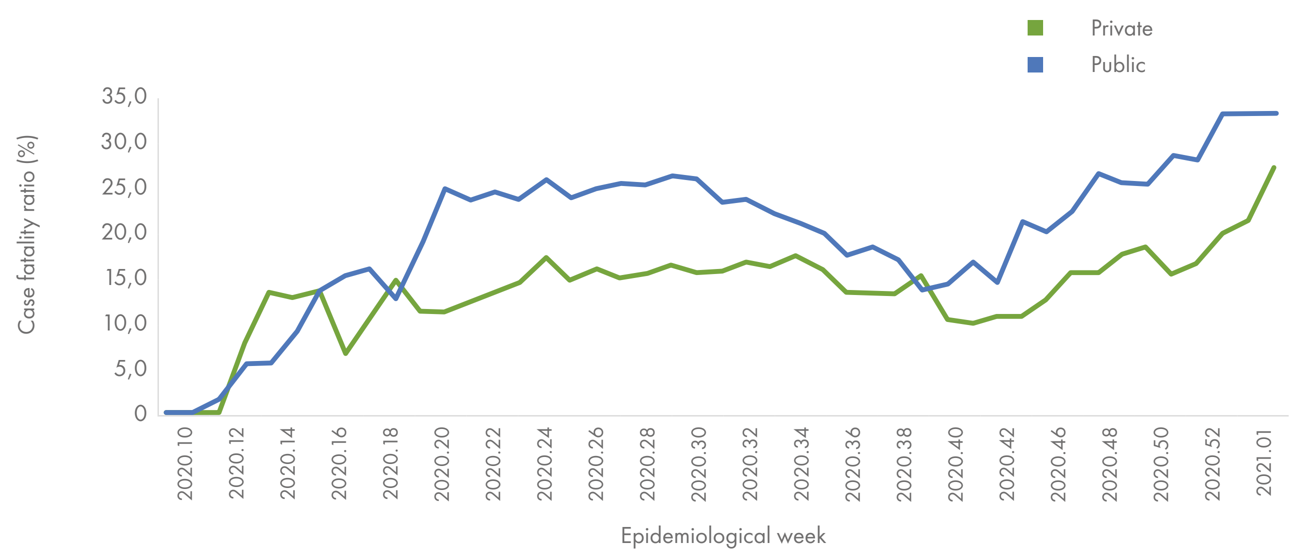

Figure 3. Weekly COVID-19 in-hospital case fatality ratio reported per week by health sector and epidemiologic week, South Africa, 5 March 2020-2 January 2021.

Demographic characteristics of admissions and deaths

There was an increasing incidence risk of admissions with increasing age, with the highest incidence risk observed amongst individuals older than 60 years. This trend was similar in the first and second waves (Figure 4).

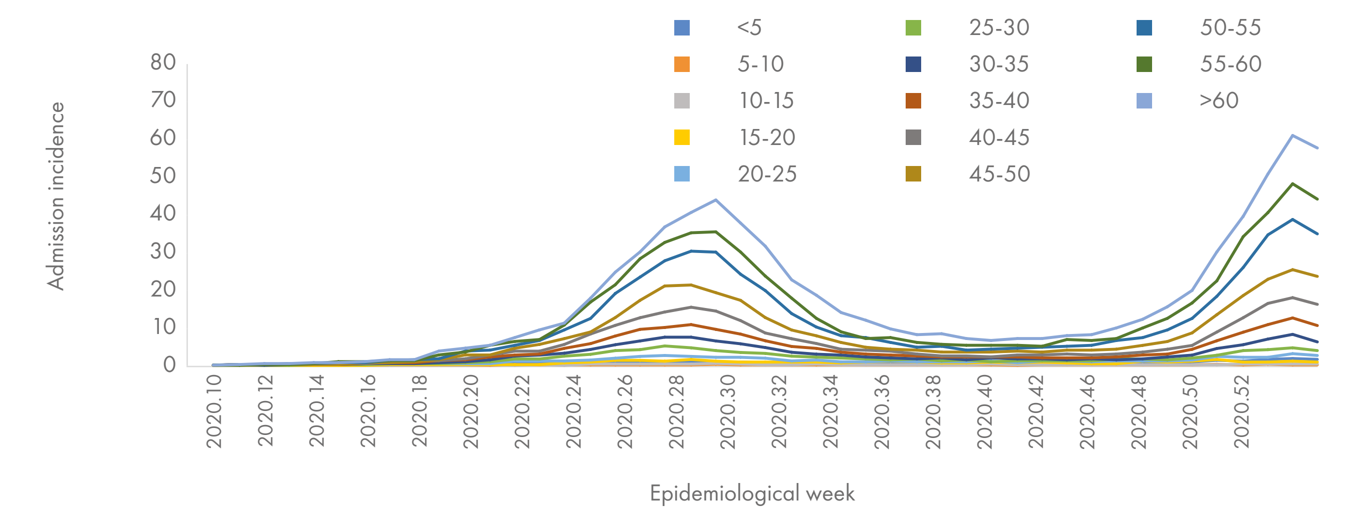

Figure 4: Incidence risk per 100,000 population of COVID-19 admissions by age group in years, South Africa, 5 March 2020-2 January 2021, n=147,308.

A higher proportion of patients older than 50 years was hospitalised during the peak of the first and second waves. There is no apparent increase in the proportion of young people admitted in the second wave (Figure 5)

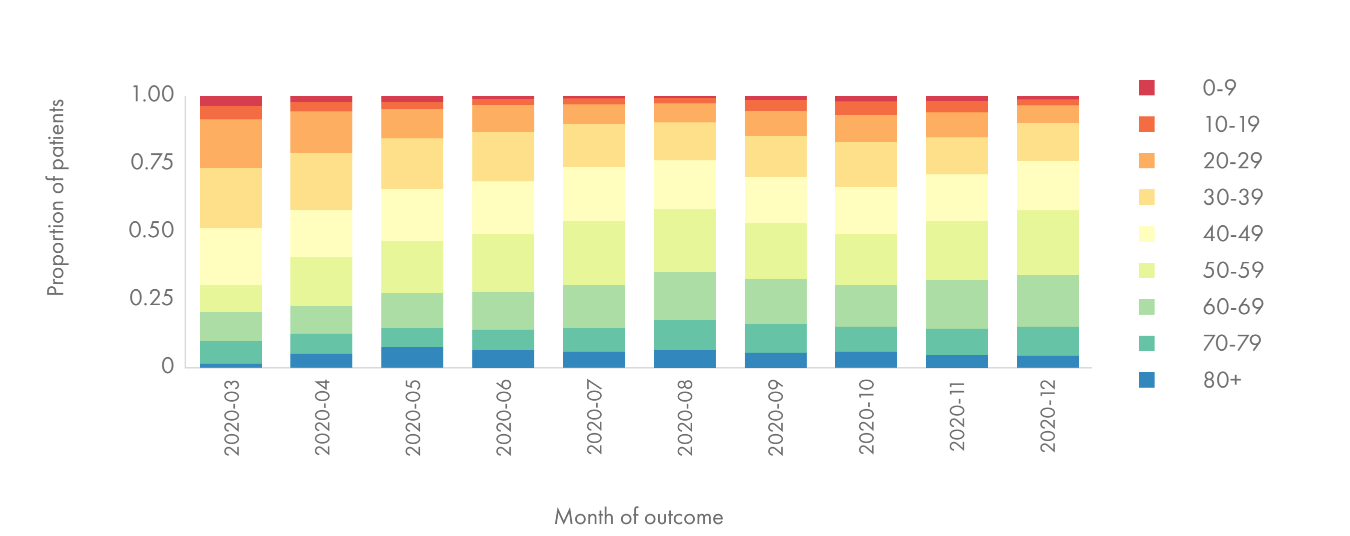

Figure 5. Proportion of COVID-19 admissions by month and age group in years, South Africa, 5 March 2020-9 January 2021, n=133,679.

* Figure courtesy of Prof Juliet Pulliam (SACEMA), produced using DATCOV data

There was an increasing incidence risk of in-hospital deaths with increasing age, with the highest incidence risk observed amongst individuals older than 60 years. This trend appears to be similar in the first and second waves (Figure 6).

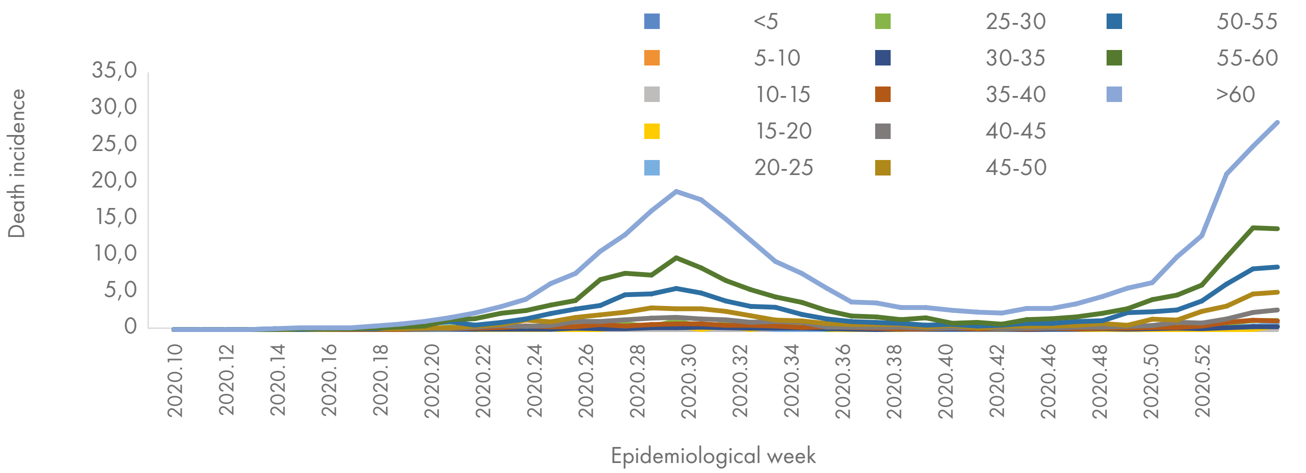

Figure 6: Incidence risk per 100 000 population of COVID-19 in-hospital deaths by age group in years, South Africa, 5 March 2020-2 January 2021, n=26,143.

The monthly CFR was higher in older age groups, particularly over 50 years, and increased towards the peak of the first and second waves, appearing more prominent in the older age groups (Figure 7).

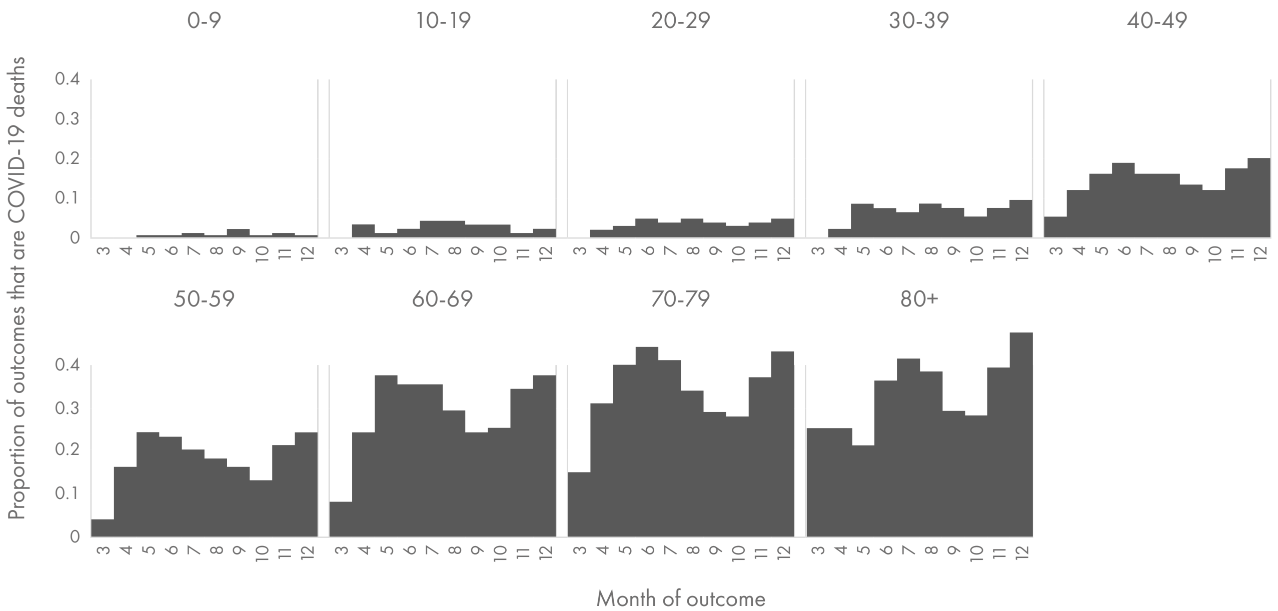

Figure 7. COVID-19 in-hospital case fatality ratio per month by age group in years (amongst admissions with in-hospital outcome), South Africa, 5 March 2020-9 January 2021.

* Figure courtesy of Prof Juliet Pulliam (SACEMA), produced using DATCOV data

Nelson Mandela Bay Metro

The weekly numbers of COVID-19 admissions in Nelson Mandela Bay Metro peaked at 495 in the first wave and 700 in the second wave. The time the district took to go from 5 admissions per 100,000 to 40 admissions per 100,000 population in the first wave was 9 weeks and in the second wave was 5 weeks (Figure 8).

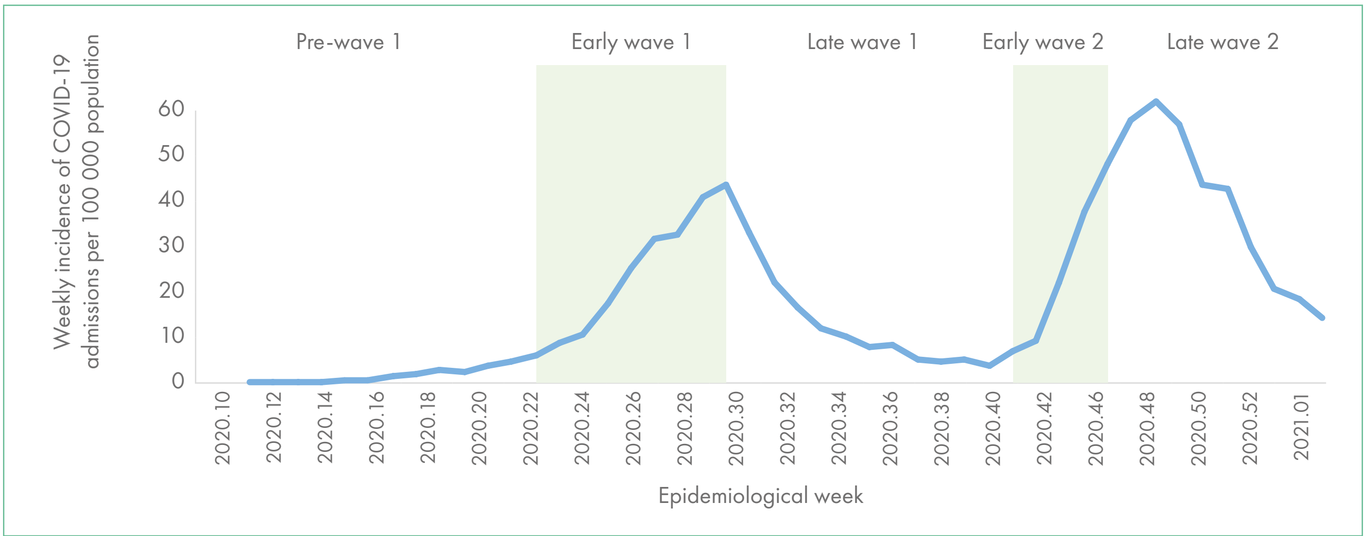

Figure 8: Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows the time period from 5 admissions per 100,000 to 40 admissions per 100,000 in the first and second waves, Nelson Mandela Bay Metro, 5 March 2020-9 January 2021, n=9,399.

Using the time period from incidence risk of 5 admissions per 100,000 to peak to define the early wave, the period of analysis of the pre-wave 1, early wave 1, late wave 1 and early wave 2 are depicted in Figure 9.

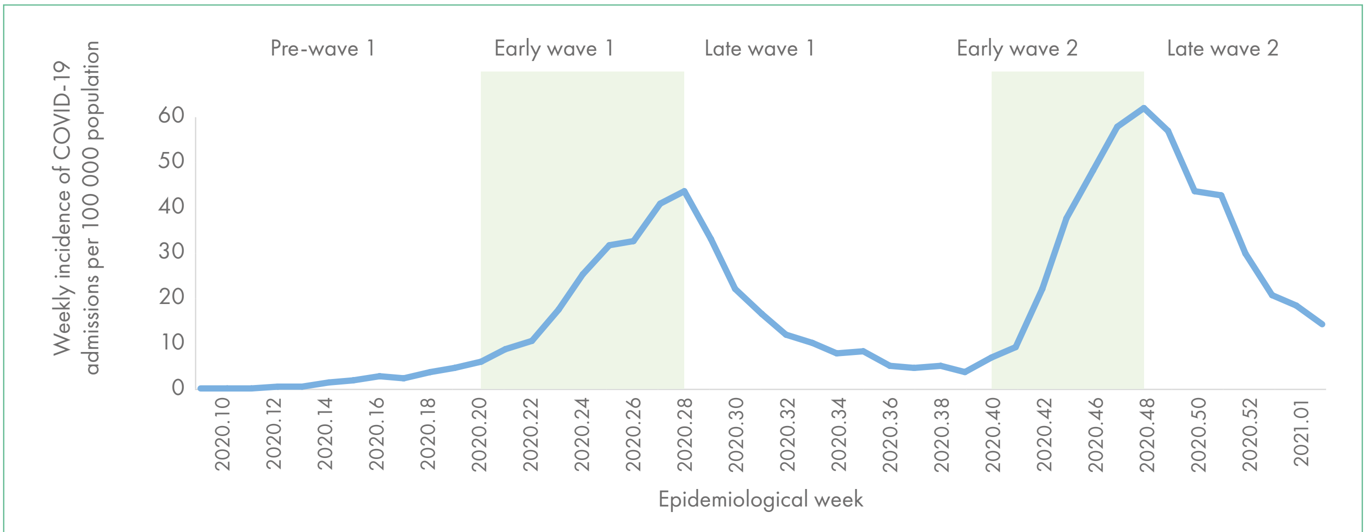

Figure 9. Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows the time periods of early first and second waves, Nelson Mandela Bay Metro, 5 March 2020-9 January 2021, n=9,399.

The weekly in-hospital CFR increased towards the peak of each wave and decreased between the first and second waves; and was lower in the second wave (Figures 10).

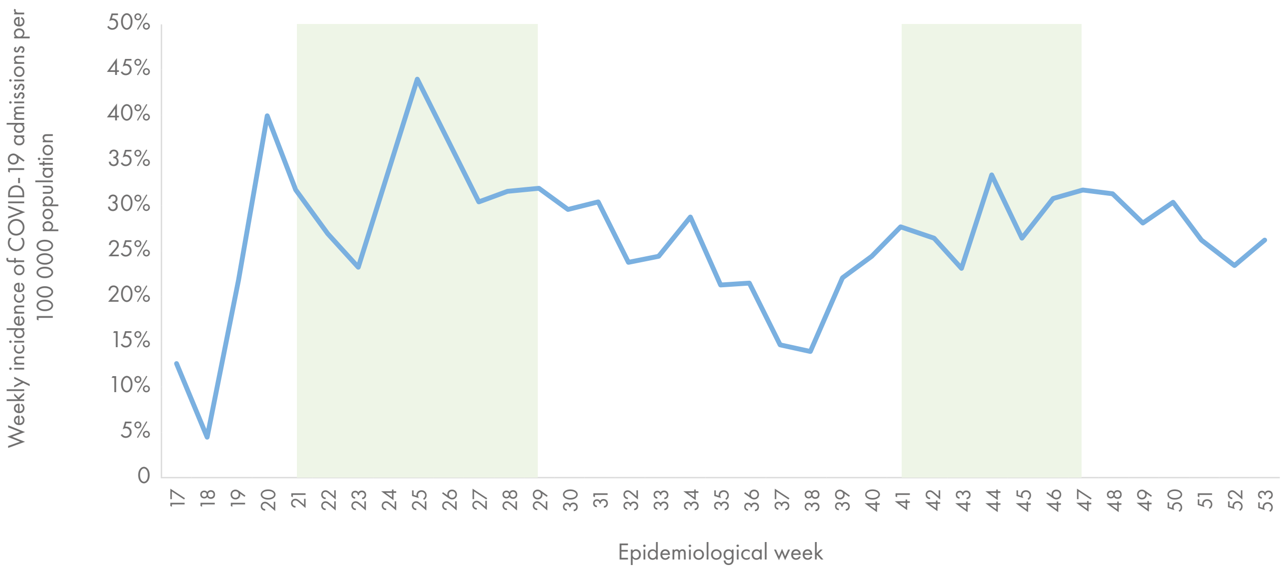

Figure 10: COVID-19 in-hospital case fatality ratio reported per week by health sector and epidemiologic week. Shading shows the time periods of the early first and second waves, Nelson Mandela Bay Metro, 5 March 2020-2 January 2021.

Multivariable analysis, comparing characteristics of hospitalised individuals in the early first and second waves, after adjusting for weekly district hospital admissions, shows that there was no increase in in-hospital mortality in the second wave [aOR 0.9, 95% CI (0.8 – 1.1)]. The factors more common in the second wave were admission in the public sector [aOR 1.2, 95% CI (1.0 – 1.5)], high weekly admissions [aOR 2.3, 95% CI (1.9 – 2.8)] and very high weekly admissions [aOR 5376.4, 95% CI (334.1 – 86510.4)] compared to low weekly admissions. The factors less common in the second wave were age 40-64 years [aOR 0.8, 95% CI (0.6 – 0.9)], and >60 years [aOR 0.8, 95% CI (0.6 – 0.9)], compared to <40 years; male sex [aOR 0.8, 95% CI (0.7 – 0.9)]; Black [aOR 0.7, 95% CI (0.5 – 0.9)] compared to White race; presence of a comorbid condition [aOR 0.8, 95% CI (0.6 – 0.9)]; and medium level of weekly admissions [aOR = 0.6, 95% CI (0.5 – 0.8)] (Table 4).

Multivariable analysis, after adjusting for weekly district hospital admissions, shows that the factors associated with in-hospital COVID-19 mortality were age 40-64 years [aOR 4.2, 95% CI (3.4 – 5.2)], and >60 years [aOR 11.2, 95% CI (8.9 – 14.0)], compared to <40 years; male sex [aOR 1.2, 95% CI (1.0 – 1.3)]; Black [aOR 1.6, 95% CI (1.2 – 2.0)] compared to White race; presence of a comorbid condition [aOR 1.4, 95% CI (1.2 – 1.6)]; and admission in the public sector [aOR 1.8, 95% CI (1.6 – 2.1)]. Compared to weeks with low numbers of district hospital admissions, there was an increased risk of mortality in weeks with medium level of weekly admissions [aOR 1.4, 95% CI (1.1 – 1.6)], high weekly admissions [aOR 1.3, 95% CI (1.1 – 1.6)] and very high weekly admissions [aOR 1.4, 95% CI (1.1 – 1.8)]. Compared to early wave 1, there was reduced risk of mortality in the late wave 1 period [aOR 0.8, 95% CI (0.6 – 0.9)]; and no difference in mortality in early wave 2 [aOR 1.0, 95% CI (0.8 – 1.1)]. (Table 5).

Table 4. Multivariable analysis of factors associated with the second COVID-19 wave among hospitalised individuals*, Nelson Mandela Bay Metro, 5 March 2020-9 January 2021.

Characteristic	First wave n (%) N=2450	Second wave n (%) N=2756	Adjusted OR	95% CI	Adjusted OR	95% CI
			Unadjusted for weekly admissions		Adjusting for weekly admissions	
Age group						
<40 years	485 (19.8)	636 (23.1)	Ref		Ref	
40-64 years	1415 (57.8)	1447 (52.5)	0.9	0.8-1.1	**0.8**	0.6-0.9
≥65 years	549 (22.4)	672 (24.4)	1.0	0.9-1.3	**0.8**	0.6-0.9
Sex						
Female	1326 (54.1)	1601 (58.1)	Ref		Ref	
Male	1124 (45.9)	1155 (41.9)	**0.8**	0.7-0.9	**0.8**	0.7-0.9
Race						
White	180 (7.4)	181 (6.6)	Ref		Ref	
Black	1717 (70.1)	1588 (57.6)	**0.6**	0.5-0.8	**0.7**	0.5-0.9
Coloured	273 (11.1)	517 (18.8)	1.2	0.9-1.6	1.0	0.7-1.5
Indian	17 (0.7)	8 (0.3)	**0.3**	0.1-0.7	0.3	0.1-1.2
Other	11 (0.5)	4 (0.2)	**0.2**	0.1-0.7	0.2	0.0-1.0
Unknown	252 (10.3)	458 (16.6)	**1.5**	1.2-2.0	1.3	0.9-1.9
Comorbid condition						
No co-morbidity	587 (24.0)	647 (23.5)	Ref		Ref	
Co-morbid condition	1306 (53.3)	881 (32.0)	**0.7**	0.6-0.9	**0.8**	0.6-0.9
Unknown	557 (22.7)	1228 (44.6)	**2.2**	1.8-2.7	**1.5**	1.2-1.9
Health sector						
Private sector	1157 (47.2)	1023 (37.1)	Ref		Ref	
Public sector	1293 (52.8)	1733 (62.9)	1.2	0.9-1.4	**1.2**	1.0-1.5
Outcome						
Discharged alive	1568 (68.2)	1809 (70.6)	Ref		Ref	
Died	731 (31.8)	754 (29.4)	1.1	0.9-1.2	0.9	0.8-1.1
Weekly admissions						
Low <200	479 (19.6)	180 (6.5)			Ref	
Medium 200-399	1015 (41.4)	251 (9.1)			**0.6**	0.5-0.8
High 400-599	956 (39.0)	972 (35.3)			**2.3**	1.9-2.8
Very high >600	0	1353 (49.1)			**5376.4**	334.1-86510.4

* Statistically significant estimates are shown in black colour

OR=Odds Ratio; CI=Confidence Interval

Table 5. Multivariable analysis of factors associated with mortality among individuals hospitalised with COVID-19, Nelson Mandela Bay Metro, 5 March 2020-9 January 2021.

Characteristic	Case Fatality Ratio n/N (%)	Adjusted OR	95% CI	Adjusted OR	95% CI
		Including wave periods		Adjusting for weekly admissions	
Age group					
<40 years	146/1774 (8.2)	Reference		Reference	
40-64 years	1238/4478 (27.7)	**4.3**	3.5-5.4	**4.2**	3.4-5.2
≥65 years	1049/2153 (48.7)	**11.4**	9.1-14.3	**11.2**	8.9-14.0
Sex					
Female	1280/4674 (27.4)	Reference		Reference	
Male	1153/3735 (30.9)	**1.2**	1.0-1.3	**1.2**	1.0-1.3
Race					
White	211/731 (28.9)	Reference		Reference	
Black	1376/4554 (30.2)	**1.6**	1.3-2.0	**1.6**	1.2-2.0
Coloured	394/1684 (23.4)	**1.3**	1.0-1.7	**1.3**	1.0-1.7
Indian	13/44 (29.6)	1.3	0.6-3.0	1.3	0.6-3.0
Other	7/22 (31.8)	2.0	0.7-5.8	2.1	0.7-6.2
Unknown	432/1375 (31.4)	**2.0**	1.5-2.6	**2.0**	1.5-2.6
Comorbid condition					
No co-morbidity	621/2275 (27.3)	Reference		Reference	
Co-morbid condition	1249/3314 (37.7)	**1.4**	1.2-1.6	**1.4**	1.2-1.6
Unknown	563/2821 (20.0)	**0.6**	0.4-0.7	**0.5**	0.4-0.7
Health sector					
Private sector	1089/3771 (28.9)	Reference		Reference	
Public sector	1344/4639 (29.0)	**1.8**	1.6-2.1	**1.8**	1.6-2.1
Wave period					
Pre-wave 1	46/176 (26.1)	**0.6**	0.4-0.9	0.8	0.5-1.1
Early wave 1	731/2299 (31.8)	Reference		Reference	
Late wave 1/post	324/1337 (24.2)	**0.7**	0.6-0.8	**0.8**	0.6-0.9
Early wave 2	754/2563 (29.4)	1.0	0.9-1.2	1.0	0.8-1.1
Weekly admissions					
Low <200	364/1566 (26.2)			Reference	
Medium 200-399	553/1764 (32.1)			**1.4**	1.1-1.6
High 400-599	553/1798 (30.8)			**1.3**	1.1-1.6
Very high >600	385/1247 (30.9)			**1.4**	1.1-1.8

* Statistically significant estimates are shown in black colour

OR=Odds Ratio; CI=Confidence Interval

City of Cape Town

The weekly numbers of COVID-19 admissions in City of Cape Town Metro peaked at 1251 in the first wave and 2330 in the second wave. The time the district took to go from 5 admissions per 100,000 to 30 admissions per 100,000 population in the first wave was 9 weeks and in the second wave was 4 weeks (Figure 11).

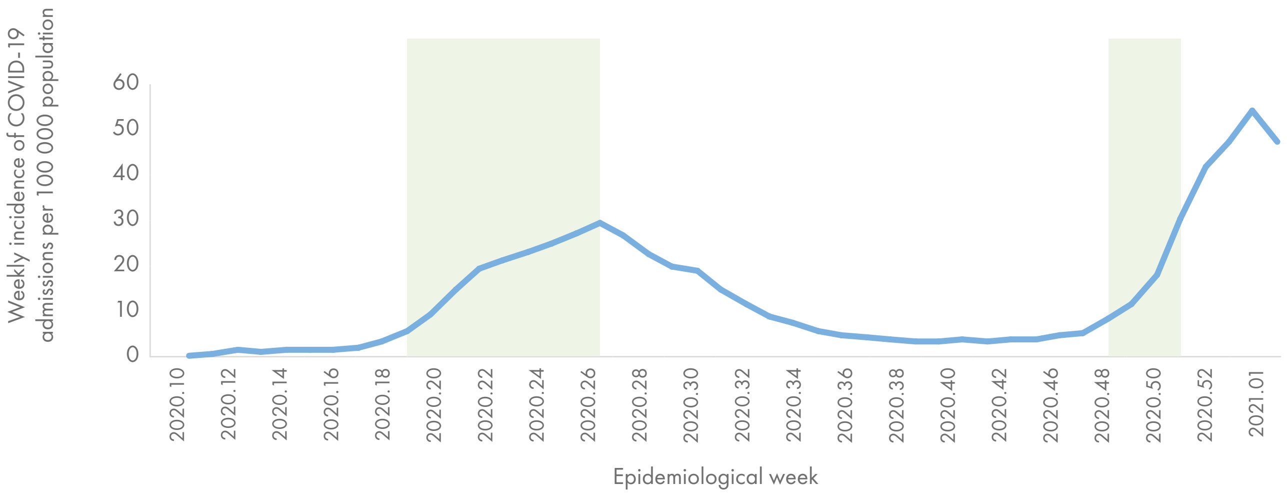

Figure 11. Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows the time period from 5 admissions per 100,000 to 30 admissions per 100,000 in the first and second waves, City of Cape Town Metro, 5 March 2020-9 January 2021, n=26,554.

Using the time period from incidence risk of 5 admissions per 100,000 to peak to define the early wave, the period of analysis of the pre-wave 1, early wave 1, late wave 1 and early wave 2 are depicted in Figure 12.

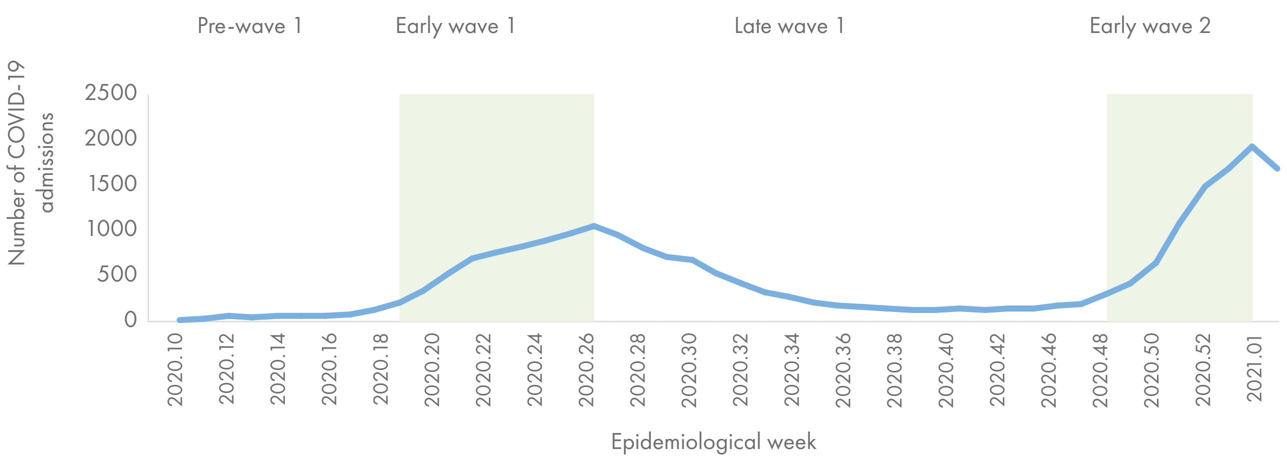

Figure 12. Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows the time periods of early first and second waves, City of Cape Town Metro, 5 March 2020-9 January 2021, n=26,554.

The weekly in-hospital CFR increased towards the peak of each wave and decreased between the first and second waves; and was similar between the first and second waves (Figure 13).

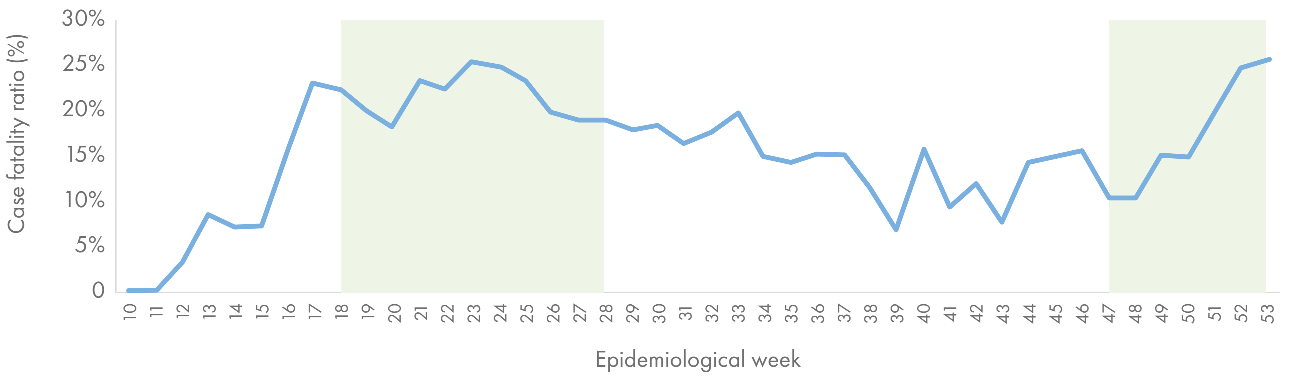

Figure 13. COVID-19 in-hospital case fatality ratio reported per week by health sector and epidemiologic week. Shading shows the time periods of the early first and second waves, City of Cape Town Metro, 5 March 2020-2 January 2021.

Multivariable analysis, comparing characteristics of hospitalised individuals in the early first and second waves, after adjusting for weekly district hospital admissions, shows that there was no increase in in-hospital mortality in the second wave [aOR 1.0, 95% CI (0.9 – 1.2)]. The factors more common in the second wave were high weekly admissions [aOR 1.4, 95% CI (1.2 – 1.6)] and very high weekly admissions aOR 3513.7, 95% CI (219.0 – 56363.8)]. Less common factors in the second wave were male sex [aOR 0.8, 95% CI (0.7 – 0.9)]; Black [aOR 0.2, 95% CI (0.2 – 0.3)] compared to White race; presence of a comorbid condition [aOR 0.4, 95% CI (0.3 – 0.5)]; admission in the public sector [aOR 0.7, 95% CI (0.6 – 0.8)] and medium level of weekly admissions [aOR = 0.1, 95% CI (0.1 – 0.1)] compared to low level of weekly admissions (Table 6).

Multivariable analysis, after adjusting for weekly district hospital admissions, shows that the factors associated with in-hospital COVID-19 mortality were age 40-64 years [aOR 3.4, 95% CI (3.0 – 3.8)], and >60 years [aOR 8.2, 95% CI (7.3 – 9.3)], compared to <40 years; male sex [aOR 1.4, 95% CI (1.3 – 1.5)]; Black [aOR 1.7, 95% CI (1.3 – 2.2)] and Coloured race [aOR 1.6, 95% CI (1.3 – 2.1)] compared to White race; presence of a comorbid condition [aOR 1.7, 95% CI (1.5 – 1.9)]; and admission in the public sector [aOR 1.4, 95% CI (1.3 – 1.6)]. Compared to weeks with low numbers of district hospital admissions, there was increased risk of mortality in weeks with medium level of weekly admissions [aOR 1.4, 95% CI (1.2 – 1.5)], high weekly admissions [aOR 1.2, 95% CI (1.1 – 1.4)] and very high weekly admissions [aOR 1.8, 95% CI (1.5 – 2.1)]. Compared to early wave 1, there was reduced risk of mortality in the late wave 1 period [aOR 0.8, 95% CI (0.7 – 0.9)]; and no difference in mortality in early wave 2 [aOR 1.0, 95% CI (0.9 – 1.1)] (Table 7).

Table 6. Multivariable analysis of factors associated with the first and second waves among individuals hospitalised with COVID-19, City of Cape Town Metro, 5 March 2020-9 January 2021.

Characteristic	First wave n (%) N=7429	Second wave n (%) N=9041	Adjusted OR	95% CI	Adjusted OR	95% CI
			Unadjusted for weekly admissions		Adjusting for weekly admissions	
Age group						
<40 years	2002 (27.0)	1892 (20.9)	Reference		Reference	
40-64 years	3700 (49.8)	4527 (50.1)	**1.3**	1.1-1.4	1.1	0.9-1.3
≥65 years	1722 (23.2)	2566 (28.4)	**1.2**	1.1-1.4	1.1	0.9-1.3
Unknown	5 (0.1)	56 (0.6)	**9.4**	3.0-30.1	**5.5**	1.4-21.7
Sex						
Female	4081 (54.9)	4937 (54.6)	Reference		Reference	
Male	3348 (45.1)	4101 (45.4)	**0.8**	0.8-0.9	**0.8**	0.7-0.9
Unknown	0	3 (0)	2.2	0.1-48.6	<0.1	<0.1-<0.1
Race						
White	159 (2.1)	218 (2.4)	Reference		Reference	
Black	3367 (45.3)	491 (5.4)	**0.1**	0.1-0.2	**0.2**	0.2-0.3
Coloured	898 (12.1)	1081 (12.0)	0.8	0.6-1.0	1.1	0.8-1.5
Indian	46 (0.6)	34 (0.4)	**0.5**	0.3-0.8	0.6	0.3-1.3
Other	4 (0.1)	0	0.1	0.0-2.1	0.1	0.0-2.8
Unknown	2955 (39.8)	7217 (79.8)	**2.6**	2.1-3.3	**3.2**	2.3-4.4
Comorbid condition						
No co-morbidity	803 (10.8)	2288 (25.3)	Reference		Reference	
Co-morbid condition	4955 (66.7)	4140 (45.8)	**0.4**	0.3-0.4	**0.4**	0.3-0.5
Unknown	1671 (22.5)	2613 (28.9)	1.0	0.8-1.1	1.1	0.9-1.3
Health sector						
Private sector	2471 (33.3)	4008 (44.3)	Reference		Reference	
Public sector	4958 (66.7)	5033 (55.7)	**0.8**	0.7-0.9	**0.7**	0.6-0.8
Outcome						
Discharged alive	5739 (78.4)	6282 (77.9)	Reference		Reference	
Died	1584 (21.6)	1786 (22.1)	**1.1**	1.0-1.2	1.0	0.9-1.2
Weekly admissions						
Low <600	627 (8.4)	851 (9.4)			Reference	
Medium 600-1199	5551 (74.7)	760 (8.4)			**0.1**	0.1-0.1
High 1200-1799	1251 (16.8)	3074 (34.0)			**1.4**	1.2-1.6
Very high >1800	0	4356 (48.2)			**3513.7**	219.0-56363.8

* Statistically significant estimates are shown in black colour

OR=Odds Ratio; CI=Confidence Interval

Table 7. Multivariable analysis of factors associated with mortality among individuals hospitalised with COVID-19, City of Cape Town Metro, 5 March 2020-9 January 2021.

Characteristic	Case Fatality Ratio n/N (%)	Adjusted OR	95% CI	Adjusted OR	95% CI
		Including wave periods		Adjusting for weekly admissions	
Age group					
<40 years	363/5950 (6.1)	Reference		Reference	
40-64 years	2254/11694 (19.3)	**3.4**	3.0-3.9	**3.4**	3.0-3.8
≥65 years	2248/6309 (35.6)	**8.3**	7.4-9.4	**8.2**	7.3-9.3
Unknown	7/80 (8.8)	1.7	0.7-4.0	1.8	0.7-4.2
Sex					
Female	2385/13172 (18.1)	Reference		Reference	
Male	2487/10859 (22.9)	**1.4**	1.3-1.5	**1.4**	1.3-1.5
Unknown	0/2 (0)	0.5	0.0-10.2	0.4	0.0-8.4
Race					
White	90/593 (15.2)	Reference		Reference	
Black	1045/5552 (18.8)	**1.7**	1.3-2.2	**1.7**	1.3-2.2
Coloured	503/2753 (18.3)	**1.6**	1.3-2.1	**1.6**	1.3-2.1
Indian	18/111 (16.2)	1.3	0.7-2.3	1.3	0.7-2.3
Other	0/4 (0)	1.2	0.1-26.3	1.5	0.1-33.0
Unknown	3216/15020 (21.4)	**1.4**	1.1-1.8	**1.5**	1.1-1.9
Comorbid condition					
No co-morbidity	492/4283 (11.5)	Reference		Reference	
Co-morbid condition	339013548 (25.0)	**1.7**	1.5-1.9	**1.7**	1.5-1.9
Unknown	990 (16.0)	**1.2**	1.1-1.4	**1.2**	1.1-1.4
Health sector					
Private sector	1521/9401 (16.2)	Reference		Reference	
Public sector	3351/14632 (22.9)	**1.5**	1.3-1.6	**1.4**	1.3-1.6
Wave period					
Pre-wave	71/466 (15.2)	0.8	0.6-1.0	1.0	0.8-1.4
Early wave 1	1584/7323 (21.6)	Reference		Reference	
Late wave 1/post	1215/7453 (16.3)	**0.7**	0.7-0.8	**0.8**	0.7-0.9
Early wave 2	1786/8068 (22.1)	**1.1**	1.0-1.2	1.0	0.9-1.1
Weekly admissions					
Low <600	708/5043 (15.8)			Reference	
Medium 600-1199	2179/10504 (22.2)			**1.4**	1.2-1.5
High 1200-1799	828/4146 (20.0)			**1.2**	1.1-1.4
Very high >1800	941/3617 (26.0)			**1.8**	1.5-2.1

* Statistically significant estimates are shown in black colour

OR=Odds Ratio; CI=Confidence Interval

eThekwini Metro

The weekly numbers of admissions in eThekwini Metro peaked at 1087 in the first wave and 1397 in the second wave. The time the district took to go from 5 admissions per 100,000 to 30 admissions per 100,000 population in the first wave was 6 weeks and for the second wave was 4 weeks (Figure 14).

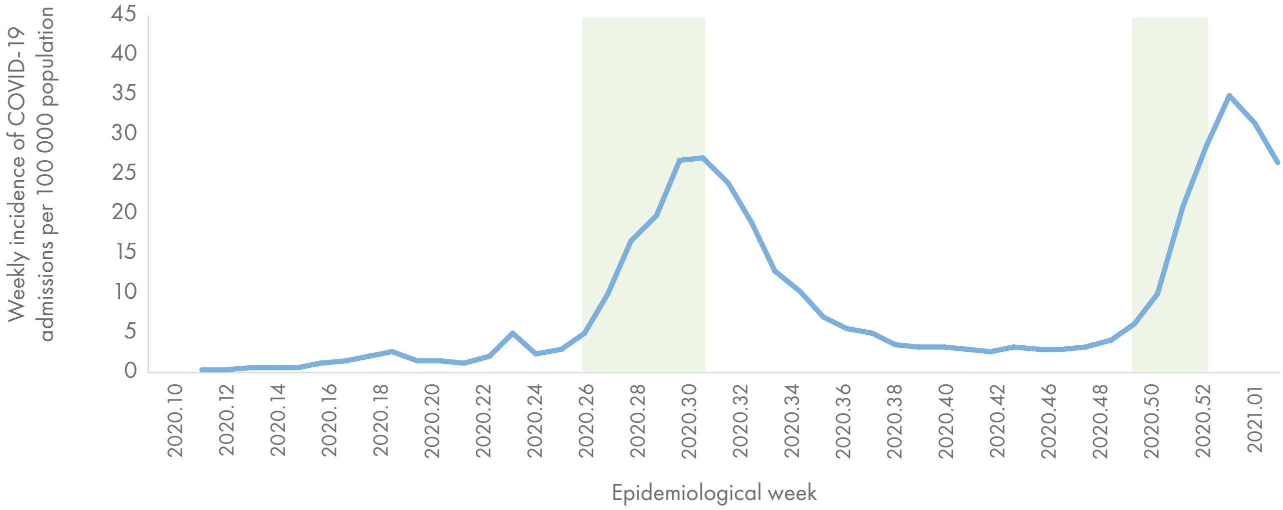

Figure 14. Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows time period from 5 admissions per 100,000 to 30 admissions per 100,000 in the first and second wave, eThekwini Metro, 5 March 2020-9 January 2021, n=15,734.

Using the time period from incidence risk of 5 admissions per 100,000 to peak to define the early wave, the period of analysis of the pre-wave 1, early wave 1, late wave 1 and early wave 2, are depicted in Figure 15.

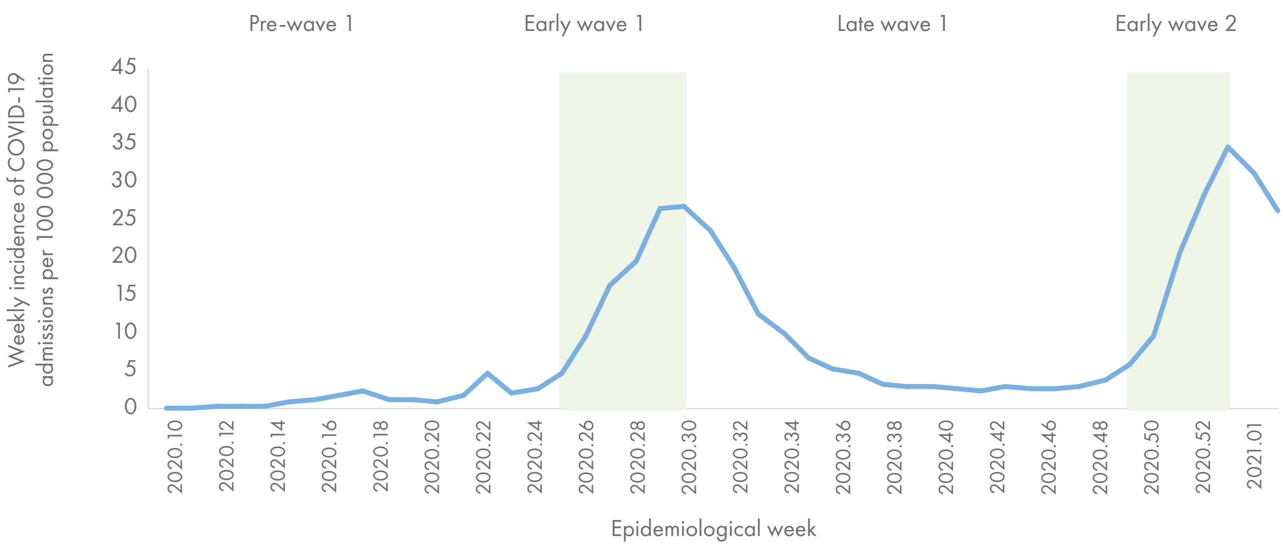

Figure 15. Weekly incidence per 100,000 population of COVID-19 admissions by epidemiologic week. Shading shows the time periods of the early first and second waves, eThekwini Metro, 5 March 2020-9 January 2021, n=15,734.

The weekly in-hospital CFR increased towards the peak of each wave, but remained high in the post wave 1 period for a further 10 weeks. The CFR increased in the second wave to a higher level than the first wave (Figure 16).

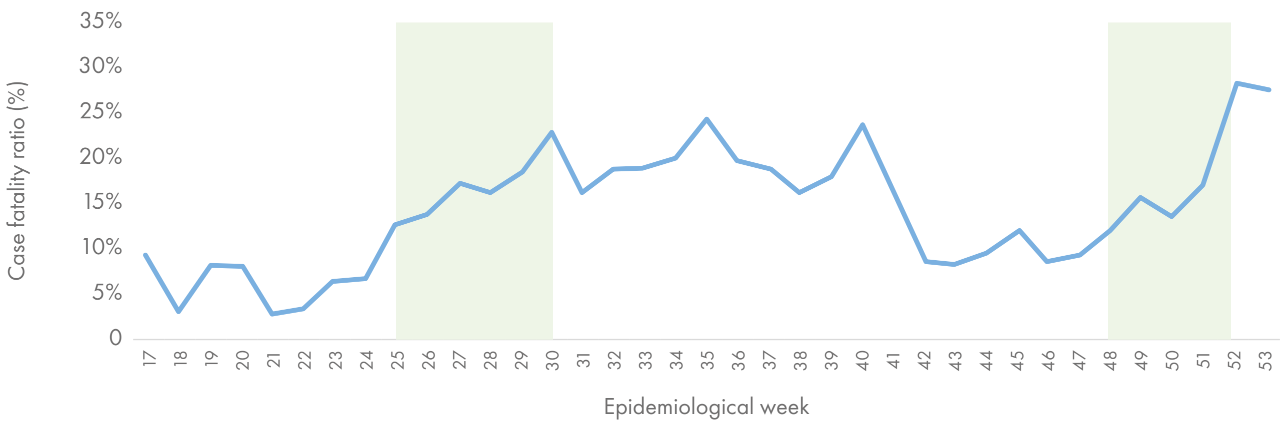

Figure 16. COVID-19 in-hospital case fatality ratio reported per week by health sector and epidemiologic week. Shading shows the time periods of the early first and second waves, eThekwini Metro, 5 March 2020-2 January 2021.

Multivariable analysis, comparing characteristics of hospitalised individuals in the early first and second waves, after adjusting for weekly district hospital admissions, shows that there was no increase in in-hospital mortality in the second wave [aOR 1.1, 95% CI (0.9 – 1.3)]. The factors more common in the second wave were very high level of weekly admissions [aOR = 1808.9, 95% CI (112.7 – 29035.7)] compared to low level of weekly admissions. The factors less common in the second wave were Black [aOR 0.4, 95% CI (0.3 – 0.5)] and Indian race [aOR 0.6, 95% CI (0.5 – 0.9)] compared to White race; presence of a comorbid condition [aOR 0.7, 95% CI (0.6 – 0.8)]; and medium level of weekly admissions [aOR = 0.5, 95% CI (0.4 – 0.6)] or high level of weekly admissions [aOR = 0.4, 95% CI (0.4 – 0.5)] compared to low level of weekly admissions (Table 8).

Multivariable analysis, after adjusting for weekly district hospital admissions, shows that the factors associated with in-hospital COVID-19 mortality were age 40-64 years [aOR 3.1, 95% CI (2.6 – 3.7)], and >65 years [aOR 10.3, 95% CI (8.6 – 12.4)], compared to <40 years; male sex [aOR 1.3, 95% CI (1.2 – 1.4)]; presence of a comorbid condition [aOR 1.7, 95% CI (1.5 – 1.9)]; and admission in the public sector [aOR 1.8, 95% CI (1.6 – 2.1)]. Compared to weeks with low numbers of district hospital admissions, there was increased risk of mortality in weeks with medium level of weekly admissions [aOR 1.2, 95% CI (1.0 – 1.4)], high weekly admissions [aOR 1.2, 95% CI (1.1 – 1.4)] and very high weekly admissions [aOR 1.6, 95% CI (1.3 – 2.0)]. Compared to early wave 1, there was reduced risk of mortality in the pre-wave 1 period [aOR 0.7, 95% CI (0.5 – 0.9)] and late wave 1 period [aOR 0.8, 95% CI (0.7 – 0.9)]; and no difference in mortality in early wave 2 [aOR 1.1, 95% CI (0.9 – 1.3)] (Table 9).

Table 8. Multivariable analysis of factors associated with the first and second wave among individuals hospitalised with COVID-19, eThekwini Metro, 5 March 2020-9 January 2021.

Characteristic	First wave n (%) N=4168	Second wave n (%) N=3990	Adjusted OR	95% CI	Adjusted OR	95% CI
			Unadjusted for weekly admissions		Adjusting for weekly admissions	
Age group						
<40 years	1049 (25.2)	846 (21.2)	Reference		Reference	
40-64 years	2323 (55.7)	2296 (57.5)	1.0	0.9-1.2	1.0	0.9-1.2
≥65 years	794 (19.1)	836 (21.0)	0.9	0.7-1.0	0.8	0.7-1.0
Unknown	2 (0.1)	12 (0.3)	2.2	0.4-13.2	1.7	0.3-9.6
Sex						
Female	2400 (57.6)	2183 (54.7)	Reference		Reference	
Male	1768 (42.4)	1803 (45.2)	1.0	0.9-1.1	0.9	0.8-1.1
Unknown	0	4 (0.1)	14.7	0.8-280.1	22.1	1.1-450.9
Race						
White	121 (2.9)	187 (4.7)	Reference		Reference	
Black	2901 (69.6)	1768 (44.3)	**0.4**	0.3-0.5	**0.4**	0.3-0.5
Coloured	55 (1.3)	95 (2.4)	1.1	0.7-1.7	1.0	0.6-1.7
Indian	924 (22.2)	968 (24.3)	**0.7**	0.5-0.9	**0.6**	0.5-0.9
Other	5 (0.1)	3 (0.1)	0.5	0.1-2.8	0.4	0.1-3.2
Unknown	162 (3.9)	969 (24.3)	**3.4**	2.6-4.7	**3.2**	2.3-4.4
Comorbid condition						
No co-morbidity	1533 (36.8)	2145 (53.8)	Reference		Reference	
Co-morbid condition	1856 (44.5)	1379 (34.6)	**0.7**	0.6-0.8	**0.7**	0.6-0.8
Unknown	779 (18.7)	466 (11.7)	**0.6**	0.5-0.7	**0.6**	0.5-0.7
Health sector						
Private sector	2672 (64.1)	2915 (73.1)	Reference		Reference	
Public sector	1496 (35.9)	1075 (26.9)	1.1	0.9-1.2	1.0	0.9-1.2
Outcome						
Discharged alive	3233 (80.5)	2526 (77.4)	Reference		Reference	
Died	782 (19.5)	739 (22.6)	**1.2**	1.0-1.4	1.1	0.9-1.3
Weekly admissions						
Low <500	569 (13.7)	624 (15.6)			Reference	
Medium 500-899	1443 (34.6)	835 (20.9)			**0.5**	0.4-0.6
High 900-1299	2156 (51.7)	1136 (28.5)			**0.4**	0.4-0.5
Very high >1300	0	1395 (35.0)			**1808.9**	112.7-29035.7

* Statistically significant estimates are shown in black colour
OR=Odds Ratio; CI=Confidence Interval

Table 9. Multivariable analysis of factors associated with mortality among individuals hospitalised with COVID-19, eThekwini Metro, 5 March 2020-9 January 2021.

Characteristic	Case Fatality Ratio n/N (%)	Adjusted OR	95% CI	Adjusted OR	95% CI
		Including wave periods		Adjusting for weekly admissions	
Age group					
<40 years	190/3325 (5.7)	Reference		Reference	
40-64 years	1277/7141 (17.9)	**3.2**	2.7-3.8	**3.1**	2.6-3.7
≥65 years	1164/2806 (41.5)	**10.5**	8.8-12.6	**10.3**	8.6-12.3
Unknown	2/23 (8.7)	2.1	0.5-8.1	2.1	0.5-8.1
Sex					
Female	1349/7495 (18.0)	Reference		Reference	
Male	1284/5793 (22.2)	**1.3**	1.2-1.4	**1.3**	1.2-1.4
Unknown	0/7 (0)	0.2	0.0-3.6	0.2	0.0-3.5
Race					
White	129/588 (21.9)	Reference		Reference	
Black	1275/7276 (17.5)	1.2	0.9-1.5	1.1	0.9-1.4
Coloured	42/213 (19.7)	1.0	0.6-1.5	1.0	0.6-1.5
Indian	656/3231 (20.3)	1.2	0.9-1.5	1.2	0.9-1.5
Other	3/15 (20.0)	3.2	0.8-13.2	3.3	0.8-13.6
Unknown	528/1972 (26.8)	**1.9**	1.5-2.4	**1.9**	1.4-2.4
Comorbid condition					
No co-morbidity	985/6126 (16.1)	Reference		Reference	
Co-morbid condition	1309/4927 (26.6)	**1.7**	1.5-1.9	**1.7**	1.5-1.9
Unknown	339/2242 (15.1)	**0.8**	0.6-0.9	**0.8**	0.6-0.9
Health sector					
Private sector	1758/9224 (19.1)	Reference		Reference	
Public sector	875/4071 (21.5)	**1.8**	1.6-2.1	**1.8**	1.6-2.1
Wave period					
Pre-wave	85/827 (10.3)	**0.6**	0.5-0.7	**0.7**	0.5-0.9
Early wave 1	782/4015 (19.5)	Reference		Reference	
Late wave 1/post	699/4144 (16.9)	**0.8**	0.7-0.9	**0.8**	0.7-0.9
Early wave 2	739/3265 (22.6)	**1.2**	1.1-1.4	1.1	0.9-1.3
Weekly admissions					
Low <500	586/3918 (15.0)			Reference	
Medium 500-899	630/3313 (19.0)			**1.2**	1.0-1.4
High 900-1299	812/3966 (20.5)			**1.2**	1.1-1.4
Very high >1300	277/1054 (26.3)			**1.6**	1.3-2.0

* Statistically significant estimates are shown in black colour
OR=Odds Ratio; CI=Confidence Interval

Discussion

In the metros of Nelson Mandela Bay, City of Cape Town and eThekwini, weekly COVID-19 cases, admissions and in-hospital deaths in the second wave exceeded the numbers in the first wave. There was also a faster increase of weekly incidence for COVID-19 admissions in the second wave. The second COVID-19 wave in South Africa is associated with the emergence of a new lineage 501Y.V2, with preliminary data suggesting this lineage made up the majority of cases in the three provinces first affected by the second wave.[2]

Nationally and in all three districts, the in-hospital CFR increased toward the peak of the first and second waves. On multivariable analysis, in all three districts, there was increased risk for mortality in weeks with medium, high or very high levels of weekly admissions. In weeks with very high weekly district admissions, mortality increased by 40% in Nelson Mandela Bay Metro, 60% in eThekwini Metro, and 80% in City of Cape Town Metro, compared to weeks with low weekly district admissions. The observed increase in mortality of hospitalized patients at the peaks of the first and second waves reflects increasing pressure on the health system. An important focus of the COVID-19 response in districts where case numbers are still increasing should be efforts to strengthen health system readiness and prepare for ongoing surges in case numbers.

Multivariable analysis, when adjusted for weekly district hospital admissions, showed that there was no difference in in-hospital mortality between the first and second wave in all three districts. While we did not have individual-level data on infecting lineage for cases included in this analysis, our data do not suggest that there is an increased mortality associated with the new lineage. It is however possible that in-hospital COVID-19 mortality would have decreased in the second wave because of the introduction of interventions proven to improve outcomes, such as steroids and high flow oxygen. It is also important to note that ecological analyses like these have intrinsic limitations as many factors can change between periods.

In the second wave in all three districts, individuals having comorbidities and being of Black race were less likely to be admitted to hospital in comparison to the first wave. In one district admissions were generally younger during the second wave but age distribution was similar in the other two districts. The lower proportion of reported comorbidities in the second wave, even accounting for age distribution, could reflect differences in clinician practice, survival bias, variation in reporting of comorbidities or changing manifestation in individuals without underlying illness.

A major limitation of this analysis is possible residual confounding as we could not adjust for several factors including burden of non-COVID-19 admissions, changes in treatment administration, the impact of national restrictions and change in individual preventive behaviour. In addition, we did not have data on the lineage type infecting individuals included in the analysis. Individual level studies comparing outcomes of people with and without the new lineage based on sequencing data are needed. Our analysis of epidemiologic characteristics of cases and in-hospital mortality in the first and second wave only included three districts and therefore may not be generalizable to the rest of South Africa.

Limitations of the DATCOV surveillance programme

DATCOV now includes reporting from all hospitals with COVID-19 admissions, but many hospitals are yet to reach complete submission of historic data. Data quality in a surveillance system is dependent on the information submitted by healthcare institutions. It is not possible for the National Institute for Communicable Diseases (NICD) to verify or check the quality of all these data although the NICD does have some built-in data quality checks. Delays in reporting of admissions and deaths may affect the numbers reported in the most recent week. The National Department of Health is in the process of recruiting data capturers to support hospitals to improve data submission.

DATCOV only reports hospital-based admissions and deaths and therefore current data do not include deaths occurring outside hospitals. DATCOV now has a module to record out-of-hospital deaths.

Acknowledgements

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