Supplementary material:

Prevalence of anti-SARS-CoV-2 antibodies in the Eswatini population and subsequent severity of the fourth Covid-19 epidemic wave.

Supplementary Appendix

SUPPLEMENTARY METHODS

Study setting and sero-survey

The vaccination programme in Eswatini was initiated in March 2021 and by May 2021 after administering 35 000 doses (3% of the national population), vaccination stopped until August 2021 due to limited vaccine supply. Currently, approximately 40% of the Eswatini population ever received a Covid-19 vaccine.

RESULTS

Decoupling of cases

Stratifying analyses by region indicated Shiselweni's first wave was the mildest peaking approximately 4 weeks after the onset of the first wave in the other 3 regions. Additionally, Shiselweni had the highest number of cases during the third compared to the fourth wave, unlike the other 3 regions, and had the earliest decoupling of cases from deaths and hospitalizations evident as early as during the third wave (Figure 1B-E).

DISCUSSION

Study limitations:

Similar to other resource constraints settings, limitations in Covid-19 testing may have inadvertently led to under-reporting of cases and over estimation of case fatality rates. The converse is true where under-reporting of deaths could have under-estimated mortality, excess mortality estimates are helpful in addressing under ascertainment of Covid-19 related deaths and such data are not available in Eswatini.

Variability in case numbers and disease severity by region may partly be driven by differences in access to health care and testing facilities by region. There could be differences in testing rates across the waves which may have contributed to differences in case numbers across the four waves.

Another limitation may be in over-emphasizing decoupling of Covid-19 cases from hospitalisations and deaths if infection and severity in earlier waves systematically selected against more susceptible individuals during the first two waves resulting in fewer high-risk individuals in subsequent waves.

Supplementary Table S1: Cumulative reported Covid-19 cases, hospitalizations and recorded deaths in Eswatini by region and Covid-19 wave

Outcomes	Wave 1	Wave 2	Wave 3	Wave 4	TOTAL
Period of case wave	Feb. 24, 2020 - Oct. 12 2020	Oct. 13, 2020 – May 24, 2021	May 2,5 2021 – Nov. 21, 2021	Nov. 22, 2021 – June 23, 2022	
Eswatini					
Recorded cases -no†	6008	7399	13492	26583	53482
Cumulative case rate per 100,000 population	517.9	637.8	1163	2291.4	4610.1
Proportion of total cumulative cases, %	11.2	13.8	25.2	49.7	100.0
Hospitalizations– no.‡	1871	3876	3436		9183
Cumulative hospitalisation rate per 100,000 population	161.3	334.1	296.2		791.6
Reported cases: recorded Covid-19 hospitalisation ratio	3.2	1.9	3.9		5.8
Recorded deaths in wave – no.	179	536	530	167	
Cumulative recorded death rate per 100,000 population	15.4	46.2	45.7	11.3	
Reported cases: recorded Covid-19 deaths ratio	33.6	13.8	25.5	159.2	
Case Fatality Risk, %	3.0	7.2	3.9	0.6	0.0
Hhohho					
Recorded cases -no†	1447	1658	3784		6889
Cumulative case rate per 100,000 population	428.3	490.7	1120		2039
Proportion of total cumulative cases, %	21.0	24.1	54.9	0.0	1
Hospitalizations– no.‡	727	879	818		
Cumulative hospitalisation rate per 100,000 population	215.2	260.1	242.1		
Reported cases: recorded Covid-19 hospitalisation ratio	2.0	1.9	4.6		
Recorded deaths in wave – no.	97	141	143		
Cumulative recorded death rate per 100,000 population	28.7	41.7	42.3		
Reported cases: recorded Covid-19 deaths ratio	14.9	11.8	26.5		
Case Fatality Risk, %	6.7	8.5	3.8		0.0
Lubombo					
Recorded cases -no†	1795	1653	1812		5260
Cumulative case rate per 100,000 population	827.6	762.1	835.4		
Proportion of total cumulative cases, %	0.3	0.3	0.3	0	1
Hospitalizations– no.‡	297	532	371		1200
Cumulative hospitalisation rate per 100,000 population	136.9	245.3	171		553.2
Reported cases: recorded Covid-19 cases ratio	6.0	3.1	4.9		4.4
Recorded deaths in wave – no.	10	76	29		

Cumulative recorded death rate per 100,000 population	4.6	35	13.4			
Reported cases: recorded Covid-19 deaths ratio	179.5	21.8	62.5			
Case Fatality Risk, %	0.6	4.6	1.6			0.0
Manzini						
Recorded cases -no†	2281	2926	3102			8309
Cumulative case rate per 100,000 population	609.6	781.9	829			
Proportion of total cumulative cases, %	0.3	0.4	0.4	0		1
Hospitalizations– no.‡	465	1431	1693			
Cumulative hospitalisation rate per 100,000 population	124.3	382.4	452.4			
Reported cases: recorded Covid-19 hospitalisations ratio	4.9	2.0	1.8			
Recorded deaths in wave – no.	60	233	234			
Cumulative recorded death rate per 100,000 population	16.0	62.3	62.5			
Reported cases: recorded Covid-19 deaths ratio	38.0	12.6	13.3			
Case Fatality Risk, %	0.03	0.08	0.08			0.00
Shiselweni						
Recorded cases -no†	485	1162	4794			6441
Cumulative case rate per 100,000 population	209.8	502.7	2073.9			
Proportion of total cumulative cases, %	8	18	74	0		100
Hospitalizations– no.‡	382	1034	554			
Cumulative hospitalisation rate per 100,000 population	165.3	447.3	239.6			
Reported cases: recorded Covid-19 hospitalisations ratio	1.3	1.1	8.7			
Recorded deaths in wave – no.	12	86	124			
Cumulative recorded death rate per 100,000 population	5.2	37.2	53.6			
Reported cases: recorded Covid-19 deaths ratio	40.4	13.5	38.7			
Case Fatality Risk, %	2.5	7.4	2.6			0.0

Covid-19 waves were defined as wave 1 Feb. 24, 2020 - Oct. 12 2020; wave 2 Oct. 13, 2020 – May 24, 2021; wave 3 May 2,5 2021 – Nov. 21, 2021 and wave 4 Nov. 22, 2021 – June 23, 2022.

Case fatality risk was calculated as number of deaths from total cases and ratio of reported cases: reported deaths was calculated as the inverse of case fatality risk

SUPPLEMENTARY REFERENCES

1. Madhi SA, Kwatra G, Myers JE, et al. Population Immunity and Covid-19 Severity with Omicron Variant in South Africa. New Eng J Med 2022;386:1314-26.