Supplemental Material

Supplemental Acknowledgements

Supplemental Methods

Baseline data were obtained from participants from the following clinical research sites (CRS): Aurum Institute Klerksdorp CRS, CAPRISA eThekwini CRS, CAPRISA Vulindlela CRS, Clinical HIV Research Unit (CHRU)/Helen Joseph CRS, Emavundleni CRS, Groote Schuur HIV CRS, Isipingo CRS, Josha Research CRS, Masiphumelele Clinical Research Site (MASI), Ndlovu Research Centre CRS, Nelson Mandela Academic Research Unit CRS, Qhakaza Mbokodo Research Clinic CRS, Rustenburg CRS, Soweto - Kliptown CRS, Synergy Biomed Research Institute, Synexus Stanza Clinical Research Centre CRS, TASK Central, Tembisa Clinic 4, Tongaat CRS, University of Cape Town Lung Institute CRS, and Wits RHI Ward 21 CRS. The protocol was approved by all local Institutional Review Boards and participants gave informed consent.

Participant symptom data were considered available and used for analysis if daily symptom data were entered into the study database for at least five of the seven post-PCR positive days, or if data were entered for between one and four of the seven days and an overall assessment was completed and the outcome consistent with daily symptoms that were entered.

Participants' PCR positivity was reported by SARS-CoV-2 serostatus and $CD4^+$ T-cell category overall and jointly with 95% confidence intervals and compared using chi-squared tests. Logistic regression was used to assess the relationship between PCR positivity and CD4 count, adjusting for baseline serostatus. CD4 counts were modeled on the log10 scale. Results from the adjusted and interaction models are summarized below. All tests were two-sided, and p-values < 0.05 were considered statistically significant.

Model	Parameter	Est. log odds	Std. err	Est. odds	p-value
Adjusted	log10(CD4)	-1.18	0.40	0.31 (0.14, 0.67)	0.003
	Seronegative	2.32	1.08	10.15 (1.23, 83.83)	0.032
	Seropositive	1.73	1.11	5.66 (0.64, 50.12	0.119
Interaction	(Intercept)	1.44	1.40		0.303
	log10(CD4)	-0.85	0.52		0.099
	Seropositive	1.56	2.22		0.481
	Seropositive x log10(CD4)	-0.78	0.80		0.331

Supplemental Tables and Figures

Supplemental Table 1. Prevalence of asymptomatic SARS-CoV-2 infection upon entry in vaccine studies.

Trial	Vaccine (developer)	Location	Dates	Predominant variant	Total participants	SARS-CoV-2 PCR+ [†]	Prevalence
COVE (CoVPN 3001; NCT04470427)	mRNA-1273 (Moderna)	US	Aug-Oct 2020	Ancestral	30,022	182	0.6%
Teen COVE (NCT04649151)	mRNA-1273 (Moderna)	US	Dec 2020-Feb 2021	Ancestral	3,469	22	0.6%
Ensemble (CoVPN 3003; NCT04505722.)	Ad26.COV2.S (Janssen)	US, South Africa, S. America	Sept 2021-Jan 2020	USA: ancestral South Africa: Beta S. America: Gamma, ancestral, P.2	Overall: 41,273 PWH[§]: 1,227	Overall: 227 PWH[§]: 7	Overall: 0.55% PWH[§]: 0.58%
Sisonke substudy (NCT04838795)	Ad26.COV2.S (Janssen)	South Africa	June-Aug 2021	Delta	1,604	39	2.4%
Ubuntu (CoVPN 3008; NCT05168813)	mRNA-1273 (Moderna)	South Africa	Dec 2021-ongoing	Omicron	719*	162*	23%

[†] At time of vaccination visit
[§] Most enrollment of people with HIV (PWH) occurred in South Africa
* Participants with baseline data as of Jan 20, 2022
Asymptomatic was defined as clinically well and without COVID-19 symptoms.

Supplemental Table 2. SARS-CoV-2 PCR positivity by South African province and participant serostatus.

	Total participants	SARS-CoV-2 PCR+	Prevalence
Serostatus			
SARS-CoV-2 Seronegative	317	95	30%
SARS-CoV-2 Seropositive	402	67	17%
Total	**719**	**162**	**23%**
Province			
Gauteng	142	44	31%
KwaZulu Natal	291	58	20%
Eastern Cape	64	9	14%
Limpopo	18	6	33%
Western Cape	112	29	26%
Mpumalanga	57	12	21%
North West	7	2	29%
Free State	28	2	7%
Total	**719**	**162**	**23%**

Supplemental Table 3. SARS-CoV-2 PCR positivity by CD4$^+$ T-cell count in PWH.

CD4$^+$ T-cell count (cells/mm^3)	SARS-CoV-2 PCR positive* (n)	Total (n)	% PCR positive (95% confidence interval)
Among total study population of PWH			
500 and above	66	354	19% (15%, 23%)
less than 500	51	153	33% (26%, 41%)
Total	**117**	**507**	**23% (20%, 27%)**
Among PWH by baseline SARS-CoV-2 serology			
SARS-CoV-2 seronegative			
500 and above	33	145	23% (17%, 30%)
less than 500	37	92	40% (31%, 50%)
Total	**70**	**237**	**30% (24%, 36%)**
SARS-CoV-2 seropositive			
500 and above	33	209	16% (12%, 21%)
less than 500	14	61	23% (14%, 35%)
Total	**47**	**270**	**17% (13%, 22%)**

*Positive cases are assumed to be Omicron, based on initial sequencing of some cases and epidemiological data.

Supplemental Table 4. Summary of cycle threshold (Ct) values by Fisher Taqpath for those samples with S gene drop out (n=56).

Target	n	Mean Ct	SD Ct	Min Ct	Median Ct	Max Ct
N gene	56	25.8	5.3	14.5	25.8	35.7
ORF1ab	56	25.2	5.5	14.4	25.7	34.1
Average N and ORF1a	56	25.4	5.4	14.4	25.8	34.9

Note Ct values of 20 and 25 correspond to log10 viral loads of approximately 6.5 and 5, respectively.

Supplemental Table 5. Persistence of asymptomatic presentation by SARS-CoV-2 serostatus.

Serostatus	Asymptomatic through 7 days follow up	Total	% Asymptomatic
SARS-CoV-2 seronegative	34	57	60%
SARS-CoV-2 seropositive	18	30	60%
Total	**52**	**87**	**60%**

Supplemental Table 6. Prevalence of asymptomatic SARS-CoV-2 infection by PCR in Sisonke substudy from enrollment through 6 months.

	Predominant variant(s)*	No. of participants	SARS-CoV-2 PCR+	Prevalence
Enrollment	Beta, Delta	1,604	39	2.4%
Week 3	Delta	1,447	51	3.5%
Week 6	Delta	1,260	25	2.0%
Month 6	Omicron	577	91	16%
HIV positive	*Omicron*	*169*	*27*	*16%*
HIV negative	*Omicron*	*405*	*62*	*15.3%*

*Source: https://covariants.org/per-country)

Month 6 participants sub divided by HIV status are in italics.
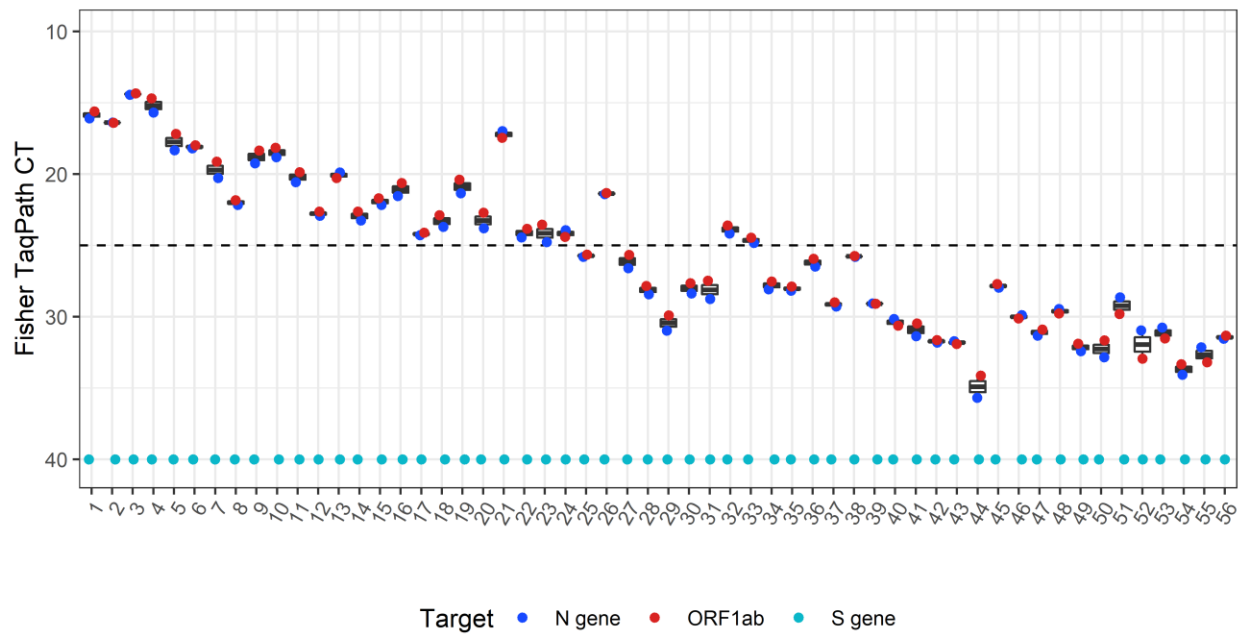
Supplemental Figure 1. Summaries of cycle threshold values. Ubuntu baseline positive swabs (x axis) with S gene target failure (n=56). Fisher Taqpath Ct arranged in order of increasing Abbott cycle number. Dotted line denotes Ct of 25. Note Ct values of 20 and 25 correspond to log10 viral loads of approximately 6.5 and 5, respectively.