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A cost-effectiveness analysis of South Africa's COVID-19 vaccination programme

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ABSTRACT

Background: COVID-19 vaccines were rolled out in South Africa beginning in February 2021. In this study we retrospectively assessed the cost-effectiveness of the vaccination programme in its first two years of implementation.
Method: We modelled the costs, expressed in 2021 US$, and health outcomes of the COVID-19 vaccination programme compared to a no vaccination programme scenario. The study was conducted from a public payer's perspective over two time-horizons – nine months (February to November 2021) and twenty-four months (February 2021 to January 2023). Health outcomes were estimated from a disease transmission model parameterised with data on COVID-19-related hospitalisations and deaths and were converted to disability adjusted life years (DALYs). Deterministic and probabilistic sensitivity analyses (DSA and PSA) were conducted to assess parameter uncertainty.
Results: Incremental cost-effectiveness ratio (ICER) was estimated at US$1600 per DALY averted during the first study time horizon. The corresponding ICER for the second study period was estimated at US$1300 per DALY averted. When 85% of all excess deaths during these periods were included in the analysis, ICERs in the first and second study periods were estimated at US$1070 and US$660 per DALY averted, respectively. In the PSA, almost 100% of simulations fell below the estimated opportunity cost-based cost-effectiveness threshold for South Africa (US$2300 DALYs averted). COVID-19 vaccination programme cost per dose had the greatest impact on the ICERs.
Conclusion: Our findings suggest that South Africa's COVID-19 vaccination programme represented good value for money in the first two years of rollout.

1. Introduction

The rollout of COVID-19 vaccination programmes in many countries contributed to halting the global COVID-19 pandemic. However, initial supply of COVID-19 vaccines was highly skewed in favour of high-income countries, with many low- and middle-income countries facing significant supply shortages. As a result, the rollout of COVID-19 vaccines was delayed in several African countries, with potential implications for the health benefits and cost-effectiveness of COVID-19 vaccination programmes in these settings [1].

South Africa rolled out its COVID-19 vaccination programme in February 2021. Prior to this, South Africa had experienced two waves of COVID-19, driven by the ancestral and Beta variants, respectively (Fig. 1), resulting in 217,891 recorded COVID-19-related hospitalisations and 47, 786 recorded in-hospital COVID-19 deaths between March 2020 and February 2021 [2]. The National Department of Health

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(NDOH) showed great commitment to rolling out the COVID-19 vaccination programme, and allocated a total of US$ 608 million[1] of domestic funds (representing 15% of total health budget) to the programme between March 2021 and February 2022 [3]. However, due to shortfalls in the supply of vaccines, a risk-based phased approach was adopted. In the first phase (February to May 2021), only healthcare workers were targeted with the Janssen (by Johnson and Johnson) vaccine as part of the Sisonke Trial. From May 2021, the COVID-19 vaccines were rolled out to the general population, starting with individuals over the age of 60 years and followed sequentially by individuals aged 50–59 years and individuals aged 35–49 years. By this time, both the Janssen (by Johnson and Johnson) and Comirnaty (by Pfizer-BioNTech) vaccines were being offered. The third phase of the vaccination programme began in August 2021, targeting individuals between the ages of 18 and 34 years. From mid-November 2021, COVID-19 vaccines were offered to all individuals over the age of 12 years, and by February 2022, all individuals over the age of 18 years were eligible to receive booster doses.

To maximise the pace of vaccine rollout, five delivery channels were utilised[4]. These included hospitals, primary healthcare facilities, mobile outreach channels and other outreach channels not traditionally used for vaccine delivery in South Africa, such as fixed outreach channels (mass vaccination sites) and temporary outreach channels [4]. Primary healthcare facilities and hospitals offered COVID-19 vaccines from specially designated areas within each facility while mobile outreach channels offered COVID-19 vaccines alongside other routine primary healthcare services. On the other hand, fixed and temporary outreach channels were used solely for administering COVID-19 vaccines to eligible populations.

The rollout of vaccines to the general population, starting in May 2021, coincided with the start of the third wave of COVID-19 (Fig. 1) which was the most fatal of the waves in South Africa[5]. Although at the time of the vaccine rollout, COVID-19 seroprevalence was estimated to be as high as 59% in some sub-populations[6], suggesting a high proportion of the population had developed immunity conferred by previous exposure to COVID-19, delays in mass vaccination across multiple age groups was likely a missed opportunity to avert many of the hospital admissions and deaths associated with the third wave.

In this study, we assessed the cost-effectiveness of South Africa's COVID-19 vaccination programme in its first two years of implementation. We compared the cost and health outcomes of the vaccination programme to a hypothetical counterfactual scenario where no vaccines were administered. In addition, we assessed the implication of South Africa's phased approach against the backdrop of high infection-derived immunity and the consecutively circulating milder COVID-19 Omicron variant, to inform ongoing discussions on targeted strategies as South Africa progresses towards a programme fully integrated into routine primary healthcare. While most studies have adopted a prospective approach in estimating the health and economic benefits of various prioritisation strategies under different scenarios [1,7,8,9,10,11,12,13], in this study, we retrospectively assessed an established programme; examining the health and economic impact of the vaccination programme over two time-horizons that represented different levels of vaccine coverage in different sub-populations and different predominant circulating COVID-19 variants at the time (Table 1 & Fig. 1).

From February 2022, the vaccination programme in South Africa began to evolve into an integrated model where COVID-19 vaccines

Table 1
Characteristics of study time horizon.

	Study period 1	Study period 2
CEA analysis period	February – November 2021	February 2021 – January 2023
Predominant COVID-19 variant	Delta	Delta + Omicron
Population targeted for vaccination	>18-year-olds	>12-year-olds + Boosters doses
Vaccination coverage by age group (%)		
12–17	5.7	34.63
18–34	26.82	40.09
35–49	45.69	55.04
50–59	58.65	65.56
60+	63.22	66.68
Total vaccine coverage	36.44	49
Total vaccination doses administered	24 886 437	38 418 222

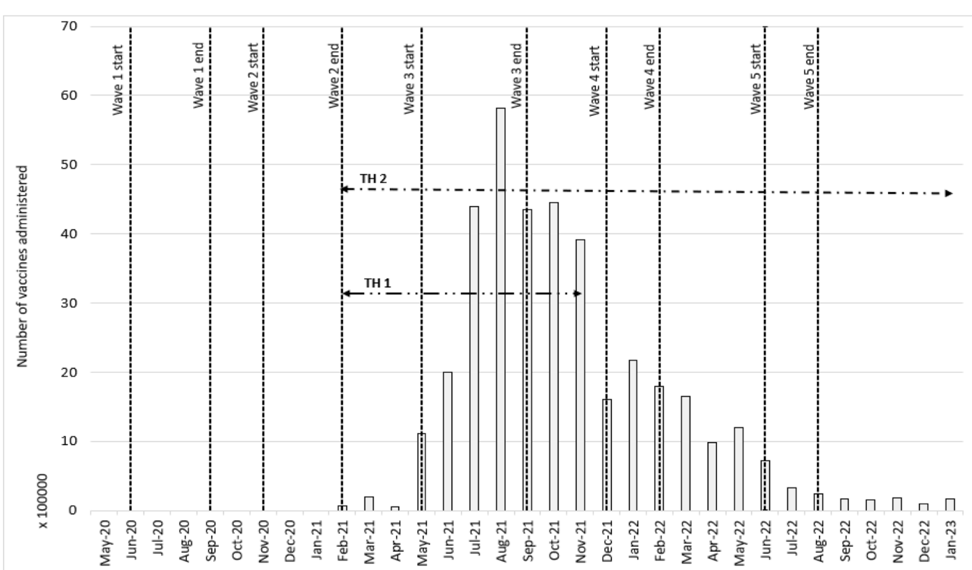


Fig. 1. COVID-19 waves, number of COVID-19 vaccine administered and study time horizon (TH), May 2020 to January 2023.

were offered as part of routine healthcare services in primary health facilities, hospitals, and mobile clinics and the gradual phase out of fixed and temporary outreach services. By February 2023, the programme had

[1] Estimated using an average 2021 US$-ZAR exchange rate of ZAR 16.61.

become fully integrated into existing service with the complete phase out of all fixed and temporary outreach services. Our approach to estimating the cost-effectiveness of the COVID-19 vaccination programme over two time-horizons provides useful insights to inform resources allocation decisions not only during future pandemics but also resource allocation decisions as the COVID-19 vaccination programme evolves in South Africa.

2. Methods

We developed an economic model to assess the cost-effectiveness of the COVID-19 vaccination programme over two study time horizons – nine months (from February 2021 to November 2021), and 24 months (from February 2021 to January 2023). The first period captured the initial phase of the programme when vaccination supply and uptake were at a peak [14] (Fig.1). The second period additionally captured the expansion phase of the programme to include wider age groups and the delivery of booster doses to eligible populations (Fig. 1). During this time, vaccine coverage had stagnated at approximately 50% of the eligible population [14]. The features of both study periods are summarised in Table 1. In each period, the vaccination programme was compared to a no vaccination scenario and the analysis was conducted from a public health payers' perspective. The economic model used epidemiological outputs from a COVID-19 disease transmission model [15] adapted to assess the health impact of the COVID-19 vaccination programme in South Africa.

3. Disease transmission model

We used outputs from a National COVID-19 Vaccine Model (NCVM) adapted from the National COVID-19 Epi Model (NCEM)[15]. A detailed description of the NCEM and NCVM, including the modelling assumptions and parameters such as vaccine effectiveness,[2] are provided elsewhere[15,16]. Briefly, the NCEM is an age-structured, multi-strain, compartmental transmission model of COVID-19, calibrated to estimate the incidence of COVID-19 infections, hospitalisations, and deaths in South Africa. The model follows a generalised Susceptible-Exposed-Infectious-Removed (SEIR) structure and accounts for disease severity (ranging from asymptomatic to critical conditions) and treatment pathways (including outpatient and inpatient care). The NCVM was adapted from the NCEM to account for COVID-19 vaccination of susceptible and naturally immune populations. The NCVM allows for immunity derived from vaccination, previous infection, and hybrid immunity against both infection and disease, as well as for vaccine waning and reinfections following vaccinations. This model provided decision-making support to the South African government from the rollout of the vaccination programme, through the delta and Omicron waves of infection [17,18,19]. The NCVM was calibrated to local sero-prevalence, admissions, mortality, vaccination and variant data between 2021 and 2023 to simulate retrospectively, the number of hospital admissions and deaths under the COVID-19 vaccination programme and estimated counterfactuals under a hypothetical no vaccination programme scenario. Hospital admissions were disaggregated by levels of inpatient care – intensive care unit (ICU) and non-ICU admissions; and deaths included both in-hospital and out-of-hospital deaths. In the absence of a system for reporting out-of-hospital COVID-19-related deaths, 85% of estimated excess deaths per month was assumed to be attributable to COVID-19 [20,21].

[2] Please see SACMC vaccineModelSupplementaryfile.pdf (sacovid19mc.github.io) for an overview of the model structure and parameters [16].

4. Economic model

4.1. Base case analysis

The economic model estimated the costs and health outcomes of the COVID-19 vaccination programme compared to a no vaccination scenario drawing on outputs from the NCVM. Costs included direct medical costs of inpatient management of COVID-19 and cost per vaccine dose administered. Inpatient care costs per day for each level of care (ICU and non-ICU) included therapeutics, diagnostics, respiratory support and accessories, equipment and human resources [22]. Costs of each level of care was estimated by multiplying number of ICU and non-ICU cases estimated from the NCVM to the corresponding inpatient costs per day and the average length of stay by level of care (Table 2). To adequately account for the distribution of inpatient management costs of COVID-19, we assumed that 5% of non-ICU bed admissions were admissions to high care wards and 95% were general ward admissions [23]. Following Edoka et al [22] we defined general wards as wards providing care to inpatients with less severe COVID-19 symptoms requiring supplemental oxygen therapy, high care wards as wards providing care to patients with severe COVID-19 requiring higher levels of respiratory support, and ICUs provided care to critical patients requiring mechanical ventilation [22]. For the vaccination programme, COVID-19 vaccination programme cost per dose was multiplied by total population vaccinated in each study time horizon (Table 2). COVID-19 vaccination programme cost per dose included vaccine procurement cost and vaccine delivery cost estimated from one district in South Africa. [24]. Edoka et al [24] estimated both financial and economic costs from a public payer's perspective by collecting data on cost incurred at the national level (vaccine procurement costs) and from five delivery channels implemented in the West Rand district (vaccine delivery costs). In this study,

Table 2
Economic model parameters.

Parameters	Base Case	Standard Error	Distribution	Source
Life expectancy by age group (years)				[19]
15–34	42			
35–59	28			
60–64	18			
65–69	15			
70–74	12			
75+	10			
Cost per patient day (US $2021)				
General ward	207.58	41.52	Gamma	[16]
High care ward	491.89	98.38	Gamma	[16]
Intensive care unit	1 429.12	285.82	Gamma	[16]
Vaccination programme cost per dose (US$2021)				
Vaccine procurement + delivery cost	21.85	4.37	Gamma	[18]
Disability Weight				
Intensive care unit	0.66	0.07	Beta	[21,22]
High care ward	0.13	0.04	Beta	[21,22]
General ward	0.13	0.01	Beta	[21,22]
Length of stay (days)				
Intensive care unit	15.52	0.14	Gamma	[17]
High care ward (HCW)	11.58	0.05	Gamma	[17]
General ward	11.58	0.05	Gamma	[17]
Proportion of HCW admissions in general ward admissions	0.05	0.01	Beta	[17]
Total Population Vaccinated				
February - November 2021	24 886 437			[12]
February 2021 - January 2023	38 418 222			[12]

we used economic cost per dose estimated as the total economic costs of the vaccination programme in the district divided by total number of doses administered in the district across all delivery channels. All costs were expressed in 2021 US$.

Health outcomes were expressed as disability-adjusted life years (DALYs) estimated as the sum of years of life lost (YLL) and years lived in disability (YLD). To estimate YLL, age group-stratified number of deaths obtained from the NCVM were applied to estimates of remaining life expectancy from WHO life tables for South Africa [25]. YLD associated with hospital admissions was estimated by applying disability weights by disease severity [26] to length of stay in ICU or non-ICU wards [23]. We used disability weights recommended by the European Burden of Disease Network Consensus COVID-19 model [26]based on the Global Burden of Disease Study (GBD) 2019 [27] and the European Disability Weight study [28]. All parameters used in the economic model are summarised in Table 2.

The results of the cost-effectiveness analysis were expressed as incremental cost-effectiveness ratios (ICERs) estimated as the ratio of the difference in costs between the COVID-19 vaccination programme and the no vaccination programme scenario to corresponding differences in DALYs lost. Cost-effectiveness of the COVID-19 vaccination programme was determined using a cost-effectiveness threshold of ZAR 38 500/US$ 2 318[3] which represents the marginal productivity of the South African health system, or the health opportunity cost of healthcare spending in South Africa [29].

4.2. Sensitivity analysis

Sensitivity analyses, including deterministic and probabilistic sensitivity analyses (DSA and PSA) were conducted to assess the impact of parameter uncertainty on the ICER. The DSA was conducted by varying individual parameters, sequentially, over a specified range defined by the standard error or 95% confidence intervals of each parameter. Where standard errors or 95% confidence intervals were not available, the standard error was assumed to be 20% the mean value of the parameter [30] (Table 2). The PSA assessed the impact of parameter uncertainty jointly by fitting appropriate distributions (Table 2) to each parameter and running 10,000 Monte Carlo simulations that drew inputs randomly from these distributions [31]. Similarly, standard errors of each parameter were used to determine the range for the PSA but when not available, standard errors were assumed to be 20% parameter mean value.

5. Results

5.1. Base case analysis

In the first study period, the vaccination programme was estimated to avert 34,007 hospital admissions and 17,635 in-hospital deaths. In the second study period, the number of estimated averted hospital admissions and deaths increased substantially – 70,764 hospital admissions and 28,519 hospital deaths were averted during this period (Table 3). When deaths occurring both within and out of hospitals were considered, deaths averted was estimated at 28,003 and 51,068 in the first and second study periods respectively (Table 3).

Table 4 summarises the results of the cost-effectiveness analysis. The incremental cost of the vaccination programme in the first study period was estimated at approximately US$380 million, increasing to approximately US$514 million in the second period. Similarly, total DALYs averted when only estimated hospital COVID-19 deaths were counted increased from approximately 235,500 in the first period to approximately 395,000 in the second period. ICERs was estimated at US$1,614 and US$1,301 per DALY averted, in the first and second study periods, respectively. When both in-and-out of hospital deaths were included in the analysis, ICERs decreased to approximately US$1,070 and US$660 per DALY averted in the first and second study periods, respectively. Overall, across both time horizons modelled, base case ICERs were below the cost-effectiveness threshold used.

5.2. Sensitivity analysis

The results of the deterministic sensitivity analysis shows that uncertainty in vaccination programme cost per dose administered had the greatest impact on ICERs in both study periods (Fig. 2&3). However, at higher values of cost per dose modelled, the ICER remained lower than the cost-effectiveness threshold except in the first study period when only in-hospital deaths were modelled (Fig. 2). Here, at the high value of vaccine programme cost per dose, the ICER increased to approximately US$2,500 per DALY averted. The results of the PSA (Fig. 3) showed that at a cost-effectiveness threshold of approximately US$2,300 per DALY averted, the probability of cost-effectiveness was approximately 100% for both in-and-out of hospital deaths in both study periods (Fig. 4).

6. Discussion

In this study, we retrospectively assessed the cost-effectiveness of the COVID-19 vaccination programme in South Africa over time horizons (nine months and twenty-four months) that represented different phases of vaccine rollout. In both study periods, the vaccination programme was shown to have been cost-effective with a high degree of certainty-approximately 100% of the model simulations in the probabilistic sensitivity analysis fell below the cost-effectiveness threshold assumed. Although a narrower public payers' perspective was adopted in the quantification of costs, we accounted for broader health benefits of the vaccination programme by including the potential impact of the programme on estimated out-of-hospital deaths due to COVID-19 that would not traditionally be reported on data systems. This resulted in substantially lower ICERs in both study periods.

The prioritisation of frontline health workers and older age populations as well as the fast pace of vaccination rollout may explain the favourable health and economic outcomes observed in our study. Our findings also suggest that as the programme was expanded to include wider sub-populations and booster doses to eligible populations, the programme averted a proportionately higher number of deaths, hospitalisations and DALYs, thus, resulting in comparatively lower ICERs.

Our findings are consistent with previous studies that have demonstrated the health and economic benefits of COVID-19 vaccination programmes under different modelling assumptions and scenarios—rapidly rolled out COVID-19 vaccination programmes, and strategies that prioritise older populations have been shown to be the most cost-effective strategies in other LMIC settings including Pakistan and Kenya [7,9,10]. However, unlike previous studies we adopted a retrospective approach and assessed the cost-effectiveness of an established COVID-19 vaccination programme.

Our study has some limitations. First, to estimate epidemiological outcomes in the absence of a COVID-19 vaccination programme, assumptions were made with regards to the behaviours of both the public and the government in response to growing numbers of COVID-19 infections and hospital admissions. We assumed that the population would exhibit the same behavioural response to increasing mortality due to COVID-19 in the presence and absence of the vaccination programme. However, it is likely that the population would exhibit more cautious behaviour in the absence of a vaccination programme, thereby leading to reduced incidence, admissions, and deaths. Therefore, the counterfactual scenario of no vaccination cannot be validated and should be interpreted with caution.

Second, the benefits of vaccination need to be contextualised both retrospectively and prospectively. Prospectively, immunity against

[3] The US$ equivalent was estimated using an average 2021 US$-ZAR exchange rate of ZAR 16.61.

Table 3
Epidemiological cases (Base case analysis).

	Study comparators	GW admissions	HCW admissions	ICU admission	Total hospital admissions	Hospital deaths	Excess deaths
Study period 1	Vaccination programme	160 772	8 462	20 782	190 016	71 944	130 160
	No vaccination programme	132 236	6 960	16 814	156 010	54 309	102 157
	Cases averted	28 536	1 502	3 968	34 007	17 635	28 003
	% Cases averted	18 %	18 %	19 %	18 %	25 %	22 %
Study period 2	Vaccination programme	234 403	12 337	28 363	275 103	99 180	184 459
	No vaccination programme	174 529	9 186	20 624	204 339	70 660	133 391
	Cases averted	59 1874	3 151	7 739	70 764	28 519	51 068
	% Cases averted	26 %	26 %	27 %	26 %	29 %	28 %

GW-general ward; HCW- High care ward; ICU- intensive care unit.

Table 4
Incremental costs, DALYs lost and Incremental cost-effectiveness ratio (probabilistic)- base case analysis.

	Study period 1			Study period 2		
	Total costs (US$)	DALYs lost (Hospital death)	DALYs lost (Excess death)	Total costs (US$)	DALYs lost (Hospital death)	DALYs lost (Excess death)
No vaccination programme	897 419 147.60	1 251 318	2 598 906	1 260 844 715	1 698 575	3 854 858
Vaccination programme	1 277 596 224.67	1 015 774	2 243 904	1 775 169 846	1 303 481	3 075 690
Difference	**Incremental Costs (US$)**	**DALYs averted**	**DALYs averted**	**Incremental Costs (US$)**	**DALYs averted**	**DALYs averted**
	380 177 077.07	235 544	355,002	514 325 131	395 094	779 168
ICER (US$/DALY averted)		1 614.04	1 070.92		1 301.78	660.10

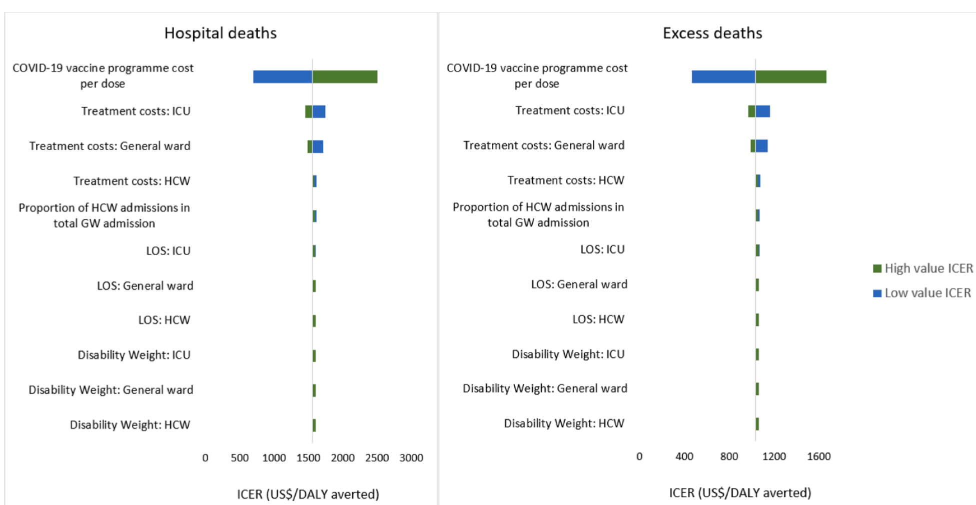


Fig. 2. Tornado diagrams (Study period 1).

severe infection may last into the future, subject to the emergence of variants with immunity escape properties. This implies that the benefits of vaccination extend well beyond the study periods under consideration. Retrospectively, the benefits of vaccination extend to hospitalisations/deaths averted as well as the patient/provider/societal benefits of not being infected.

Third, we adopted a narrower study perspective in the quantification of costs. The inclusion of costs incurred by patients, both in accessing care and in lost productivity would have resulted in lower ICERs compared to our basecase ICERs [7]. Furthermore, our study did not account for the health and economic benefits of COVID-19 vaccines in averting long COVID-19 which may results in more favourable ICERs.

Fourth, although we used vaccination programme cost per dose estimated in South Africa, this was based on costs from one of 52 districts in South Africa in the first year of programme rollout [24]. Therefore, our estimate of programme unit costs may not be representative of average cost incurred across the country. Furthermore, in the second year of the programme, the vaccination programme shifted towards an integrated model with COVID-19 vaccines being offered as part of existing healthcare services. Therefore, programme costs during this period are likely to be different from cost estimates modelled in our study. These have important implications for our estimated ICERs given that programme cost per dose was shown, through the DSA, to have the biggest impact on the ICER.

Finally, in the second year of the programme, the COVID-19 vaccination programme was expanded to include a wider age group. During this time, booster doses were administered to eligible populations. Although we observed more favourable cost-effectiveness outcomes during this period, we are unable to distinguish if this effect was due to the expansion of the vaccination programme to wider population groups or due to the provision of booster doses.

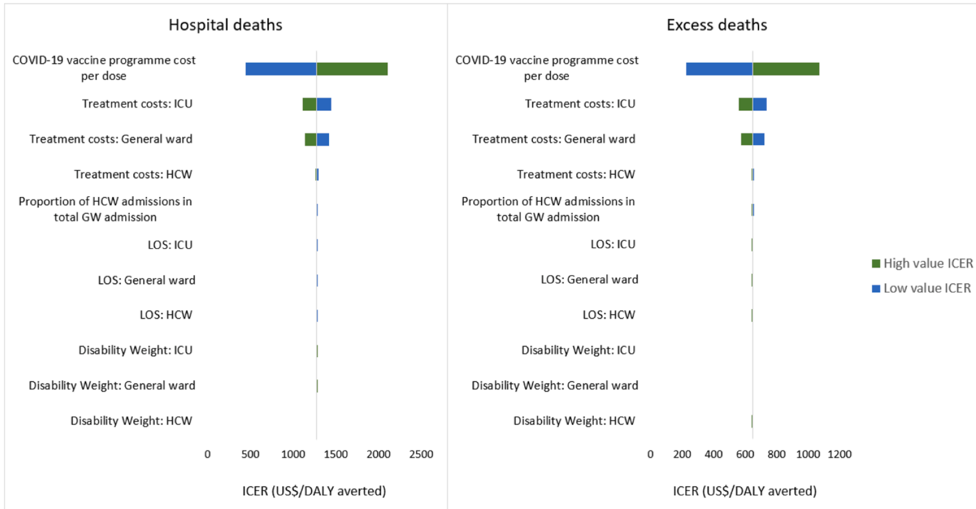
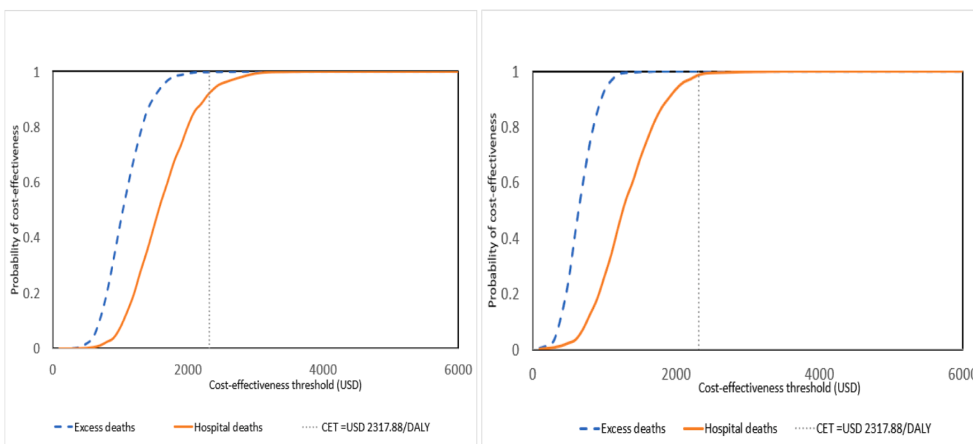


Fig. 3. Tornado diagrams (Study period 2).



A. Study period 1 **B.** Study period 2

Fig. 4. Cost-effectiveness acceptability curves **A.** Study period 1 **B.** Study period 2.

7. Conclusion

Overall, our findings suggest that the investment made in rolling out the COVID-19 vaccination programme in South Africa represented good value for money. The phased age-based approach adopted appeared to have maximised health benefits in face of limited vaccine supply during the first year of the programme. In addition, the gradual expansion of the vaccination programme to include wider age groups and the administration of booster doses further increased the cost-effectiveness of the programme. As South Africa moves towards a fully integrated approach to COVID-19 vaccine delivery, the likelihood of a decrease in vaccination uptake as a consequence, would need to be balanced against the costs of the integrated programme to assess if an integrated approach continues to represent good value for money and for which population age groups.

CRediT authorship contribution statement

Ijeoma Edoka: Writing – original draft, Validation, Formal analysis, Data curation, Conceptualization. **Sheetal Silal:** Writing – review & editing, Validation, Formal analysis, Conceptualization. **Lise Jamieson:** Writing – review & editing, Data curation, Conceptualization. **Gesine Meyer-Rath:** Writing – review & editing, Validation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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