

Research Article

Public Health Evaluation of COVID-19 Vaccine Acceptability and Health Behaviors in South Africa: Past, Current, and Future Implications (2020–2022)

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South Africa is facing a high burden of COVID-19 pandemic with low-vaccine coverage in the African Region. We aimed to investigate the temporal changes and impacts in health behaviors on vaccine acceptability in pre-, during-, and post-vaccine roll-out periods. In this cross-sectional study, we used the combined data from the nationally conducted "COVID-19 Vaccine Surveys (CVACS)" (May 2020–February/March 2022). Semiparametric regression models were used to capture the nonlinear association between the vaccine acceptability and health behaviors. Our study provided compelling evidence for a substantial decline in COVID-19 vaccine trust which shifted from 62%–70% to 26%–42% overtime. Participants younger than 40 years of age were less likely to receive the vaccine before it became available. However, this association changed in the postvaccine period with significant uptake in vaccine acceptance in younger groups. South Africans who identified themselves as black were more likely to intend to receive (aORs ranged: 1.93–3.60) and to trust the vaccine's safety and efficacy (aORs ranged: 1.79–1.23) in all time periods. "Mask wearing" and "frequent hand washing" were the most commonly reported behaviors. Given the lower rates of vaccine acceptability and a reduction in preventative health behaviors, monitoring the spread of infections is crucial and may have significant clinical and epidemiological implications.

1. Introduction

South Africa has one of the highest burden of coronavirus disease 2019 (COVID-19) related comorbidities in the African region [1–3]. The country also had delays in vaccine delivery programs which was also observed in other low- and-middle-income countries [2–5]. As of November 2022, ~50% of the adults had received one or more doses of vaccine compared to 70% of the global average [6]. There is growing evidence that vaccine hesitancy, a phenomenon observed globally, is also contributing to lower vaccine uptake in African countries, including South Africa [7–12]. There is overwhelming evidence for the benefits of vaccination and high vaccine coverage in reducing COVID-19-related hospitalizations and death

[13–15]. This is particularly crucial for South Africa since the country is also the epicenter of the human immunodeficiency virus (HIV) infection and has one of the highest tuberculosis (TB) rates in the world which have been adversely impacted by the pandemic [1, 16]. Besides the adverse biological interactions between these infections, HIV and TB testing and treatment have also declined substantially since the beginning of the pandemic [1, 2].

Using the combined data from the seven rounds of nationally representative surveys (May 2020–February/March 2022), the current study aimed to investigate the temporal changes in vaccine acceptability and health behaviors using the semiparametric regression models [17]. These flexible statistical techniques can capture changes in an exposure without imposing

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linearity assumption overtime while adjusting for potential confounders. Our combined survey population provided a unique opportunity to identify the correlates and temporal changes in vaccine acceptability and health behaviors across the three clinically and epidemiologically important time periods: (1) prevaccine roll-out (May–December 2020); (2) during-vaccine roll-out (February–November 2021); and (3) postvaccine roll-out periods (February–March 2022). In our analysis, we also estimated age-specific individual and population-level impacts of vaccine roll-out periods on vaccine acceptability and changes in health behaviors such as mask wearing, social distancing, and hand washing/sanitizing. These investigations potentially be crucial for evaluation of past and current vaccine promotion campaigns and can be used in planning and modifying future vaccine implementation programs.

2. Materials and Methods

2.1. Study Design and Population. The current study used the combined data from the national surveys conducted to measure COVID-19 vaccine acceptability among adult South Africans. Details of the surveys are described elsewhere [18–24]. We summarized them briefly as follows.

2.1.1. National Income Dynamics Study-COVID-19 Rapid Mobile (NIDS-CRAM) Survey. The survey investigated the socioeconomic impacts of the national lockdown associated with the State of Disaster declared in South Africa in March 2020, and the social and economic consequences of the global COVID-19 pandemic [18–22]. NIDS-CRAM is a follow-up with a subsample of adults from households in the National Income Dynamics Study (NIDS) Wave 5 (2017). Five rounds of surveys were telephonically conducted during the period of May 2020–2021 among those who consented to participate in the surveys (N= 30,370).

2.1.2. COVID-19 Vaccine Surveys (CVACS) 1 and CVACS 2. The CVACS were designed to collect information on barriers to COVID-19 vaccine uptake in South Africa. In CVACS 1, conducted between 15 November and 15 December 2021, the study team interviewed (via telephone) 3,510 individuals who were unvaccinated against COVID-19 (vaccination status was self-reported). In CVACS 2, from 23 February to 25 March 2022, the study team attempted to reinterview the original CVACS 1, sample of 1,386 were successfully reinterviewed, with 386 reporting vaccination between the surveys. Additionally, a new sample of 2,222 unvaccinated individuals was interviewed, bringing the total to 3,608 unvaccinated individuals for the second survey [23, 24]. Design weights were applied to account for sample selection and nonresponse.

All surveys included individuals 18 years or older and the data are collected with computer-assisted telephone interviewing (CATI). Participants provided informed consent, indicating that they understood the purpose of the survey and agreed to participate voluntarily. All surveys aimed to measure multiple outcomes, such as vaccination knowledge, attitudes, and beliefs (including specific concerns); vaccination intentions (plans to get vaccinated), vaccine access constraints, and information seeking. Data from all surveys were aggregated across the time periods in such a manner that respondents from different surveys, such as CVACS and NIDS-CRAM participants, were categorized based on the time periods of their participation. For example, individuals who participated in any of these surveys during the "prevaccine" period were collectively categorized as "prevaccine" respondents, regardless of the specific survey they were part of. Consequently, each time period—"prevaccine," "during-vaccine," and "postvaccine" phases—consisted of unique individuals. Therefore, the study was considered to have as cross-sectional design.

2.2. Measurements. The surveys employed CATI for data collection, with trained interviewers using this system to conduct standardized, telephone-based surveys, and record responses in real-time. Prior to each interview, informed consent was obtained from participants, ensuring they understood the survey's purpose, voluntary nature, and the confidentiality of their responses. Demographic data collected included age, sex, education (<grade 12 vs. grade 12+), and employment status (employed vs. not employed), along with specific variables related to COVID-19, such as vaccine knowledge, attitudes, intentions, barriers to access, and information-seeking behaviors. CATI's structured approach guaranteed consistent questioning and immediate data entry, enhancing data quality and accuracy. Additionally, strict data privacy protocols were followed to ensure participant anonymity and secure data storage, accessible only to authorized team members.

2.2.1. Outcome Measurements. In this combined population, we considered the following vaccine acceptability and health behaviors as outcome measurements: (1) intention to receive vaccine (i.e., "I would definitely get vaccinated") (yes/no); (2) trusting vaccine's safety and efficacy, i.e., vaccine is safe (i.e., "no side effects, vaccine prevents getting COVID-19 and dying from COVID-19") (yes/no); (3) self-perceived risk: no risk ("I would definitely not get sick with COVID-19") (yes/no); behavior changes since the pandemic; (4) "always wears a mask in public" (yes/no); (5) "washing hands frequently" (yes/no); and (6) "avoiding crowd/social distancing" (yes/no). The survey time points were categorized and grouped as: (1) "before-vaccine roll-out" (May-December 2020); (2) "during-vaccine roll-out" (February-November 2021); and (3) "postvaccine roll-out" (February-March 2022). Since the COVID-19-related behavior changes were only available in NIDS-CRAM surveys, we regrouped the rounds of surveys as: (1) "before vaccine roll-out" (May-December 2020); (2) "during vaccine roll-out" (February–March 2021); and (3) "postvaccine roll-out" (April-May 2021). We only used nonmissing data.

2.3. Statistical Analysis. Percentages and χ^2 tests were used to compare the characteristics of the study populations across the three survey periods: (1) before-, (2) during-, and (3) post-vaccine roll-out. Multivariable logistic regression models were used to identify the significant correlates of the primary outcome variables while accounting for the multistage sampling design (weighted). Adjusted odds ratios (aORs) and their 95% confidence intervals (CIs) were presented. We also assessed

the significant features of the changes in vaccine acceptability and behavior changes in two steps.

Step 1: Quantitative and Visual Assessments of Changes in Vaccine Acceptability and Health Behaviors.

We used semiparametric regression models to capture nonlinear association between the outcome variable(s) and the age, which was analyzed as a continuous variable and fitted as a smoothed function of splines for a binary outcome variable [17]:

Logit
$$(P(\text{intention to receive vaccine}_{ij} = 1)) = s(t_i) + U_{1i} + \varepsilon_{ij}.$$
(1)

Intention to receive vaccine corresponds to the *i*th individual at *j*th time was formulated as a function of penalized spline:

$$s(t_i) = \beta_i t + \sum_{k=1}^{K} s_k^G z_k(t).$$
 (2)

For each individual, (t_i) ; $z_1(.), ..., z_k(.)$ is the spline functions and σ_s^2 is the penalization of the spline coefficients $s_1(.), ..., s_k(.)$; $U_{1j} \sim N(0, \sigma_u^2)$, the random component due to the repeated measures; $\varepsilon_{ij} \sim N(0, \sigma_e^2)$ and overall error associated with the model where "degrees of freedom" (*e.d.f*) were estimated for each model and p < 0.05 were interpreted as significant evidence for a nonlinear association between an outcome variable and the study visits. Using a "weighted average" of the binary outcomes, the methodology was also able to plot a smoothed curve of adjusted ORs across the age.

Step 2: Identifying Threshold Age Using "Zero-Crossing Derivatives" Method.

If the semiparametric model presents an evidence for a nonlinear association between the ORs of an outcome variable (e.g., vaccine acceptability) as a continuous function of age (i.e., e.d.f > 2), then we used the "zero-crossing" technique which produces "first and second derivatives" to identify the threshold for age when the odds ratios changed significantly [25]. In this setting, the first and second derivatives of the regression curves and their confidence bands were also presented. Increases/decreases of the model estimated fits were interpreted as significant "curvature" if their confidence bands cross the "zero-line."

2.3.1. Population-Level Impact of Survey Periods on "Vaccine Acceptability" and "Health Behaviors". We estimated the proportion of "vaccine acceptability" and "changing health behaviors" was associated with the vaccine roll-out periods. The population attributable risk percent (PAR(%)) was estimated using the prevalence of an exposure and aORs from the multivariable models [16]:

$$PAR(\%) = \frac{\sum_{s=1}^{S} p_s(OR_s - 1)}{1 + \sum_{s=1}^{S} p_s(OR_s - 1) + 1} = 1 - \frac{1}{\sum_{s=1}^{S} p_sOR_s},$$
(3)

where OR_s and p_s , s = 1, ..., S. Data were analyzed using Stata 16.0 (College Station, TX). We also used the software package "SemiPar" ([R-3.5.3 (2019-03-11)]) [26], with a "logit" link function. The scripts were written using the R-software package (3.5.3) (https://cran.r-project.org/web/packages/Se miPar/SemiPar.pdf) and presented in *Supplementary 1*.

3. Results

Overall, the median age of the survey participants was 38 years (interquartile range (IQR): 29-50). Approximately 81% of all survey participants identified themselves as Black. Table 1 describes and compares the various sociodemographic characteristics by three periods: "before-vaccine development/roll-out," "during-vaccine roll-out," and "postvaccine roll-out." Compared to those at postvaccine roll-out period, survey participants in pre-/during-vaccine roll-out periods were significantly more likely to be female (47% vs. 62% and 61%, respectively), low educated (40% vs. 53% (both)). In our combined population, vaccine acceptability declined significantly from 62% to 26% in pre- and postvaccine roll-out periods, respectively (*p*-value < 0.001) (Table 1). Similar declines were observed in proportion of those who indicated trusting vaccine's safety and efficacy (77% to 42%, p < 0.001). Meanwhile, a proportion of those who indicated wearing masks in public increased from 6% to 30% overtime while frequent hand washing declined from 62% to 50%. Less than 10% of the study population indicated avoiding crowd/ social distancing as their main health behavior change since the pandemic started.

3.1. Correlates of Vaccine Acceptability. The demographic and socioeconomic correlates of "intention to receive vaccine," and "trusting vaccine's safety and efficacy" are presented in Table 2. Compared to the other ethnicities, Black ethnicity was more likely to intend to receive a vaccine in all three time periods (aOR: 1.93, 2.28, and 3.60, respectively) (Table 2). They were also more likely to trust the vaccine's safety and efficacy (aORs: 1.79, 2.17, and 1.23 for pre-, during-, and post-vaccine roll-out). Older participants (40+) were 60% and 66% more likely to intend to receive a vaccine in pre- and during-vaccine roll-out only. Lower socioeconomic indicators including low education and unemployment were also correlated with increased odds of vaccine acceptability and trust during and post vaccine roll-out. These characteristics were correlated with individuals who had low perceived risk.

3.2. Age-Specific Temporal Changes in Vaccine Acceptability and Trust: Visual and Quantitative Assessments. Our findings from semiparametric regression models confirmed significant nonlinear associations between age and intention to receive vaccine overtime and appeared more prominent in the postvaccine period (Figure 1(a)). Model estimated degrees of freedom (*e.d.f*) were 6.31 (p<0.001), 4.05 (<0.001), and 2.96 (p = 0.0456). Results from the "zero-crossing" method confirmed the age 40 to be the cut-point when the odds of having intention to get vaccinated were changed significantly

Characteristics	Prevaccine roll out (May-December 2020)	te roll out (May–December 2020) During-vaccine roll out (February–November 2021) Post	Postvaccine roll out (February–March 2022)	<i>p</i> -Value
Age, median (IQR)	37 (29–49) years	38 (29–51) years	37 (30–51) years	
<30 years	26%	29%	23%	<0.001
30–39 years	27%	28%	34%	
40–49 years	20%	20%	16%	I
50–59 years	12%	11%	15%	
60+ years	15%	12%	12%	
Sex		Ι	Ι	<0.001
Male	38%	39%	53%	
Female	62%	61%	47%	
Ethnicity	I	I	I	<0.001
Other	14%	21%	23%	I
Black	86%	29%	77%	
Education	I	1	I	<0.001
<grade 12<="" td=""><td>53%</td><td>53%</td><td>40%</td><td>I</td></grade>	53%	53%	40%	I
≥Grade 12	47%	47%	80%	
Employment status		1	I	<0.001
Employed/income	46%	43%	43%	I
Unemployed	54%	57%	57%	
Vaccine beliefs and attitudes		1	I	I
Intention to receive vaccine	62%	70%	26%	<0.001
Trusting vaccine's safety and efficacy	77%	68%	42%	I
Self-perceived low risk	66%	62%	73%	<0.001
Changed behavior due to COVID-19				
Wearing mask in public	6%	25%	30%	<0.001
Washing hand frequently	63%	52%	50%	<0.001
Avoid crowd/social distancing	11%	8%	6%	<0.001
^a CRAN and CVACS surveys.				

TABLE 1: Characteristics of the study populations by vaccine roll-out period^a (N = 30, 370).

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Sex Male Female	Adjusted OR ^a (95% CI) Preventioer 2020)	cember 2020) <i>p</i> -Value	During-vaccine roll out (February–November 2021) Adjusted OR ^a (95% CI) p-Valu	November 2021) <i>p</i> -Value	Postvaccine roll out (February–March 2022) Adjusted OR ^a (95% CI) p-Valu	March 2022) <i>p</i> -Value
Sex Male Female		4	Intention to get vaccinated			4
Male Female						
Female	1		1		1	
	$0.95\ (0.85,\ 1.06)$	0.395	1.00 (0.90, 1.12)	0.955	1.60(1.42, 1.77)	<0.001
Ethnicity						
Others	1		1	Ι	1	
Black	1.93(1.64, 2.25)	<0.001	2.28 (1.96, 2.65)	<0.001	3.60(4.03, 4.26)	<0.001
Age						
<40 years	1	I	1	I	1	
40+ years	1.60(1.42, 1.76)	<0.001	1.66 (1.49, 1.85)	<0.001	0.98(0.88, 1.09)	0.657
Education level						
≥Grade 12	1		1		1	
<grade 12<="" td=""><td>1.09 (0.97, 1.20)</td><td>0.145</td><td>1.38 (1.24, 1.54)</td><td><0.001</td><td>$1.74 \ (1.56, 2.00)$</td><td><0.001</td></grade>	1.09 (0.97, 1.20)	0.145	1.38 (1.24, 1.54)	<0.001	$1.74 \ (1.56, 2.00)$	<0.001
Employment status						
Employed	1	I	1	I	1	
Not employed	1.02(0.91, 1.13)	0.771	1.10 (0.99, 1.23)	0.079	1.45(1.30, 1.61)	<0.001
			Trusting vaccine's safety and/or efficacy	or efficacy		
Sex						
Male	1	Ι	1	Ι	1	I
Female	1.01 (0.90, 1.15)	0.855	1.02 (0.91, 1.14)	0.776	1.47 (1.31, 1.61)	<0.001
Ethnicity						
Others	1	I	1	I	1	
Black	1.79 $(1.50, 2.08)$	<0.001	2.17 (1.89, 2.50)	<0.001	1.23 (1.10, 1.37)	<0.001
Age						
<40 years	1		1		1	
40+ years	1.23(1.10, 1.37)	<0.001	1.54 (1.37, 1.75)	<0.001	1.12(1.03, 1.23)	0.012
Education level						
≥Grade 12	1		1	I	1	
<grade 12<="" td=""><td>1.02(0.90, 1.15)</td><td>0.770</td><td>1.32 (1.20, 1.47)</td><td><0.001</td><td>1.30(1.18, 1.43)</td><td><0.001</td></grade>	1.02(0.90, 1.15)	0.770	1.32 (1.20, 1.47)	<0.001	1.30(1.18, 1.43)	<0.001
Employment status						
Employed	1		1		1	
Not employed	0.97 (0.85, 1.10)	0.610	1.02 (0.01, 1.15)	0.680	1.20 (1.08, 1.20)	<0.001

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			TABLE 2: Continued.			
	Prevaccine roll out (May–December 2020)	cember 2020)	During-vaccine roll out (February–November 2021)	November 2021)	Postvaccine roll out (February–March 2022)	-March 2022)
Unaracteristics	Adjusted OR ^a (95% CI)	<i>p</i> -Value	Adjusted OR ^a (95% CI)	<i>p</i> -Value	Adjusted OR ^a (95% CI)	<i>p</i> -Value
			Perceived low-risk			
Sex						
Male	1	I	1	I	1	
Female	1.00(0.90, 1.12)	0.978	1.02(0.92, 1.14)	0.699	0.71 (0.64, 0.79)	<0.001
Ethnicity						
Others	1		1	I	1	I
Black	1.50 (1.28, 1.75)	<0.001	1.57 (1.35, 1.82)	<0.001	0.70 (0.62, 0.80)	<0.001
Age						
<40 years	1	Ι	1	Ι	1	I
40+ years	0.83 (0.75, 0.92)	0.001	0.83(0.74, 0.92)	<0.001	0.69 (0.62, 0.76)	<0.001
Education level						
≥Grade 12	1	I	1	Ι	1	
<grade 12<="" td=""><td>1.40 (1.26, 1.56)</td><td><0.001</td><td>1.32(1.19, 1.47)</td><td><0.001</td><td>1.64 (0.58, 0.71)</td><td><0.001</td></grade>	1.40 (1.26, 1.56)	<0.001	1.32(1.19, 1.47)	<0.001	1.64 (0.58, 0.71)	<0.001
Employment status						
Employed	1	I	1	Ι	1	
Not employed	1.97 (1.76, 2.19)	<0.001	1.67(1.51, 1.86)	<0.001	$0.88 \ (0.80, \ 0.97)$	0.012
^a Odds ratios are from t	^a Odds ratios are from the multivariable logistic regression model.	lel.				

6

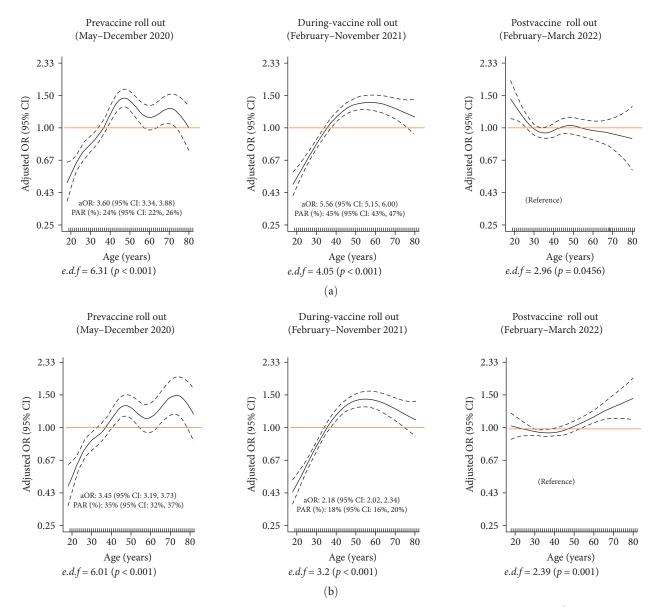


FIGURE 1: Age-specific temporal trends in vaccine acceptability by vaccine roll-out: NIDS-CRAM and CVACS surveys[§]: (a) Intention to get vaccinated and (b) trusting vaccine's safety and efficacy. [§]aOR, adjusted (for age, sex, ethnicity, education, and employment status) odds ratios for the outcomes (i.e., vaccine acceptability); *e.d.f*, expected degrees of freedoms from the semiparametric regression models; PAR (%), percent vaccine acceptability (i.e., intention to get vaccinated) associated with the vaccine roll-out periods. For example, compared to the "postvaccine" period, those who participated in "prevaccine" period were 3.6 times more likely to indicate that they would get vaccinated when the vaccine developed; in a combined study population 24% of the mask users were exclusively associated with prevaccine period; this proportion increased to 45% during the vaccine roll-out period.

in pre- and during-vaccine (*Supplementary 2*). However, these associations appeared to disappear at the postvaccine roll-out (*Supplementary 2*). Similar trends were observed in trusting the vaccine's safety and efficacy with e.d.f = 6.01, 3.2, and 2.39 in pre-, during-, and post-vaccine roll-out periods, respectively (Figure 1(b)). There was a marked shift in age distribution between pre-/during- and post-vaccine roll-out where the odds of vaccine acceptability increased from 0.43 to 0.80 in pre-/during-vaccine periods to 1.10–2.33 in postvaccine roll-out period (Figure 1(b)).

3.3. Age-Specific Temporal Changes in Health Behaviors: Visual and Quantitative Assessments. We observed an inverse U-shape association between age and the most commonly reported health behavior changes including "wearing mask" and "frequent hand washing" overtime with *e.d.f.* from the semiparametric regression models ranging from 2.21 to 3.62 (Figure 2(a)). Results from the "zero-crossing" method confirmed the age group of 40–60 years of age, which were the approximate cut-point when the odds of wearing mask increased significantly in all time periods. At a population-level,

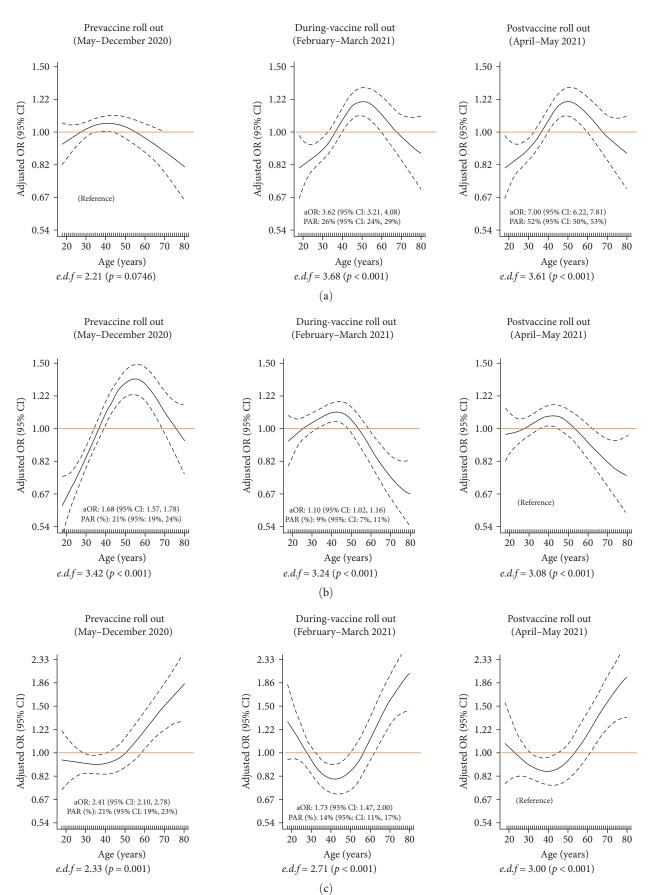


FIGURE 2: NIDS-CRAM surveys: age-specific temporal trends in changing behaviors due to COVID-19[§]: (a) wearing mask in public, (b) washing hands frequently, and (c) avoiding crowds/social distancing. [§]aOR, adjusted (for age, sex, ethnicity, education, and employment status) odds ratios for the outcomes (i.e., behavior changes); *e.d.f.*, expected degrees of freedoms from the semiparametric regression models;

PAR (%), percent behavior changes (mask, washing hands or avoiding crowds/social distancing) associated with the vaccine roll-out periods. For example, compared to the "prevaccine" period, those who participated in "postvaccine" period were seven times more likely to report "wearing mask in public"; in a combined study population 52% of the mask users were exclusively associated with postvaccine period.

more than 52% of the mask users were exclusively associated with postvaccine roll-out period. This substantial impact was due to the strong association between this healthy behavior and postvaccine period (aOR: 7.00). Odds ratios associated with ages 40–60 were substantially higher for "frequent hand washers" compared to those outside these cut-points, conversely, they were less likely to report "avoiding crowd/social distancing" (Figures 2(b) and 2(c), respectively).

4. Discussion

Results from our study provided compelling evidence for a significant decline in vaccine acceptability which shifted from 62%–70% in pre- (May–December 2020) and duringvaccine roll-out periods (February 2021) to 26% (November 2021–March 2022) in postvaccine period. We also observed a significant decline in the proportion of people who trusted the vaccine's safety and efficacy which essentially mirrored the trends observed for those who intended to receive a vaccine in all time periods. These results are not surprising since concerns around safety and efficacy of the vaccine have been strongly associated with vaccine hesitancy and widely reported globally as well as in other African populations [9–11, 27–31].

Our estimates are comparable with the studies conducted in before-vaccine development and delivery. High rates of vaccine acceptability were previously reported in China, the United Kingdom, the United States, and European countries [27–33]. Shortly after COVID-19 was declared as pandemic, 80% of the "COVID-19-SCORE Global Survey" participants indicated intention to receive a vaccine when vaccines become available. However, our study is the first to report substantial decline in vaccine acceptability in the postvaccine period based among South African adults.

Despite the substantial decline overtime, the highest rates of vaccine acceptability were observed in Black South Africans and groups with lower socioeconomic conditions including low education and unemployment which were all significantly associated with increased odds of vaccine acceptability in all time periods. These factors have recently been associated with low vaccine acceptability in other African countries including Ghana, Kenya, and Nigeria [3, 9, 10, 34]. In contrast to our findings, higher socioeconomic conditions have been frequently linked to vaccine acceptability and uptake in African countries such as Kenya as well as other countries [10, 30, 34, 35]. High education and income were previously associated with vaccine uptake in African countries [34, 35]. The trends observed in our study were previously reported in school-age children vaccination, where families with low socioeconomic conditions were more likely to allow their child to be vaccinated, compared to those with high socioeconomic conditions [36, 37]. As expected, correlates of trusting vaccine's safety and efficacy were similar to those who intend to receive vaccine in all time periods. In our study population, individuals who trusted vaccine's safety and efficacy were 23 times more likely to be vaccine acceptant than those who did not (data not shown).

The semiparametric regression models brought further insights into the age-specific vaccine acceptability across the vaccine development and roll-out periods. Results from the "visual" and "quantitative" analysis from these flexible statistical models, revealed a significant shift in age distribution and intention to receive vaccine overtime. Survey participants younger than 40 years of age were less likely to have the intention to receive a vaccine at pre- and during-vaccine development periods. However, this association flipped in the postvaccine period with significant uptake in vaccine acceptance among those younger than 40 years of age. Consistent with these results, younger survey participants were also more likely to express concerns around safety and efficacy of the vaccine early on, in pre- and during-vaccine rollout. However, this association appeared to disappear in the postvaccine period when rates of trusting vaccine's safety and efficacy increased among the younger survey participants, while primarily declined in older age. These results collectively indicate that despite some increases in vaccine acceptability in younger groups in the postvaccine roll-out period, semiparametric regression models revealed flat regression curves which may be due to declines in vaccine acceptability in older age survey participants.

In terms of health behaviors, results from our analysis also highlighted substantial temporal changes in health behaviors reported by the survey participants. Despite a decline from 62% to 50% overtime, frequent hand-washing was reported as the most common health behavior reported to prevent COVID-19 in all time periods. Wearing masks increased from 6% in prevaccine period to 30% postvaccine period which was previously reported in other populations. This significant increase was primarily attributed to the mask-mandate imposed by the government during the pandemic (https://www.samedical.org/) [38], which was also reported previously. Along with social distancing, mask wearing was one of the first behavior changes imposed in many countries since the pandemic started in 2020 [39-41]. However, our findings provide empirical evidence for relatively low acceptance rates of mask wearing among South Africans which was also reported in other African countries including Ghana and Uganda [42–45]. Despite advice from the medical and epidemiological researchers to keep mask requirements, as of June 23, 2022, South Africa lifted the mask requirements in public. Social distancing and avoiding crowds were significantly less common in this population and reported as 11% when the pandemic emerged and dropped to 6% in the postvaccination period.

More than 3 years into the pandemic, South Africa continues to have a high burden of infections with excess mortality rates which are primarily linked to COVID-19-related complications [38, 46]. The effectiveness of the vaccines for reducing COVID-19-related hospitalizations and death is overwhelming [9, 10]. Despite this, as of November 2022, compared to the global vaccine coverage of 70%, less than 50% of the adults in South Africa have had at least one dose of vaccine [6]. The country also has the significant burden of HIV and TB infections globally which have been impacted adversely by the pandemic in many ways including a significant decline in testing and treatment across the country [1]. Therefore, low vaccination coverage in South Africa may have far more serious clinical and public health implications of widespread infection not just of COVID-19 but HIV and TB.

5. Limitations of This Study

The current study has several limitations, and results should be interpreted with a caution. We analyzed the data if they were collected in all seven surveys. Survey questions were self-reported, therefore subject to recall bias. The authors recognize that participants with no education may have different beliefs and attitudes compared to those with some or higher education. However, the small proportion of participants with no schooling (4% in CVACS and 3% in NIDS-CRAM) limited our ability to conduct a robust analysis using this specific categorization. Most of our analyses, including population-level impacts of vaccine hesitancy in South Africa are novel to this study and cannot be compared with previous research.

6. Conclusion

Our study found a significant drop in vaccine acceptability in South Africa, from 62%–70% to 26% postvaccine, a trend not seen in countries like China, the United Kingdom, or the United States. This decline was accompanied by decreased trust in vaccine safety and efficacy. Notably, Black South Africans and those with lower socioeconomic status showed higher vaccine acceptability, contrary to trends in other African countries. Younger participants, under 40, demonstrated increased vaccine acceptance in the postvaccine period. While hand-washing remained common, mask-wearing increased, likely due to government mandates. Given these findings, we recommend targeted interventions to address vaccine hesitancy, especially among older adults, and sex-specific strategies to close the vaccination gap. Mandates and awareness campaigns emphasizing the risks of COVID-19, along with leveraging vaccinated individuals as ambassadors, could also be effective. These findings suggest that the reasons for low rates of vaccine acceptability and a reduction in protective health behaviors in South Africa may differ from those in other regions, highlighting the need for country-specific public health strategies. We recommend targeted interventions to address vaccine hesitancy, especially among older adults, and sex-specific strategies to close the vaccination gap. Moreover, promoting culturally and socially relevant awareness about vaccination, reinforcing social norms, and highlighting the health risks associated with COVID-19 could be effective.

Data Availability

The current study used the several publicly available data from https://www.datafirst.uct.ac.za/. Analytical codes were written using the publicly available R-Software package "SemiPar" ([R-Version 3.5.3 (2019-03-11)]) (https://cran. r-project.org/web/packages/SemiPar/SemiPar.pdf) (*Supplementary 1*). If the paper gets accepted, the authors will share all data (publicly available) and software code written in publicly available software ([R-Version 3.5.3 (2019-03-11)]) (http://cran.r-project.org/) using a public repository.

Ethical Approval

The current study is used an open access (publicly available) data set and does not require further ethical approval.

Consent

Data were collected using telephone surveys. Therefore, a verbal consent obtained from the participants by asking if they wanted to participate the survey. Those who said "yes" were included in the surveys.

Disclosure

There was no study or analytic plan registration. However, the authors prepared a statistical analysis plan before they analyze the data. Surveys were undertaken by the Southern Africa Labour and Development Research Unit (SALDRU) (University of Cape Town).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Handan Wand, Sarita Naidoo, and Jayajothi Moodley prepared the concept sheet. Handan Wand and Tarylee Reddy extracted database and analyzed the data. Handan Wand prepared the first draft. All authors interpreted the results.

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Supplementary Materials

Supplementary 1. Using "SemiPar" to analyse vaccine acceptability and health behaviours by age. Supplementary 1 provides analytical codes developed with the R-Software package "*SemiPar*" (R-Version 3.5.3, released on 2019-03-11) for the analysis of vaccine acceptability and health behaviours by age.

This file includes the specific R codes used in our study to model the data on how age influences vaccine acceptability and associated health behaviours, using the semi-parametric regression models. The included code is designed to guide researchers through the process of data analysis, from data preparation to the execution of semi-parametric models. (https://cran.r-project.org/web/packages/SemiPar/SemiPar. pdf).

Supplementary 2. "Zero Crossing". This file includes visual presentations from the "Zero Crossing" method to determine critical age threshold(s) where changes in vaccine acceptance behaviour become statistically significant. After fitting the semiparametric regression models, the "Zero Crossing" technique is applied through first and second derivative plots. This approach is illustrated by analysing the intention to receive a vaccine across three distinct phases: Pre-vaccine rollout, During-vaccine rollout, and Post-vaccine rollout.

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