COVID-19 Vaccine Breakthrough Infections and Associated Factors in Kwekwe City, Zimbabwe, 2021

**Nyashadzashe Cosmas Makova[1], Mary Muchekeza[2], Addmore Chadambuka[1*],
Emmanuel Govha[1], Tsitsi Patience Juru[1], Notion Tafara Gombe[1,3], Mufuta Tshimanga[1]**

[1]Department of Primary Health Care Sciences, University of Zimbabwe, Harare, Zimbabwe
[2]Kwekwe City Council Department of Health, Kwekwe, Zimbabwe
[3]African Field Epidemiology Network, Harare, Zimbabwe
Email: *achadambuka1@yahoo.co.uk

Abstract

Background: To break the spread of COVID-19, people must adopt preventive health measures such as vaccination. A vaccine breakthrough infection is the detection of SARS-CoV-2 RNA or antigen in a specimen collected from a person $\geq$ 14 days after receipt of all recommended vaccine doses. Kwekwe City experienced an increase in breakthrough cases from one case (12 June 2021) to 39 cases (7 July 2021). The study was conducted to determine factors associated with breakthrough infections. **Methods:** We conducted an unmatched 1:2 case-control study. A case is defined as a patient who had two doses of a COVID-19 vaccine and had a positive SARS-CoV-2 antigen/PCR test at least two weeks after the date of receiving the second dose of the vaccine in Kwekwe City from June 12, 2021. An interviewer-administered questionnaire was used to collect data. We used the Epi Info software to generate means, frequencies, and proportions, to calculate measures of associations that include odds ratios. **Results:** Fifty-four cases in the records met the case definition for breakthrough infections, and two had died giving a case fatality rate of 3.7%. Fifty-one of the remaining 52 cases and 102 controls were recruited. Being within the age of 55 - 64 years (aOR = 12.22; 95% CI (1.15 - 129.81) and being unemployed (aOR = 0.26; 95% CI (0.07 - 0.93) were the independent factors associated with breakthrough infection. The median duration in days between getting the second dose of the vaccine and getting tested was 57.0 (Q_1 = 33; Q_3 = 81) and 46 (Q_1 = 33; Q_3 = 64) for cases and controls respectively. There were significant differences in overall knowledge, controls had good knowledge compared to cases (p = 0.01). **Conclusion:** Individuals who were within the 55 - 64 years age group were more likely to

have breakthrough infections. Those who had breakthrough infections had overall poor knowledge of COVID-19. Non-pharmacological interventions such as mask-wearing, social distancing, and frequent hand washing protect against having breakthrough infections. We recommended that residents get continuous education on the transmission, control, and prevention of the SARS-CoV-2 virus. The elderly should get booster doses of the vaccine.

Keywords

Breakthrough Infections, COVID-19, Kwekwe

1. Background

Coronavirus disease 2019 (COVID-19) is defined as an illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 which was first identified in the middle of an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China [1] [2]. It was initially reported to the World Health Organization (WHO) on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency [3]. On March 11, 2020, the WHO declared COVID-19 a global pandemic. The emergence of SARS-CoV-2 has shaken the globe in fundamental ways, and sub-Saharan Africa has been no exception [4]. Moreover, the emergence of SARS-CoV-2 variants threatens progress toward control of the COVID-19 pandemic [5].

COVID-19 disease has had several impacts on the livelihoods of Zimbabweans. Results from the rapid phone survey data collected by the Zimbabwe National Statistics Agency (ZIMSTAT) showed that 19% of rural households and 23% of urban ones were unable to access medical treatment when needed. Only 25% of rural school-going children continued learning after schools were closed, compared to 70% of urban school-going children. Approximately, 21% of those who were working pre-COVID no longer worked in July 2020. Urban people were most affected and 40% of urban wage workers that kept working saw their pay reduced [6]. There was a considerable fall in household income since the onset of the COVID-19 pandemic as 90 percent of households that operated a non-farm business reported a drop in revenue [7].

To stop the spread of COVID-19, people must adopt preventive health measures [8]. COVID-19 vaccines are a critical tool for controlling the ongoing global pandemic [9]. Vaccines were found to be safe and efficacious in preventing symptomatic, laboratory-confirmed COVID-19 [9]. In February 2021, the Medicines Control Authority of Zimbabwe (MCAZ) authorised the use of Sinopharm, Sinovac, Sputnik V, and Covaxin vaccines. In early 2021, the Zimbabwe Government started a campaign to vaccinate citizens against COVID-19. The programme started with the vaccination of frontline workers such as nurses, doctors, uniformed forces, teachers, people suffering from chronic illnesses, and the

elderly [8].

Sinopharm with two doses, administered at an interval of 21 days, has an efficacy of 79% against symptomatic SARS-CoV-2 infection 14 or more days after the second dose. Vaccine efficacy against hospitalization was 79% [10]. Sinovac trials showed 50.7% efficacy in Brazil, or 62.3% with longer dosing intervals, while Turkish researchers reported 83.5% efficacy [11]. Covaxin had an efficacy of 93.4% against severe COVID-19 disease, and overall vaccine efficacy of 77.8% against symptomatic infections confirmed by PCR tests. Against asymptomatic COVID-19, the efficacy was 63.6% [12]. Sputnik V vaccine efficacy, based on the number of confirmed COVID-19 cases from 21 days after the first dose of the vaccine, was reported as 91.6% [13]. Despite the level of vaccine efficacy, a percentage of fully vaccinated persons will develop infections with SARS-CoV-2, the virus that causes COVID-19 [14] [15] [16]. These infections are referred to as vaccine breakthrough infections. A vaccine breakthrough infection is the detection of SARS-CoV-2 RNA or antigen in a specimen collected from a person ≥ 14 days after receipt of all recommended doses of a vaccine [17].

On June 12, 2021, Kwekwe City identified the first case of breakthrough COVID-19 infection and cases have been constantly rising. As of July 7, 2021, there has been a cumulative 39 cases of fully vaccinated individuals in the city. A total of 127 fully vaccinated individuals have been tested for COVID-19, which gave a positivity rate of 30.1% which is comparable to the positivity rate among the non-vaccinated population. Furthermore, two of the 43 deaths that had occurred were among fully vaccinated individuals. It was against this background that we investigated the factors associated with COVID-19 vaccine breakthrough infection in Kwekwe City, 2021. There has been limited evidence to date on factors associated with breakthrough COVID-19 infections.

2. Methods and Materials

2.1. Study Setting

The study was conducted in Kwekwe City. The city of Kwekwe was established in 1898 by the British South African Company (BSAC) as a mining town due to large gold deposits in the area. Kwekwe lies along with the Harare-Bulawayo highway and in the Great Dyke area, a geological formation that is endowed with several minerals. Kwekwe is the fifth largest city in Zimbabwe. It offers several functions including, mining, industrial, educational, commercial, and social activities. According to the Zimbabwe National Statistics Agency (ZIMSTATS), Midlands Province District Population Projections Report of 2021, the current population of Kwekwe City is approximately 117,116. The majority of the residents is informally employed and practice artisanal mining.

2.2. Study Design

We conducted an unmatched 1:2 case-control study. A case is defined as a patient who had two doses of a COVID-19 vaccine and had a positive SARS-CoV-2 anti-

gen/PCR test at least two weeks after the date of receiving the second dose of the vaccine in Kwekwe City from June 12, 2021, to August 31, 2021. A control was defined as a patient who had two doses of a COVID-19 vaccine and had a negative SARS-CoV-2 antigen/PCR test at least two weeks after the date of receiving the second dose of the vaccine in Kwekwe City from June 12, 2021, to August 31, 2021.

2.3. Study Population

The study population consisted of individuals who had been fully vaccinated and had been tested for COVID-19. In addition, records consisting of vaccination cards were also part of the study population.

2.3.1. Inclusion Criteria
Any individual who consented to participate in the study was included despite age and had received two doses of the approved vaccine.

2.3.2. Exclusion Criteria
Any individual who refuses to participate or who had not received the two doses of the vaccine.

2.4. Sample Size and Sampling Technique

The sample size was calculated using the Fleiss formula on StatCalc based on a study by Sharma *et al.* (2021) in Delhi, India [17]. Assumptions are that having no prior history of COVID-19 infection is a significant risk factor of having breakthrough infections with an odds ratio of 3.8. The percentage of controls who had no prior history of COVID-19 infection was 82.5%. A 1:2 case-control study, 95% confidence interval, and 80% power was conducted. Assuming a 10% refusal rate, the sample size will be 93 cases and 186 controls. The total sample size was 279.

The tested individual line lists from clinics were used as the sampling frame. We checked if Kwekwe City combined its line lists with those of the private facilities and Kwekwe General Hospital. From the line lists of the tested individuals, the details of those who are fully vaccinated were extracted and we created a separate line list. The individuals who met the criteria for the case definition were less than the minimum sample size; therefore a census of all the 51 cases was done. For controls, systematic random sampling was done on the line lists from June 12, 2021, to August 31, 2021.

2.5. Data Collection

Interviewer administered questionnaires were used for cases and controls to get information on demographics, risk factors for contracting COVID-19, history of chronic medical conditions, knowledge, attitudes, and practices. These interviews were conducted at the participant's households. Individuals were phoned in advance to book an appointment before going to their places of residence.

Vaccination cards were reviewed for assessment of duration between vaccines doses. In addition, they were used to ascertain the date of the last second dose. Result slips of the tests were used to ascertain the date of the test.

Variables that we captured include age, gender, occupation, prior history of COVID-19, number of chronic illnesses, history of hypertension, type of vaccine administered, and history of contact with a COVID-19 patient, smoking history, history of tuberculosis, and HIV status.

2.6. Measurement of Knowledge and Attitudes

To measure COVID-19 knowledge, 12 items were adopted from Teng [18]. There were four items regarding clinical presentations, three regarding transmission routes, and five regarding prevention and control. "True", "false", or "I don't know". responses were offered for these items. Correct answers were scored "1" and incorrect/unknown answers scored "0". The score total range for knowledge items was 0 - 12, with higher scores indicating better knowledge about COVID-19. We used Bloom's cut-off of 80% (≥ 9.6) to determine good knowledge [19]. Attitudes were measured with a three-item scale adopted from Twinamasiko [20]. "Yes", "maybe" or "no" responses were offered for these items.

2.7. Data Analysis

We checked questionnaires for completeness and internal consistency before being entered in Epi info version 7.2.4.0. We used the Epi Info software to generate means, frequencies, and proportions, to calculate measures of associations that include odds ratios and their corresponding 95% confidence intervals. Bivariate analysis to identify risk and protective factors were carried out. For variables with more than two categories, one of the categories was assigned to be the reference category. Stratified analysis was done to identify possible confounding or effect modification. Logistic regression analysis was done to determine the independent factors associated with contracting breakthrough COVID-19 infection. All variables that were associated with contracting breakthrough COVID-19 infection in the bivariate analysis with a p-value $</= 0.25$ were included in the logistic regression model. Results of both the descriptive and analytic data were presented as figures and tables after analysis.

2.8. Permission to and Ethical Considerations

We sought and obtained permission to conduct the study from the Health Studies Office and the Kwekwe City Director of Health. Informed consent was obtained from all the interviewees and they were assured of confidentiality. Participants were told that participation was voluntary and that they can withdraw from the study at any time during the study. Any information that was obtained in connection with this study was not linked to the participants. Participants' identities were kept confidential thus participants were not required to put their

names on the questionnaire.

3. Results

Fifty-four cases in the records met the case definition for breakthrough infections; two had died giving a case fatality rate of 3.7%. Fifty-one of the remaining 52 cases and 102 controls were recruited. The response rate was 98.1%.

3.1. Characteristics of Respondents and Symptoms

The majority of the respondents were females, 28 (54.9%) and 71 (69.6%) for cases and controls respectively. There was no statistical difference in gender between cases and controls (p = 0.07). Most of the cases 16/51 (31.4%) were in the 35 - 44 years age group whilst most of the controls 36/102 (35.3%) were in the 25 - 34 age group. The median age for cases was 48.0 years (Q_1 = 38; Q_3 = 58) and 34.5 years (Q_1 = 28; Q_3 = 47) for controls (Table 1). The median interval for the

Table 1. Socio-demographic characteristics of study participants in Kwekwe City, Zimbabwe 2021.

Variable	Category	Cases n = 51 (%)	Controls n = 102 (%)	p value
Sex	Female	28 (54.9)	71 (69.6)	
	Male	23 (45.1)	31 (30.4)	0.07
Age in years	18 - 24	2 (3.9)	15 (14.7)	
	25 - 34	5 (9.8)	36 (35.3)	
	35 - 44	16 (31.4)	23 (22.6)	
	45 - 54	14 (27.5)	19 (18.6)	
	55 - 64	7 (13.7)	2 (1.9)	
	65+	7 (13.7)	7 (6.9)	**0.00**
Median age in years		48.0 (Q_1 = 38; Q_3 = 58)	34.5 (Q_1 = 28; Q_3 = 47)	
Occupation	Health worker	20 (39.2)	26 (25.5)	
	Teacher	9 (17.8)	9 (8.8)	
	Student	1 (2.0)	18 (17.7)	
	Unemployed	8 (15.7)	27 (26.4)	
	Other	13 (25.5)	22 (21.6)	**0.01**
Level of education	Primary	5 (9.8)	2 (2.0)	
	Secondary	12 (23.5)	18 (17.7)	
	Tertiary	34 (66.7)	82 (80.3)	0.05
Comorbidity	Yes	30 (58.8)	34 (33.3)	
	No	21 (41.2)	68 (66.7)	0.00

vaccination period for cases was 28 days (Q_1 = 14; Q_3 = 28) and for controls was also 28 days (Q_1 = 15; Q_3 = 30). The median duration of days between getting the second dose of the vaccine and getting tested for SARS-CoV-2 was 57.0 (Q_1 = 33; Q_3 = 81) and 46 (Q_1 = 33; Q_3 = 64) for cases and controls respectively. A total of 64 respondents (30 cases and 34 controls) had chronic diseases, with 26 (40.6%) being in the age group 45 - 54 years. Figure 1 shows the frequency of chronic conditions of the respondents. Of the 51 cases, 14 (27.5%) had no symptoms. Of the remaining 37 who had symptoms, 34 (91.2%) had mild to moderate symptoms with 3 (8.2%) having severe symptoms. Only 1 (2.0%) of the cases was admitted. The most common symptoms were headache with 24 (47.1%), fever with 20 (39.2%), and cough with 19 (37.3%). On the other hand, the least common symptoms were a sore throat 4 (7.8%), runny nose 2 (3.9%), and nausea 1 (2.0%). The median days for the duration of symptoms was 7 days (Q_1 = 4; Q_3 = 20).

3.2. Knowledge, Attitudes, and Practices

There were significant differences in overall knowledge level with controls having good knowledge compared to cases (p = 0.01). However, knowledge on transmission, prevention, and control were mostly comparable between the two groups (Table 2). There were no significant differences in attitudes between cases and control, however, there were significant differences in practices with controls adhering more to hand washing practices (p = 0.02) and adhering more to social distancing practices (p = 0.04) (Table 3).

3.3. Factors Associated with Breakthrough Infections

The significant risk factors for having COVID-19 breakthrough infection were being in the age of 35 - 44 years (OR = 5.53; 95% CI (1.08 - 28.18), having chronic illnesses (OR = 2.86; 95% CI (1.42 - 5.71), smoking (OR = 3.23; 95% CI (1.21 - 8.64) and history of tuberculosis (OR = 4.40; 95% CI (1.52 - 12.71). The significant protective factors for breakthrough COVID-19 disease were always hand washing and always observing social distance (Table 4). The association
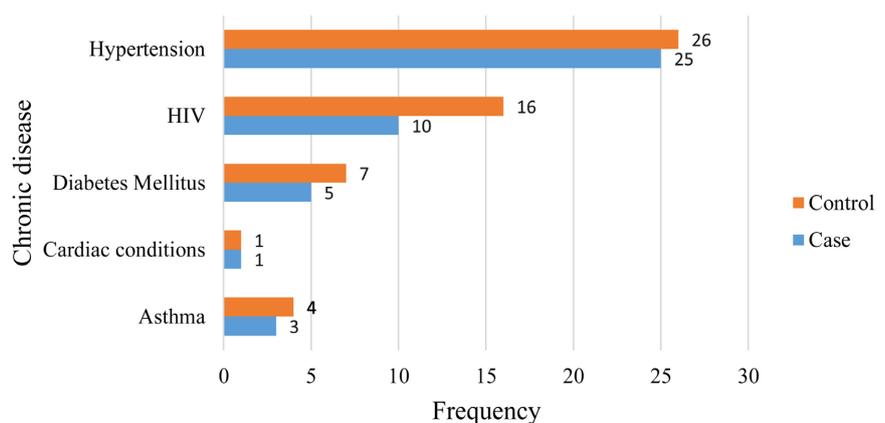
Figure 1. Frequency of medical chronic conditions of study participants in Kwekwe City, Zimbabwe 2021.

Table 2. Knowledge of participants in Kwekwe City, Zimbabwe 2021.

Variable	Cases n = 51 (%)	Controls n = 102 (%)	p-Value
Signs and Symptoms of COVID-19			
The symptoms of COVID-19 include fever, fatigue, cough, and myalgia.	51 (100.0)	102 (100.0)	1.00
Nasal congestion, runny nose, and sneezing can occur among people infected with the COVID-19 virus.	51 (100.0)	101 (99.0)	0.48
At present, there is no effective treatment for COVID-19, but early symptomatic treatment can help most patients recover from infection	47 (92.2)	101 (99.0)	**0.02**
Not all persons with COVID-19 will develop into severe cases.	45 (88.2)	99 (97.1)	**0.03**
Transmission routes			
Eating or contacting wild animals may result in infection by the COVID-19 virus	27 (52.9)	77 (75.5)	**0.00**
Persons with COVID-19 cannot pass the virus to others when a fever is not present	26 (51.0)	59 (57.84)	0.42
The COVID-19 virus spreads via respiratory droplets from infected individuals	51 (100.0)	100 (98.0)	0.31
Prevention and control			
Ordinary residents can wear general medical masks to prevent infection from the COVID-19 virus	47 (92.2)	95 (93.1)	0.82
Children and young adults don't need to take measures to prevent infection from the COVID-19 virus	29 (56.9)	85 (83.3)	**0.00**
To prevent infection by COVID-19, individuals should avoid going to crowded places such as bus stations and busy supermarkets	51 (100.0)	102 (100.0)	1.00
Isolation and treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus	51 (100.0)	102 (100.0)	1.00
People who have contact with someone infected with the COVID-19 virus should be immediately isolated in a proper place.	50 (98.0)	101 (99.0)	0.61
Summary of knowledge			
Good	46 (90.2)	101 (99.0)	**0.01**
Poor	5 (9.8)	1 (1.0)	

Table 3. Attitudes and practices of respondents in Kwekwe City, Zimbabwe 2021.

Variable	Cases n = 51 (%)	Controls n = 102 (%)	p-Value
Attitudes			
Ever since you were vaccinated, do you feel like you cannot contract COVID-19?	50 (98.0)	97 (95.1)	0.38
If you are tested for COVID-19 and the results are positive, would you believe it?	51 (100.0)	102 (100.0)	1.00
Do you think the government was right to put up the measures to prevent the spread of COVID-19?	51 (100.0)	102 (100.0)	1.00
Practices			
Hand washing adherence	28 (54.9)	75 (73.5)	**0.02**
Social distancing adherence	26 (51.0)	69 (67.7)	**0.04**
Masking adherence	29 (56.9)	74 (72.6)	0.05

Table 4. Factors associated with breakthrough COVID-19, Kwekwe City, Zimbabwe 2021.

Factor	Response	Cases n = 51 (%)	Controls n = 102 (%)	Odds Ratio (95% CI)	p value	Adjusted OR (95% CI)	p value
Gender	Female	28 (54.9)	71 (69.6)	0.53 (0.26 - 1.06)	0.07	0.88 (0.43 - 2.66)	0.89
	Male	23 (45.1)	31 (30.4)				
Age	18 - 24	2 (3.9)	15 (14.7)	Ref		Ref	Ref
	25 - 34	5 (9.8)	36 (35.3)	1.04 (0.18 - 5.98)	0.96	0.79 (0.12 - 4.91)	0.79
	35 - 44	16 (31.4)	23 (22.6)	5.22 (1.05 - 26.04)	**0.03**	4.46 (0.83 - 23.36)	0.08
	45 - 54	14 (27.5)	19 (18.6)	5.53 (1.08 - 28.18)	**0.03**	3.35 (0.51 - 22.06)	0.21
	55 - 64	7 (13.7)	2 (1.9)	26.25 (3.04 - 226.61)	**0.00**	12.22 (1.15 - 129.8)	**0.04**
	65+	7 (13.7)	7 (6.9)	7.5 (1.22 - 45.81)	**0.02**	4.89 (0.61 - 39.44)	0.14
Occupation	Health worker	20 (39.2)	26 (25.5)	Ref		Ref	
	Teacher	9 (17.8)	9 (8.8)	1.3 (0.44 - 3.88)	0.64	2.26 (0.60 - 8.58)	0.23
	Student	1 (2.0)	18 (17.7)	0.07 (0.01 - 0.59)	**0.00**	0.07 (0.00 - 1.22)	0.07
	Unemployed	8 (15.7)	27 (26.4)	0.39 (014 - 1.03)	0.05	0.26 (0.07 - 0.93)	**0.04**
	Other	13 (25.5)	22 (21.6)	0.77 (0.31 - 1.91)	0.57	0.77 (0.26 - 2.29)	0.64
History of COVID-19	Yes	3 (5.9)	10 (9.8)	0.58 (0.15 - 2.19)	0.41	* * *	
	No	48 (94.1)	92 (90.2)				
Chronic illnesses	Yes	30 (58.8)	34 (33.3)	2.86 (1.42 - 5.71)	**0.00**	1.15 (0.40 - 3.29)	0.79
	No	21 (41.2)	68 (66.7)				
History of hypertension	Yes	27 (52.9)	26 (25.5)	3.29 (1.62 - 6.67)	**0.00**	1.21 (0.30 - 4.86)	0.62
	No	24 (47.1)	76 (74.5)				
Vaccine	Sinopharm	27 (52.9)	47 (46.1)	1.32 (0.67 - 2.58)	0.42	* * *	
	Sinovac	24 (47.1)	55 (53.9)				

Continued

Contact with a COVID-19 patient	Yes	37 (75.6)	62 (60.8)	1.70 (0.82 - 3.55)	0.15	1.24 (0.51 - 3.01)	0.61
	No	14 (27.4)	40 (39.2)			
Smoking	Yes	11 (21.6)	8 (7.8)	3.23 (1.21 - 8.64)	**0.02**	3.07 (0.86 - 11.00)	0.08
	No	40 (78.4)	94 (92.2)			
History of TB	Yes	11 (21.6)	6 (5.9)	4.40 (1.52 - 12.71)	**0.00**	2.81 (0.73 - 10.77)	0.13
	No	40 (78.4)	96 (94.1)			
HIV status	Negative	41 (80.4)	86 (84.3)	0.76 (0.32 - 1.83)	0.54	* * *	
	Positive	10 (19.6)	16 (15.7)			
Hand washing adherence	Always	28 (54.9)	75 (73.5)	0.44 (0.22 - 0.89)	**0.02**	2.24 (0.64 - 7.82)	0.21
	Sometimes	23 (45.1)	27 (26.5)			
Mask wearing adherence	Always	29 (56.9)	74 (72.6)	0.50 (0.25 - 1.00)	0.05	1.60 (0.51 - 5.03)	0.43
	Sometimes	22 (49.1)	28 (27.4)			
Social distancing adherence	Always	26 (51.0)	69 (67.7)	0.50 (0.25 - 0.99)	**0.04**	0.84 (0.21 - 3.42)	0.81
	Sometimes	25 (49.0)	33 (32.3)			

Note: * not included in the logistic regression model because the p-value > 0.25.

between age and having COVID-19 breakthrough infection stratified by vaccine type was analysed. The crude odds ratio for age always was within the stratum-specific odds ratio. Therefore, the association between age and having a breakthrough infection was modified by the type of vaccine. The crude odds ratio was (OR = 5.4; 95% CI (2.00 - 13.60). The stratum specific odds ratios for the age groups were 25 - 34 years (OR = 1.2; 95% CI (0.09 - 14.69), 35 - 44 years (OR = 8.0; 95% CI (0.81 - 78.74), 45 - 54 years (OR = 12.0 95% CI (1.25 - 115.38), 55 - 64 years (OR = 48; 95% CI (2.40 - 958.29) and 65+ (OR = 7.2; 95% CI (0.59 - 87.02). Being within the age of 55 - 64 years (aOR = 12.22; 95% CI (1.15 - 129.81) and being unemployed (aOR = 0.26; 95% CI (0.07 - 0.93) were the independent factors associated with COVID-19 breakthrough infection in Kwekwe City.

4. Discussion

We found that the median interval from the second dose to the collection of a SARS-CoV-2 positive specimen was 57 days. In Chicago, Illinois, the median interval from the second dose to the collection of a positive SARS-CoV-2 specimen was 29 days (interquartile range [IQR] = 23 - 42 days) [14]. In India, the median time from receipt of the second dose to breakthrough infection was 29.5 days (interquartile range, 20 to 35) [21]. The median time from receipt of the second dose to a positive case in Kwekwe City was higher than in Chicago, Illinois, and India. This could be because the individuals in Kwekwe City had been vaccinated between the second and third wave and transmission of the SARS-CoV-2

virus could have been low. Furthermore, when cases are not high, testing for SARS-CoV-2 infection is relatively low and this could have resulted in a higher median time from second dose receipt to having a positive COVID-19 test. The results were however comparable to those by Sharma *et al.*, 2021 in Delhi, India who found that the median time until incidence of COVID-19 breakthrough infection since receiving second dose of COVID-19 vaccine was 47 (IQR = 28.5 to 55) days [17].

We found that more than a quarter of the breakthrough infections were not symptomatic and approximately 95% had mild to moderate disease. The percentage was higher than that reported in non-vaccinated individuals which shows that the vaccine is protecting against severe disease. The results were similar to those found in the United States (U.S) where (27%) of vaccine breakthrough infections were asymptomatic [9]. Despite the high percentage of mild to moderate disease, the case fatality rate remained high in Kwekwe City. The high case fatality could be attributed to the Delta variant which was in circulation during the time of the study. The delta variant was more virulent and was associated with higher mortality. Furthermore, the city had limited beds for infected individuals and was not able to cope with the high number of cases that occurred during the time which could have possibly resulted in the high case fatality rate. The case fatality was higher than that in the United States which stood at 2% [9].

In Kwekwe City the two vaccines that were being used were the Sinopharm and Sinovac vaccines. We found that the association between having breakthrough infection was modified by the type of vaccine that was used. As age increased, the odds of having breakthrough infection increased for those who were inoculated with the Sinovac vaccine. This could have resulted from the different efficacies of the vaccines. Sinopharm with two doses, administered at an interval of 21 days, has an efficacy of 79% against symptomatic SARS-CoV-2 infection 14 or more days after the second dose. Vaccine efficacy against hospitalization was 79% [10]. Sinovac trials showed 50.7% efficacy in Brazil, or 62.3% with longer dosing intervals, while Turkish researchers reported 83.5% efficacy [11].

We found that being in the age of 55 - 64 years was independently associated with having breakthrough COVID-19 infection. This could be because the risk of chronic illnesses such as hypertension and diabetes increases with age and they are also known to increase the risk of contracting SARS-CoV-2. The findings were similar to those by Butt on rate and risk factors for breakthrough infection after vaccination among US veterans who showed that the risk of contracting COVID-19 was lower among those with no comorbidities, compared with those with comorbidities [22]. Furthermore, some of the people in this group are still employed formally as the retirement age in most institutions in Zimbabwe is 65 years. When people are employed their mobility and interactions with other people are relatively high compared to those who stay at home given the lockdown measures. This then increases their risk of contracting SARS-CoV-2. Also, as people age, they become frail and increase their risk of having post-vac-

cination infections as was found in the United Kingdom [23].

In May 2021, the Zimbabwean government imposed a lockdown in Kwekwe where the delta variant had been detected. This was through the Public Health (COVID-19 Prevention, Containment and Treatment) (National Lockdown) (No. 2) (Amendment) Order, 2021 (No. 24) [24]. The lockdown restricted the movement of all the citizens in Kwekwe with only those working being allowed to move. We found that being unemployed protected against contracting SARS-CoV-2. This could be explained by the lockdown measures which restricted movement mostly among the employed. This resulted in reduced interaction with many people in turn reducing the risk of having breakthrough infections. It further shows that movement restrictions play a huge role in minimizing the transmission of SARS-CoV-2.

We found that non-pharmacological interventions such as always observing social distance, always wearing a mask, and always washing hands protected against having breakthrough COVID-19 infection. This shows that despite vaccination, people should continue to adhere to non-pharmacological interventions as they reduce the risk of contracting SARS-CoV-2. Every non-pharmaceutical intervention was aimed at slowing (in a few countries stopping) the disease progression buying time for the development, test, production, and distribution of vaccines that might ultimately protect the population [25]. Yang also noted that despite vaccination, China needed non-pharmaceutical interventions to prevent widespread outbreaks of COVID-19 in 2021 [26]. Antonelli *et al.*, 2021 cautioned about relaxing physical distancing and other personal protective measures in the post-vaccination era [23].

5. Limitations

During interviews recall and social desirability bias could have been introduced as questions were asked concerning past events. Bias might have led to overestimation or underestimation of the strength of associations between exposures and the outcome of interest. We tried to minimize recall bias by providing respondents adequate time to think before responding to the questions and the use of a well-structured data collection tool for both cases and controls. Social desirability bias was minimized by giving a brief history of the study so that the participants would not respond in a socially desirable way. African data shows 6 in 7 COVID-19 cases go undetected, there could have been misclassification bias as individuals may have had prior COVID-19 infections before first and after second doses of vaccinations. This could have underestimated or overestimated the measures of association.

6. Conclusions and Recommendations

The factors associated with contracting the SARS-CoV-2 virus in vaccinated individuals are almost similar to those in unvaccinated individuals. Being within the age group 54 - 65 years increases one's chances of having COVID-19 break-

through infections whilst being unemployed reduced the chances. The association between age and contracting SARS-CoV-2 was modified by the Sinovac vaccine. Non-pharmacological interventions such as wearing a mask correctly and consistently protect against COVID-19 breakthrough infections.

We, therefore, recommend that residents get continuous education on transmission, control, and prevention of the SARS-CoV-2 virus and that the city regularly tests individuals with symptoms of COVID-19 disease despite vaccination status. Those within the 54 - 65 years age group should minimize movement and if employed should work flexible hours or work from home. Also, those within that age group should be vaccinated using the Sinopharm vaccine. We further recommend that fully vaccinated individuals get booster doses of the vaccines. We also recommend studies that focus on antibody levels in vaccinated and their rate of decay so that appropriate recommendations on boosters can be given.

Acknowledgements

Conflicts of Interest

The authors declare no competing interests whether financial or non-financial.

Funding of the Study

Authors' Contributions

NCM, MM, AC, EG, NTG, TPJ, and MT: conception, design, and acquisition. NCM, MM, MT data analysis, and interpretation of data. NCM, MM, AC, EG, NTG, TPJ, and MT wrote the first draft of the manuscript. All authors read and approved the final manuscript for publication.

References

[1] CDC (2020) Coronavirus Disease 2019 (COVID-19). Centers for Disease Control and Prevention.
https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html

[2] (2021) Coronavirus Disease 2019 (COVID-19). Practice Essentials, Background, Route of Transmission. https://emedicine.medscape.com/article/2500114-overview

[3] WHO Declares Public Health Emergency for Novel Coronavirus.
https://www.medscape.com/viewarticle/924596

[4] Katsidzira, L., Gwaunza, L. and Hakim, J.G. (2020) Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Epidemic in Zimbabwe: Quo Vadis? *Clinical Infectious Diseases*, **71**, 2180-2183. https://doi.org/10.1093/cid/ciaa552
https://academic.oup.com/cid/article/71/16/2180/5835837

[5] Shinde, V., Bikha, S., Hoosain, Z., Archary, M., Bhorat, Q., Fairlie, L., *et al.* (2021) Efficacy of NVX-CoV2373 COVID-19 Vaccine against the B.1.351 Variant. *New England Journal of Medicine*, **384**, 1899-1909. https://doi.org/10.1056/NEJMoa2103055

[6] RAPID_PICES_Wave1.pdf. https://www.zimstat.co.zw/wp-content/uploads/publications/Income/Finance/RAPID_PICES_Wave1.pdf

[7] (2020) Monitoring COVID-19 Impact on Households in Zimbabwe. Report No. 1. https://documents1.worldbank.org/curated/en/898311610383469008/pdf/Monitoring-COVID-19-Impact-on-Households-in-Zimbabwe-Results-from-a-High-Frequency-Telephone-Survey-of-Households.pdf

[8] (2021) Monitoring COVID-19 Impact on Households in Zimbabwe. Report No. 3. https://www.unicef.org/zimbabwe/media/4686/file/Monitoring%20COVID-19%20Impact%20on%20Households%20in%20Zimbabwe.pdf

[9] Birhane, M., Bressler, S., Chang, G., Clark, T., Dorough, L., Fischer, M., *et al.* (2021) COVID-19 Vaccine Breakthrough Infections Reported to CDC—United States, January 1-April 30, 2021. *Morbidity and Mortality Weekly Report*, **70**, 792-793. https://doi.org/10.15585/mmwr.mm7021e3

[10] The Sinopharm COVID-19 Vaccine: What You Need to Know. https://www.who.int/news-room/feature-stories/detail/the-sinopharm-covid-19-vaccine-what-you-need-to-know

[11] Dyer, O. (2021) COVID-19: Chinese Vaccines May Need Changes to Improve Efficacy, Admits Official. *BMJ*, **373**, n969. https://doi.org/10.1136/bmj.n969

[12] India's "Covaxin" Vaccine Shows High Efficacy against COVID-19 Infections in Phase 3 Trial. https://www.gavi.org/vaccineswork/indias-covaxin-vaccine-shows-high-efficacy-against-covid-19-infections-phase-3

[13] Jones, I. and Roy, P. (2021) Sputnik V COVID-19 Vaccine Candidate Appears Safe and Effective. *The Lancet*, **397**, 642-643. https://doi.org/10.1016/S0140-6736(21)00191-4

[14] Teran, R.A. (2021) Postvaccination SARS-CoV-2 Infections among Skilled Nursing Facility Residents and Staff Members—Chicago, Illinois, December 2020-March 2021. *Morbidity and Mortality Weekly Report*, **70**, 632-638. https://doi.org/10.15585/mmwr.mm7017e1

[15] Cavanaugh, A.M. (2021) COVID-19 Outbreak Associated with a SARS-CoV-2 R.1 Lineage Variant in a Skilled Nursing Facility after Vaccination Program—Kentucky, March 2021. *Morbidity and Mortality Weekly Report*, **70**, 639-643. https://doi.org/10.15585/mmwr.mm7017e2

[16] Brosh-Nissimov, T., Orenbuch-Harroch, E., Chowers, M., Elbaz, M., Nesher, L., Stein, M., *et al.* (2021) BNT162b2 Vaccine Breakthrough: Clinical Characteristics of 152 Fully Vaccinated Hospitalized COVID-19 Patients in Israel. *Clinical Microbiology and Infection*, **27**, 1652-1657. https://doi.org/10.1016/j.cmi.2021.06.036

[17] Sharma, P., Mishra, S., Basu, S., Kumar, R. and Tanwar, N. (2021) Breakthrough Infection with Severe Acute Respiratory Syndrome Coronavirus 2 among Healthcare Workers in Delhi: A Single-Institution Study. *Cureus*, **13**, e19070. https://doi.org/10.7759/cureus.19070

[18] Teng, Y.-M., Wu, K.-S., Wang, W.-C. and Xu, D. (2021) Assessing the Knowledge, Attitudes and Practices of COVID-19 among Quarantine Hotel Workers in China. *Healthcare*, **9**, 772. https://doi.org/10.3390/healthcare9060772

[19] Kaliyaperumal, K. and Expert, I.E.C. (2004) Guideline for Conducting a Knowledge, Attitude and Practice (KAP) Study. 3.

[20] Twinamasiko, N., Olum, R., Gwokyalya, A.M., Nakityo, I., Wasswa, E. and Sserunjogi, E. (2021) Assessing Knowledge, Attitudes and Practices towards COVID-19 Public Health Preventive Measures among Patients at Mulago National Referral Hospital. *Rocky Mountain Health Plans*, **14**, 221-230.
https://doi.org/10.2147/RMHP.S287379

[21] Hacisuleyman, E., Hale, C., Saito, Y., Blachere, N.E., Bergh, M., Conlon, E.G., *et al.* (2021) Vaccine Breakthrough Infections with SARS-CoV-2 Variants. *New England Journal of Medicine*, **384**, 2212-2218. https://doi.org/10.1056/NEJMoa2105000

[22] Butt, A.A., Khan, T., Yan, P., Shaikh, O.S., Omer, S.B. and Mayr, F. (2021) Rate and Risk Factors for Breakthrough SARS-CoV-2 Infection after Vaccination. *Journal of Infection*, **83**, 237-279. https://doi.org/10.1016/j.jinf.2021.05.021

[23] Antonelli, M., Penfold, R.S., Merino, J., Sudre, C.H., Molteni, E., Berry, S., *et al.* (2022) Risk Factors and Disease Profile of Post-Vaccination SARS-CoV-2 Infection in UK Users of the COVID Symptom Study app: A Prospective, Community-Based, Nested, Case-Control Study. *The Lancet Infectious Diseases*, **22**, 43-55.
https://doi.org/10.1016/S1473-3099(21)00460-6

[24] SI 2021-153A Public Health (COVID-19 Prevention, Containment and Treatment) (National Lockdown) (No. 2) (Amendment) Order, 2021 (No. 24)|Veritaszim.
https://www.veritaszim.net/node/5047

[25] Gozzi, N., Bajardi, P. and Perra, N. (2021) The Importance of Non-Pharmaceutical Interventions during the COVID-19 Vaccine Rollout. *PLOS Computational Biology*, **17**, e1009346.
https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1009346

[26] Yang, J., Marziano, V., Deng, X., Guzzetta, G., Zhang, J., Trentini, F., *et al.* (2021) Despite Vaccination, China Needs Non-Pharmaceutical Interventions to Prevent Widespread Outbreaks of COVID-19 in 2021. *Nature Human Behaviour*, **5**, 1009-1020.
https://doi.org/10.1038/s41562-021-01155-z