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Article

Influenza Vaccination Hesitancy and Acceptance among Healthcare Workers in Cape Town, South Africa

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Abstract: Vaccination attitudes among healthcare workers (HCWs) is a vital factor for measuring their level of vaccination uptake and intention to recommend vaccinations to their patients. To our knowledge, no study has been conducted in South Africa to assess hesitancy to influenza vaccines among HCWs. We used questionnaire adapted from Betsch and colleagues to conduct an online and face-to-face cross-sectional study among HCWs at the start of COVID-19 vaccine roll-out prior to the flu season. Main outcome was influenza vaccine hesitancy. We used multivariate logistic regression to assess predictors of influenza vaccine hesitancy. Of 401 participants, 64.5% were women, 49.2% nurses, and 12.5% physicians. A total of 54.9% were willing to accept vaccination, 20.4% were undecided, and 24.7% intended to refuse. Older participants above 17-25 years and physicians were likely to receive the vaccine. Key predictors of vaccine acceptance were confidence in the effectiveness, consideration of benefits and risks, and willingness to be vaccinated to protect others. Influenza vaccine hesitancy was highest in those who did not trust that influenza vaccines are safe. For future flu

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seasons, tailored education programs targeting younger HCWs and more information about the composition of flu vaccines would be vital to improve vaccine uptake.

Keywords: Influenza vaccines; Vaccine hesitancy; Healthcare workers (HCWs); South Africa

1. Introduction

Influenza, also known as flu, is an acute respiratory infection that is highly contagious and considered one of the most challenging public health problems worldwide (1, 2). It may range from mild to severe illness causing hospitalizations and deaths mainly among high-risk groups (1). Seasonal influenza causes an estimated 3 to 5 million cases of severe illness and between 250,000 to 500,000 deaths worldwide every year (1). Most often, deaths associated with influenza occur among the most vulnerable individuals including young children, elderly, and chronically ill patients (1). Despite the severity of influenza, there are safe vaccines available albeit a low uptake (hesitancy) among specific risk groups resulting in the high burden of flu pandemic. Healthcare workers (HCWs) are at regular contact with ill patients and are therefore at a higher risk of contacting the influenza virus and may also transmit the disease to their patients. As such, HCWs infections may be a source of nosocomial outbreaks, with an increased risk of mortality among immunocompromised, hospitalized and high-risk patients they care for (3, 4). Further, influenza infection among health professionals is associated with a high economic burden and is mainly related to absenteeism (5).

Given the aforementioned reasons, the World Health Organization (WHO) and the U.S. Advisory Committee on Immunization Practices (ACIP) recommended annual vaccination of HCWs (6, 7) with influenza vaccines. Despite these recommendations and reported efficacy of HCWs influenza vaccination in reducing sickness, absenteeism rates mostly in the high-income parts of the world (8, 9), with annual vaccination rates varying between 44% and 54% in UK (8). Vaccine coverage among healthcare professionals remains low mainly in low- and middle-income countries (10, 11), with less than half that had received the influenza vaccine at least once in their lives and only 15.3% that were vaccinated in the 2018–2019 flu season in Tunisia (11). It is critical to understand barriers to influenza vaccination or hesitancy, and to find better ways to improve influenza vaccine uptake in this group as they are in the front line (12).

There are reports showing that influenza vaccination does not only protect against influenza but also reduces the risk of COVID-19 infection, suggesting immune cross-protection between influenza vaccination and COVID-19 to an extent (13-15). Therefore, increase HCWs flu vaccination, may provide some benefits, especially during this period of relatively high vaccine hesitancy towards COVID-19 vaccination and especially among HCWs (16). Thus, it is critical to understand the behaviour of HCWs towards flu vaccination. Hence, as an implementation research project on influenza vaccination among HCWs, we sought to find out if HCWs would take the influenza vaccine during the next flu season as the study was conceived in March when the flu season in South Africa was approaching (usually in winter between May and August) (17, 18).

Vaccine hesitancy has been described by the Strategic Advisory Group of Experts on Immunization (SAGE) as a motivational state of being conflicted about, or opposed to, getting vaccinated, including intentions and

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willingness (19). Vaccine hesitancy is a complex and context-specific issue and may vary across time, place, and type of vaccines (20). There are specific characteristics that should be considered when looking at influenza vaccine hesitancy. Influenza vaccine effectiveness varies yearly and is sometime described as too low (20); there are influenza-specific myths (e.g., the flu shot can cause the flu (21)); it is required yearly; and in most countries it is recommended for specific risk groups only. Influenza vaccine hesitancy does have unique features that requires further investigations to gain specific understanding of the phenomenon.

There are limited number of studies on vaccine hesitancy especially regarding influenza vaccine among HCWs conducted in low- and middle-income countries (22). To our knowledge, no study has been conducted in South Africa to assess acceptance and hesitancy of the influenza vaccine among HCWs. In this study, we aimed to understand the extent and the major contributors to influenza vaccine acceptance and hesitancy among HCWs in Cape Town. Findings would be vital to understand the bigger picture of the level of influenza vaccine acceptance and hesitancy among HCWs in South Africa as a whole.

2. Materials and methods

2.1. Study design and setting

The study was a cross sectional survey of HCWs working in healthcare settings in Cape Town, South Africa. Participants were HCWs from both private and government facilities that were eligible, and participation was on voluntary basis. The sample size was estimated at 300 participants based on best practice recommendations for exploratory factor analyses and scale validation published by Betsch and colleagues in 2020 (23). This sample size of 300 was enough to allow for detection of a reasonable correlation (r=0.2) with about 95% power (23). To assess the psychological antecedents of influenza vaccination in our study, we performed a qualitative assessment of confidence, complacency, constraints, calculated risk and collective responsibility as determinants of influenza vaccine hesitancy amongst HCWs as previously described by Bestch and colleagues (23-25).

2.2. Ethical consideration

The study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC: 858/2020), and permission was granted to access health facilities in Cape Town by the Western Cape Provincial Government Department of Health (WC_202101_014). In addition, permission was granted by the respective healthcare facilities managers for data to be collected. Ethical principles were adhered to, including HCW's informed consent, anonymity, and confidentiality.

2.3. Data collection and management

Data collection started prior to the preceding flu season and coincided with the start of the COVID-19 vaccination rollout among HCWs in South Africa. Participants were enrolled between 15 March and 27 May 2021. Recruitment of participants and study data were collected either through hard copy questionnaires handed to the healthcare facilities, or using online form on Research Electronic Data Capture software tools (REDCap; Vanderbilt University, Nashville, TN, USA) (26-28) hosted at the University of Cape Town server sent through a link to HCWs e-mails or HCWs WhatsApp chat groups. Once completed electronically, data was directly captured and

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stored on REDCap. Data completed on hard copies was captured and verified on the REDCap platform by two researchers. The survey instrument variables included sociodemographic characteristics, as well as attitudes, and behaviors of HCWs towards influenza vaccines. Information on sociodemographic characteristics included date of birth, age, gender, education, healthcare workers role, religion, and personal income.

Regarding contributors to influenza vaccine hesitancy in HCWs, this study adapted 15 questions published by Betsch and colleagues in 2018 (29) on five psychological antecedents of vaccinations namely constraints, confidence, calculation of risk, complacency, and collective responsibility (29), and further contextualized in our setting. In addition, questions were asked regarding HCWs religion being compatible with influenza vaccination. The detailed questionnaire employed in the study can be seen in our previous publication (16), and participants had to sign consent before attempting the questionnaires either as hard copies or an online form.

2.4. Description of variables

The explanatory variables consisted of 23 questions or statements (six on sociodemographic characteristics and 17 on attitudes toward influenza vaccination).

We treated the sociodemographic variables as follows; age transformed from a numeric to a categorical variable (17–24, 25-34, 35-44, 45-54, 55+) to be able to examine differences between specific age groups. We grouped healthcare worker roles into administrative support and clinical researchers, nurse, physician, and other HCWs to reflect the risk related to the function. We also stratified highest educational attainment into three categories: below high school, high school graduate, and University (from Bachelor to PhD). We also grouped religion into Christian, Muslim, other religions (African Spirituality, Hindu, Buddhist, Jewish, etc.), and none. For personal income per month, categories included less than 10,000.00 Rand, between 10,000.00 and 50,000.00 Rand, and more than 50,000.00 Rand. The current exchange rate is One United States Dollar to 14 South African Rands.

Each of the 17 vaccine attitude statements had seven response options: 1 for strongly disagree, 2 for moderately disagree, 3 for slightly disagree, 4 for neutral, 5 for slightly agree, 6 for moderately agree, and 7 for strongly agree. We shortened these to three responses as follows: 1 to 3 were categorized as “no”, 4 as “neutral”, and 5 to 7 as “yes”.

Our outcome variable was the intention to receive a dose of influenza vaccine. This was measured in the questionnaire by the statement “During the next influenza season, I will take the influenza vaccine”. This statement had seven response options: 1 for strongly disagree, 2 for moderately disagree, 3 for slightly disagree, 4 for neutral, 5 for slightly agree, 6 for moderately agree, and 7 for strongly agree. We transformed the seven responses to three as follows: 1 to 3 were categorised as “no” or “refusals”, 4 as “neutral” or “undecided”, and 5 to 7 as “yes” or “acceptance”. The outcome variable was further transformed to a binary variable with responses 1 to 4 categorised as “hesitancy” and 5 to 7 and “acceptance”. This dichotomisation of Likert scale responses for influenza vaccine intention has been employed previously by other recent surveys (30, 31), including our group’s recent assessment of attitudes and behaviour towards COVID-19 vaccination by HCWs (16).

2.5. Statistical analyses

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A total of 414 people completed the questionnaire. However, eight records were duplicates and five had incomplete information on age and gender. These records (13) were excluded from the statistical analyses. To describe the intention of HCWs for influenza vaccination by sociodemographic characteristics and by influenza vaccine personal consideration, frequency and percentages were used for categorical data and means with standard deviation (SD) for continuous variables.

We used multivariate logistic regression to assess the association between socio-demographic variables and intention to receive an influenza vaccine dose, followed by models including each vaccination attitude variable separately. We assessed the predictors of influenza vaccine acceptance versus hesitancy (i.e., neutral and refusal); acceptance versus neutral, excluding the refusals; acceptance versus refusal, excluding neutrals; neutral versus refusal, excluding acceptance; and refusal versus other intentions (i.e., acceptance and neutral). As a result of this process, we fitted models adjusted for age as a continuous variable and gender to assess independent predictors of influenza vaccine intention among HCWs in Cape Town. All statistical analyses, tables, and figures were processed with the R software, version 4.0.4 and models built using generalised linear model for logistic regression in R/finalfit. R,1.0.3 package. All p-values are two-sided.

3. Results

3.1. Sociodemographic characteristics of study participants

Table 1 presents the sociodemographic characteristics of 401 participants of this study as we investigated the intention to take the vaccine. Of the 401 HCWs included in the analysis, 220 (54.9%) expressed intention to take influenza vaccine, 99 (24.7%) would refuse, and 82 (24.4%) were neutral. Looking at age, participants between the ages 25-34 and 35- 44 were more willing to take the influenza vaccine, both age groups had a participation frequency of 104 (25.9%) and 103 (26.7%) with an intention to accept influenza vaccination frequency of 56 (25.5%) and 58 (26.4%), respectively. Professional classification found nurses to be the highest number of HCWs that participated in this study (49.2%) with physicians being the lowest (12.5%). Among the HCWs who expressed intention to take the shot, 135 (64.3%) female HCWs declared their intention to accept the influenza vaccine. Among all HCWs 193 (49.2%) nurses engaged in this study with 86 (40.2%) expressed intention to vaccinate for influenza, while 56 (68.3%) were neutral and 51 (53.1%) refused. More of those who completed high school and university graduates had intention to vaccinate with acceptance frequencies of 86 (40.6%) and 118 (55.7%) respectively among all HCWs. In addition, those with a personal income of between R10,000 – R50,000 per month had the highest participation frequency of 235 (64.2%), 59.1% of whom expressed intention to accept the flu vaccine. Regarding religion, 262 (71.6%) Christians participated and 73.3% expressed intention to accept the influenza vaccines.

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Table 1. Sociodemographic characteristics of study participants.

Variables	Intention for influenza vaccination			
	All N=401	**Neutral** N=82 (20.4%)	**Refusal** N=99 (24.7%)	**Acceptance** N=220 (54.9%)
Sociodemographic Variables				
Age (in years)	39.2 (12.3)	33.6 (9.34)	38.2 (12.9)	41.7 (12.3)
Age groups:				
17-24 years	40 (9.98%)	15 (18.3%)	16 (16.2%)	9 (4.09%)
25-34 years	104 (25.9%)	29 (35.4%)	19 (19.2%)	56 (25.5%)
35-44 years	103 (26.7%)	22 (26.8%)	22(22.2%)	58 (26.4%)
45-54 years	67 (16.7%)	8 (9.76%)	18 (18.2%)	41 (18.6%)
55-78 years	42 (10.5%)	1 (1.22%)	8 (8.08%)	33 (15.0%)
Gender:				
Male	136 (35.5%)	20 (25.6%)	41 (43.2%)	75 (35.7%)
Female	247 (64.5%)	58 (74.4%)	54 (56.8%)	135 (64.3%)
Health worker role:				
Admin support	51 (13.0%)	8 (9.76%)	11 (11.5%)	32 (15.0%)
Nurses	193 (49.2%)	56 (68.3%)	51 (53.1%)	86 (40.2%)
Other health workers	99 (25.3%)	17 (20.7%)	32 (33.3%)	50 (23.4%)
Physicians	49 (12.5%)	1 (1.22%)	2 (2.08%)	46 (21.5%)
Highest educational level attained:				
High School Graduate	188 (49.3%)	47 (61.0%)	55 (59.8%)	86 (40.6%)
Below High School	11 (2.89%)	0 (0.00%)	3 (3.26%)	8 (3.77%)
University	182 (47.8%)	30 (39.0%)	34 (37.0%)	118 (55.7%)
Personal income:				
Less than R10,000 per month	78 (21.3%)	15 (18.8%)	25 (28.4%)	38 (19.2%)
More than R50,000 per month	53 (14.5%)	5 (6.25%)	5 (5.68%)	43 (21.7%)
R10,000 - R50,000 per month	235 (64.2%)	60 (75.0%)	58 (65.9%)	117 (59.1%)
Religion:				
African Spirituality	4 (1.09%)	1 (1.25%)	0 (0.00%)	3 (1.54%)
Buddhist or Hindu	15 (4.10%)	5 (6.25%)	4 (4.40%)	6 (3.08%)
Christian	262 (71.6%)	55 (68.8%)	64 (70.3%)	143 (73.3%)
Jewish	4 (1.09%)	0 (0.00%)	1 (1.10%)	3 (1.54%)
Muslim	54 (14.8%)	17 (21.2%)	16 (17.6%)	21 (10.8%)
None	27 (7.38%)	2 (2.50%)	6 (6.59%)	19 (9.74%)

Values shown are absolute counts (percentages), except for age in years where the values are means (standard deviations)

3.2. Attitudes towards influenza vaccination among HCWs

We found that 49.9% (200 participants) of the HCWs had received influenza vaccine in the past (Table 2). From the 401 total participants who were included in the statistical analysis, 220 (54.9%) were willing to take the vaccine, with influenza vaccine hesitancy at 45.1% i.e., a combination of those who were undecided and those who would refuse to take the flu vaccine. A total of 167 (76.6%) of 220 who would accept the flu vaccine agreed that vaccination against influenza is compatible with their religion.

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Table 2. Attitudes towards influenza vaccination among HCWs.

Variables	Intention to get influenza vaccine			
	All	**Neutral**	**Refusal**	**Acceptance**
	N=401	N=82 (20.4%)	N=99 (24.7%)	N=220 (54.9%)
Received influenza vaccine in the past	200 (49.9%)	15 (18.3%)	30 (30.9%)	155 (72.8%)
Influenza vaccination is compatible with my religion:				
Neutral	86 (21.6%)	51 (62.2%)	11 (11.2%)	24 (11.0%)
No	100 (25.1%)	15 (18.3%)	58 (59.2%)	27 (12.4%)
Yes	212 (53.3%)	16 (19.5%)	29 (29.6%)	167 (76.6%)
I am completely confident that influenza vaccines are safe:				
Neutral	92 (23.2%)	57 (71.2%)	16 (16.2%)	19 (8.72%)
No	83 (20.9%)	11 (13.8%)	61 (61.6%)	11 (5.05%)
Yes	222 (55.9%)	12 (15.0%)	22 (22.2%)	188 (86.2%)
Influenza vaccination is effective:				
Neutral	94 (24.1%)	57 (71.2%)	21 (22.3%)	16 (7.41%)
No	75 (19.2%)	9 (11.2%)	54 (57.4%)	12 (5.56%)
Yes	221 (56.7%)	14 (17.5%)	19 (20.2%)	188 (87.0%)
I am confident that public authorities decide in the best interest of the community:				
Neutral	92 (23.2%)	38 (46.3%)	29 (29.9%)	25 (11.5%)
No	73 (18.4%)	17 (20.7%)	42 (43.3%)	14 (6.45%)
Yes	231 (58.3%)	27 (32.9%)	26 (26.8%)	178 (82.0%)
Influenza vaccination is unnecessary because flu is not common anymore:				
Neutral	97 (24.9%)	38 (47.5%)	28 (29.5%)	31 (14.5%)
No	252 (64.8%)	40 (50.0%)	50 (52.6%)	162 (75.7%)
Yes	40 (10.3%)	2 (2.50%)	17 (17.9%)	21 (9.81%)
My immune system is so strong, it also protects me against flu:				
Neutral	91 (23.4%)	37 (46.2%)	20 (21.1%)	34 (15.9%)
No	210 (54.0%)	34 (42.5%)	42 (44.2%)	134 (62.6%)
Yes	88 (22.6%)	9 (11.2%)	33 (34.7%)	46 (21.5%)
Flu infection is not so severe that I should be vaccinated:				
Neutral	88 (22.4%)	21 (26.2%)	31 (32.3%)	36 (16.7%)
No	230 (58.7%)	49 (61.3%)	34 (35.4%)	147 (68.1%)
Yes	74 (18.9%)	10 (12.5%)	31 (32.3%)	33 (15.3%)
Everyday stress will prevent me from getting vaccinated against influenza:				
Neutral	85 (21.6%)	28 (34.1%)	30 (31.9%)	27 (12.4%)
No	264 (67.0%)	46 (56.1%)	52 (55.3%)	166 (76.1%)
Yes	45 (11.4%)	8 (9.76%)	12 (12.8%)	25 (11.5%)
It is inconveniencing for me to receive vaccinations against influenza:				
Neutral	85 (21.5%)	32 (39.5%)	27 (27.8%)	26 (11.9%)
No	235 (59.3%)	44 (54.3%)	42 (43.3%)	149 (68.3%)
Yes	76 (19.2%)	5 (6.17%)	28 (28.9%)	43 (19.7%)
Visiting the vaccination clinic will make me feel uncomfortable, and this will keep me from getting vaccinated against influenza:				
Neutral	66 (16.8%)	25 (30.5%)	21 (21.9%)	20 (9.35%)
No	237 (60.5%)	34 (41.5%)	47 (49.0%)	156 (72.9%)

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Yes	89 (22.7%)	23 (28.0%)	28 (29.2%)	38 (17.8%)
When I think about getting vaccinated against influenza, I weigh benefits and risks to make the best decision possible:				
Neutral	64 (16.1%)	22 (26.8%)	18 (18.6%)	24 (11.0%)
No	77 (19.3%)	11 (13.4%)	20 (20.6%)	46 (21.0%)
Yes	257 (64.6%)	49 (59.8%)	59 (60.8%)	149 (68.0%)
For every influenza vaccine dose, I will closely consider whether it is useful for me:				
Neutral	81 (20.6%)	29 (35.4%)	27 (28.1%)	25 (11.6%)
No	74 (18.8%)	11 (13.4%)	17 (17.7%)	46 (21.4%)
Yes	238 (60.6%)	42 (51.2%)	52 (54.2%)	144 (67.0%)
It is important for me to fully understand the topic of vaccination before I get vaccinated against influenza:				
Neutral	60 (15.2%)	24 (29.6%)	19 (19.6%)	17 (7.87%)
No	55 (14.0%)	8 (9.88%)	12 (12.4%)	35 (16.2%)
Yes	279 (70.8%)	49 (60.5%)	66 (68.0%)	164 (75.9%)
When everyone is vaccinated against influenza, I don't have to get vaccinated, too:				
Neutral	81 (21.2%)	28 (35.4%)	37 (41.1%)	16 (7.51%)
No	183 (47.9%)	16 (20.3%)	23 (25.6%)	144 (67.6%)
Yes	118 (30.9%)	35 (44.3%)	30 (33.3%)	53 (24.9%)
I will get vaccinated against influenza because I will be protecting people with a weaker immune system:				
Neutral	75 (19.2%)	27 (33.3%)	33 (34.7%)	15 (6.98%)
No	60 (15.3%)	12 (14.8%)	22 (23.2%)	26 (12.1%)
Yes	256 (65.5%)	42 (51.9%)	40 (42.1%)	174 (80.9%)
Vaccination is a collective responsibility to prevent the spread of diseases like influenza:				
Neutral	70 (17.8%)	29 (35.4%)	28 (28.6%)	13 (6.10%)
No	33 (8.40%)	3 (3.66%)	14 (14.3%)	16 (7.51%)
Yes	290 (73.8%)	50 (61.0%)	56 (57.1%)	184 (86.4%)

Values shown are absolute counts (percentages)

Based on confidence (23-25), out of the 220 participants that were willing to accept flu vaccination, 188 (86.2%) HCWs believed that the influenza vaccine is safe as compared to 11 (5.05%) that did not believe. Moreover, 188 (87.0%) agreed that the influenza vaccine is effective. Of interest was that 178 (82.0%) participants expressed confidence that public authorities had the best interest of the general community at heart.

As for complacency (23-25), among the 401 participants included in the statistical analysis, 252 (64.8%) had the belief that influenza vaccination is not necessary because flu is not common anymore. Among the 220 who intended to take the flu vaccine, 162 (75.7%) believed flu vaccine was necessary and 21 (9.81%) believed it was not. Also, among the 401 participants included in the statistical analysis, 210 (54.0%) did not agree that their immune system is strong to protect them against influenza. Among the 220 who were willing to accept the influenza vaccine, 134 (62.6%) did not belief in the strength of their immune system to protect them while 46 (21.5%) did. Furthermore, among the 220 HCWs who were willing to accept the influenza vaccine, 147 (68.1%) had the belief that the flu infection is so severe for them to take a vaccine.

Regarding constraints (23), out of the 401 participants included in the statistical analysis, 264 (67.0%) of HCWs did not have the impression that every day stress will prevent them from getting vaccinated against influenza. Among the 220 who intended to take the flu vaccine, 166 (76.1%) did not have

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the impression that every day stress will prevent them from getting vaccinated against influenza while 25 (11.5%) did. On the other hand, a smaller frequency of HCWs 76 (19.2%) out of the 401 participants included in the statistical analysis thought it would be inconveniencing for them to get vaccinated against influenza. Also, with respect to convenience (23-25), few HCWs 89 (22.7%) out of the 401 participants included in the statistical analysis did think that visiting the vaccination clinic will make them feel uncomfortable, and this will further keep them from getting vaccinated against influenza. However, 237 (60.5%) did not think so, of which 156 (72.9%) out of the 220 who intended to take the flu vaccine did not think so.

Looking at risk calculation (23, 24), among the 220 who intended to take the flu vaccine, 149 (68.0%) indicated they will first weigh benefit and risk before taking a decision to get the influenza vaccine. In addition, 144 (67.0%) HCWs highlighted that they will closely monitor when it comes to decision making to accepting vaccination whether the vaccine is useful to them or not. A high frequency of HCWs 164 (75.9%) reported that it will be of importance for them to fully understand the topic of the vaccination before getting the influenza vaccine.

As far as collective responsibility is concerned (23), among the 220 who intended to take the flu vaccine, 144 (67.6%) HCWs mentioned that even if the greater population is vaccinated for influenza, they also still need to get vaccinated. Majority of HCWs 174 (80.9%) indicated that they will get vaccinated to protect their colleagues, patients, and other people with weaker immune system. Finally, 184 (86.4%) HCWs reported that they believe vaccination is a collective responsibility to prevent the spread of diseases like influenza.

3.3. Predictors of acceptance versus hesitancy of influenza vaccination

HCWs willingness to accept influenza vaccination was significantly associated with age with older HCWs (>24 years age groups) being more willing compared to the 17-24 years old. The older HCWs, 55-78 years were the most willing to accept the influenza vaccine with odds ratio (OR 9.53, 95% confidence interval (CI) 2.55-40.32, p = 0.001, Table 3). This was followed by HCWs between the ages of 45-54 years (OR 6.54, 95% CI 2.26 to 21.27, p = 0.001), and 35-44 years (OR 4.27, 95% CI 1.60 to 12.93, p = 0.006), and lastly 25-34 years old's (OR 3.31, 95% CI 1.25 to 9.97, p = 0.02). Compared to HCWs with administration role, nurses had the highest number of participants in the study with a trend towards a significant unwillingness to accept influenza vaccine (OR 0.48, 95% CI 0.21-1.09, p = 0.083) while physicians displayed a significantly higher willingness to accept the influenza vaccine (OR 24.43, 95% CI 3.97-480.39, p = 0.004). In addition, HCWs who attained higher education or university also had a significantly higher willingness for influenza vaccination (OR 1.83, 95% CI 1.01-3.37, p = 0.048) than those with high school level. Among our study participants, gender, personal income, and religion did not prove to be independent predictors of influenza vaccine hesitancy.

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Table 3. Predictors associated with acceptance versus hesitancy of influenza vaccination.

Variables		Influenza vaccine intention		Acceptance versus hesitancy	
		Hesitancy	Acceptance	OR (univariable)	OR (multivariable)
Sociodemographic characteristics					
Age groups	17-24 years	31 (77.5)	9 (22.5)	-	-
	25-34 years	48 (46.2)	56 (53.8)	4.02 (1.80-9.74, p=0.001)	3.31 (1.25-9.97, p=0.022)
	35-44 years	41 (42.7)	55 (57.3)	4.62 (2.05-11.29, p<0.001)	4.27 (1.60-12.93, p=0.006)
	45-54 years	26 (38.8)	41 (61.2)	5.43 (2.30-13.84, p<0.001)	6.54 (2.26-21.27, p=0.001)
	55-78 years	9 (21.4)	33 (78.6)	12.63 (4.64-38.09, p<0.001)	9.53 (2.55-40.32, p=0.001)
Gender	Male	61 (44.9)	75 (55.1)	-	-
	Female	112 (45.3)	135 (54.7)	0.98 (0.64-1.49, p=0.926)	1.36 (0.77-2.43, p=0.290)
Health worker role	Admin support	19 (37.3)	32 (62.7)	-	-
	Nurses	107 (55.4)	86 (44.6)	0.48 (0.25-0.89, p=0.022)	0.48 (0.21-1.09, p=0.083)
	Other health workers	49 (49.5)	50 (50.5)	0.61 (0.30-1.20, p=0.155)	0.64 (0.26-1.56, p=0.326)
	Physicians	3 (6.1)	46 (93.9)	9.10 (2.81-41.08, p=0.001)	24.43 (3.97-480.39, p=0.004)
Highest educational level	High School Graduate	102 (54.3)	86 (45.7)	-	-
	Below High School	3 (27.3)	8 (72.7)	3.16 (0.88-14.78, p=0.096)	2.81 (0.65-15.15, p=0.185)
	University	64 (35.2)	118 (64.8)	2.19 (1.44-3.33, p<0.001)	1.83 (1.01-3.37, p=0.048)
Personal income	Less than R10,000 per month	40 (51.3)	38 (48.7)	-	-
	More than R50,000 per month	10 (18.9)	43 (81.1)	4.53 (2.06-10.70, p<0.001)	0.53 (0.15-1.90, p=0.327)
	R10,000-R50,000 per month	118 (50.2)	117 (49.8)	1.04 (0.62-1.75, p=0.870)	1.01 (0.48-2.10, p=0.982)
Religion	African or Hindu or Jewish	11 (47.8)	12 (52.2)	-	-

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	Christian	119 (45.4)	143 (54.6)	1.10 (0.46-2.60, p=0.824)	1.69 (0.57-5.18, p=0.346)
	Muslim	33 (61.1)	21 (38.9)	0.58 (0.21-1.56, p=0.283)	0.79 (0.21-2.92, p=0.716)
	None	8 (29.6)	19 (70.4)	2.18 (0.69-7.18, p=0.190)	1.27 (0.32-5.24, p=0.738)
Variables related to confidence in influenza vaccines					
Received influenza vaccine in the past	No	134 (69.8)	58 (30.2)	-	-
	Yes	45 (22.5)	155 (77.5)	7.96 (5.10-12.63, p<0.001)	6.41 (3.15-13.53, p<0.001)
Compatible with religion	Neutral	62 (72.1)	24 (27.9)	-	-
	No	73 (73.0)	27 (27.0)	0.96 (0.50-1.83, p=0.890)	0.92 (0.28-2.99, p=0.891)
	Yes	45 (21.2)	167 (78.8)	9.59 (5.47-17.31, p<0.001)	1.06 (0.35-3.03, p=0.908)
Vaccines are safe	Neutral	73 (79.3)	19 (20.7)	-	-
	No	72 (86.7)	11 (13.3)	0.59 (0.25-1.30, p=0.198)	0.68 (0.15-2.81, p=0.605)
	Yes	34 (15.3)	188 (84.7)	21.24 (11.62-40.56, p<0.001)	2.31 (0.65-7.97, p=0.186)
Vaccines are effective	Neutral	78 (83.0)	16 (17.0)	-	-
	No	63 (84.0)	12 (16.0)	0.93 (0.40-2.10, p=0.859)	0.91 (0.23-3.77, p=0.900)
	Yes	33 (14.9)	188 (85.1)	27.77 (14.82-54.94, p<0.001)	5.82 (1.85-18.86, p=0.003)
Authorities have best interest	Neutral	67 (72.8)	25 (27.2)	-	-
	No	59 (80.8)	14 (19.2)	0.64 (0.30-1.32, p=0.232)	0.52 (0.16-1.65, p=0.271)
	Yes	53 (22.9)	178 (77.1)	9.00 (5.25-15.88, p<0.001)	1.72 (0.63-4.46, p=0.277)
Variables related to complacency towards influenza vaccines					
Vaccination is unnecessary	Neutral	66 (68.0)	31 (32.0)	-	-
	No	90 (35.7)	162 (64.3)	3.83 (2.35-6.37, p<0.001)	3.58 (1.83-7.22, p<0.001)
	Yes	19 (47.5)	21 (52.5)	2.35 (1.11-5.04, p=0.026)	4.44 (1.65-12.41, p=0.004)
	Neutral	57 (62.6)	34 (37.4)	-	-

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Have strong immune system	No	76 (36.2)	134 (63.8)	2.96 (1.79-4.96, p<0.001)	2.05 (1.06-3.99, p=0.034)
	Yes	42 (47.7)	46 (52.3)	1.84 (1.02-3.35, p=0.046)	1.71 (0.78-3.81, p=0.182)
Flu is not severe enough	Neutral	52 (59.1)	36 (40.9)	-	-
	No	83 (36.1)	147 (63.9)	2.56 (1.55-4.26, p<0.001)	1.23 (0.62-2.42, p=0.543)
	Yes	41 (55.4)	33 (44.6)	1.16 (0.62-2.18, p=0.637)	0.55 (0.23-1.29, p=0.169)
Variables related to constraints affecting uptake of influenza vaccines					
Everyday stress	Neutral	58 (68.2)	27 (31.8)	-	-
	No	98 (37.1)	166 (62.9)	3.64 (2.18-6.20, p<0.001)	2.05 (1.02-4.18, p=0.046)
	Yes	20 (44.4)	25 (55.6)	2.69 (1.28-5.72, p=0.009)	3.45 (1.29-9.67, p=0.016)
Inconvenient to be vaccinated	Neutral	59 (69.4)	26 (30.6)	-	-
	No	86 (36.6)	149 (63.4)	3.93 (2.33-6.78, p<0.001)	1.66 (0.81-3.42, p=0.165)
	Yes	33 (43.4)	43 (56.6)	2.96 (1.56-5.71, p=0.001)	1.85 (0.79-4.37, p=0.156)
Clinic visits uncomfortable	Neutral	46 (69.7)	20 (30.3)	-	-
	No	81 (34.2)	156 (65.8)	4.43 (2.49-8.13, p<0.001)	3.55 (1.78-7.27, p<0.001)
	Yes	51 (57.3)	38 (42.7)	1.71 (0.88-3.40, p=0.116)	1.45 (0.64-3.36, p=0.378)
Variables related to risk calculation with respect to influenza vaccines					
Weigh benefits and risks	Neutral	40 (62.5)	24 (37.5)	-	-
	No	31 (40.3)	46 (59.7)	2.47 (1.26-4.94, p=0.009)	1.19 (0.51-2.77, p=0.685)
	Yes	108 (42.0)	149 (58.0)	2.30 (1.32-4.08, p=0.004)	1.20 (0.59-2.45, p=0.608)
Consider usefulness of each dose	Neutral	56 (69.1)	25 (30.9)	-	-
	No	28 (37.8)	46 (62.2)	3.68 (1.91-7.26, p<0.001)	2.62 (1.17-5.98, p=0.020)
	Yes	94 (39.5)	144 (60.5)	3.43 (2.02-5.96, p<0.001)	2.80 (1.42-5.65, p=0.003)

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Need to fully understand	Neutral	43 (71.7)	17 (28.3)	-	-
	No	20 (36.4)	35 (63.6)	4.43 (2.05-9.92, p<0.001)	2.97 (1.20-7.58, p=0.020)
	Yes	115 (41.2)	164 (58.8)	3.61 (1.99-6.79, p<0.001)	2.09 (1.00-4.50, p=0.054)
Variables associated with collective responsibility for influenza vaccines					
Everyone vaccinated not me	Neutral	65 (80.2)	16 (19.8)	-	-
	No	39 (21.3)	144 (78.7)	15.00 (8.00-29.58, p<0.001)	6.96 (3.24-15.50, p<0.001)
	Yes	65 (55.1)	53 (44.9)	3.31 (1.75-6.54, p<0.001)	1.56 (0.72-3.51, p=0.267)
Vaccinated to protect weaker immunity	Neutral	60 (80.0)	15 (20.0)	-	-
	No	34 (56.7)	26 (43.3)	3.06 (1.44-6.68, p=0.004)	1.55 (0.57-4.33, p=0.395)
	Yes	82 (32.0)	174 (68.0)	8.49 (4.66-16.33, p<0.001)	3.44 (1.56-7.95, p=0.003)
Collective action	Neutral	57 (81.4)	13 (18.6)	-	-
	No	17 (51.5)	16 (48.5)	4.13 (1.68-10.47, p=0.002)	2.98 (0.86-10.70, p=0.087)
	Yes	106 (36.6)	184 (63.4)	7.61 (4.10-15.12, p<0.001)	2.87 (1.23-7.07, p=0.017)

Values shown are absolute counts (percentages) and odds ratios (95% confidence intervals and p values). The category “hesitancy” includes participants who were unsure whether they will take the influenza vaccine during the flu season and those who planned to refuse taking the influenza vaccine.

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Furthermore, when considering confidence in influenza vaccine, we noted that participants who had received influenza vaccine in the past were more willing to take the vaccine (OR 6.41, 95% CI 3.15-13.53, $p < 0.001$) compared to those who did not receive the vaccine. In addition, HCWs who believe that influenza vaccines are effective were more likely to accept the vaccines with an acceptance frequency of 85.1% versus 14.9% hesitancy (OR 5.82, 95% CI 1.85-18.86, $p = 0.003$) as compared to those with neutral position.

Regarding variables related to complacency, 64.3% of HCWs were likely to take the influenza vaccine and agreed that vaccination was necessary (OR 3.58, 95% CI 1.83-722, $p < 0.001$). Furthermore, 63.8% of HCWs with a significant likelihood to accept influenza immunization did not think that their immune system is strong to protect them from flu (OR 2.05, 95% CI 1.06-3.99, $p = 0.034$).

When looking at aspects of constraints as predictors of influenza vaccination among HCWs, 62.9% of HCWs were more likely to accept vaccines for influenza and did not believe that everyday stress was a hindrance (OR 2.05, 95% CI 1.02-4.18, $p = 0.046$). Still under constraints, 65.8% of participants were willing to vaccinate against influenza and did not agree that clinic visits were uncomfortable for them (OR 3.55, 95% CI 1.78-7.27, $p < 0.001$).

It is worth noting that 60.5% (OR 2.80, 95% CI 1.42-5.65, $p = 0.003$) of HCWs would consider the usefulness (benefits) of each dose of the influenza vaccine before deciding and 63.6%, (OR 2.97, 95% CI 1.20-7.58, $p = 0.020$) did not think that it is important to fully understand the topic of vaccination before getting vaccinated.

Finally, collective responsibility is of great importance as a predictor of vaccine acceptance. There were a significantly higher number of HCWs (78.7%) with a higher likelihood of accepting influenza vaccination who believed that even when most people are vaccinated against influenza, they must still get vaccinated (OR 6.96, 95% CI 3.24-15.50, $p < 0.001$). On the same note, influenza vaccine acceptance was significantly higher (68.0%) among participants who wanted to be vaccinated to protect people with weaker immune systems (OR 3.44, 95% CI 1.56-7.95, $p = 0.003$). Also, 63.4% of HCWs who considered vaccination as a collective responsibility to prevent the spread of influenza had a significantly higher likelihood to receive the influenza vaccine (OR 2.87, 95% CI 1.23-7.07, $p = 0.017$).

4. Discussion

There is huge gap in sub-Sahara Africa, and South Africa in particular, when it comes to research on influenza vaccine hesitancy among HCWs. Vaccine hesitancy represents a motivational state of being conflicted or opposed to vaccination (32). This study was strategically designed to bridge this gap and to understand the behavior of HCWs towards influenza vaccine uptake as this may also influence the community's response. It was initially reported that influenza vaccination had some protective effect or reduced the severity of COVID-19 infection. In this study, vaccine acceptance (willingness to vaccinate) was 54.9% while vaccine hesitancy (intention to refuse or undecided) was 45.1% of HCWs. The study finding reveal that some key drivers of influenza vaccine uptake among HCWs in Cape Town was confidence in the effectiveness of influenza vaccine and the collective responsibility and necessity to receive the influenza vaccine in the next flu season. Another important factor was that besides vaccination as a collective responsibility, 65.5% of HCWs had the belief that vaccination was essential to protect their co-workers, members of the community or patients with weaker immunity.

In addition, constraints as one of the predictors turned out to be a key factor considering vaccine hesitancy in HCWs. We showed that HCWs who did not believe that every day stress had an impact on decision making to vaccinate in the next flu season had a strong likelihood to accept influenza vaccination. Other vital findings of the study included positive perceptions on the efficacy, safety, trust and need to understand the science behind vaccine development and were the stronger predictors of acceptance. Other determinants of vaccine acceptance were demographic characteristics (e.g., Age, Religion, Gender, Education, and Personal income) that showed varying degrees of association

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with vaccination acceptance and uptake. Government trust was associated with vaccine acceptance and its intention to attain herd immunity.

This study is of critical importance considering that HCWs are the custodians of global healthcare. The WHO in 2012 and 2016, updated its recommendation on influenza vaccination of HCWs indicating that ''HCWs are an important priority group for influenza vaccination, not only to protect the individual and maintain healthcare delivery during influenza epidemics, but also to limit spread of influenza to vulnerable patient groups" (33, 34). The WHO also recommended that annual influenza vaccination among HCWs be mandatory to mitigate the epidemiological and economic effects of seasonal influenzas (35-37). However, influenza vaccine hesitancy among HCWs remains a major public health challenge and has been understudied or neglected in sub-Saharan Africa compared to other parts of the world.

This study found that overall coverage rate of influenza vaccination among HCWs in Cape Town, South Africa based on past behavior towards influenza vaccination was 49.9%, and the difference between those who were most likely to accept vaccination in the coming flu season (77.5%) and those who would not (22.5%) was significant. It is worth noting that vaccine coverage of 49.9% in a mixed setting of health facilities that included physicians, nurses, biomedical scientists, allied HCWs, hospital administrators, and others is quite low, and comparable to that of the only African study on hesitancy of influenza vaccination on HCWs in Tunisia which was below 50% (11). Cherif and colleagues reported that less than half of the health professionals enrolled i.e., 36.6% had received influenza vaccine at least once in the past and only 15.3% were vaccinated against influenza in the 2018–2019 influenza season when the survey was conducted (11). In line with our findings, just below half the proportion of HCWs (49.9%, however higher than what Cherif et al. found) reported to have received a shot of influenza vaccine in the past, but on the contrary, more than half (54.9%) in our study were willing to accept influenza vaccination in the coming flu season.

Interestingly, participants with high educational level were less likely to receive the influenza vaccine than those with the lowest educational level in the Tunisian study (11). This was the contrary in South Africa as we recorded a high rate of HCWs willing to accept influenza vaccination being University (55.7%) followed by high school (40.6%) graduates and also supported by a study in Italy (9). This further emphasises on the importance of tailored education programs targeting HCWs generally in Africa following previously low vaccination rate below expectation among Tunisian and South African HCWs. A key observation between our studies is that HCWs participants in Tunisia were female (80%) while we recorded 64.5% female participants about 15% less, though both studies had majority female participants.

This study was conducted at the peak of the COVID-19 pandemic and recruitment of HCWs in the study coincided with the campaigns of the COVID-19 vaccines rollout to HCWs in South Africa. This provides a better understanding on factors affecting influenza vaccination among HCWs in the next and subsequent flu seasons during the COVID-19 pandemic. Another study during the COVID-19 pandemic in Saudi Arabia with 424 HCWs as participants assessing vaccination trends from 2017 to 2020 had majority being nurses (72.2%), and physicians making up 27.8% (38). Of note is the similar sample size to our study as we included 401 HCWs in our analysis, as well as majority of participants in our study were nurses (49.2%) against 12.5% physicians which was the lowest of all HCWs roles in our study.

They reported increase in influenza vaccine uptake from 2017 to 2019 (45%, 52% and 62%) but a decrease in 2020 (59%) in the flu season during the COVID-19 pandemic. This could be because of conspiracy theories on social media and other communication platforms, lack of proper communication between governments and other community stakeholders, and most importantly complacency and inadequate education of HCWs on the importance of their vaccination to protect their patients and community. Jones and col-

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leagues in 2020 suggested that measures to control COVID-19 pandemic might be quashing the cold and flu season (39), which could influence HCWs choice towards influenza vaccination. Following multivariate logistic regression, HCWs above 40 years of age, female, nurses, and participants who were knowledgeable about flu vaccination had a higher likelihood of having received the influenza vaccine and were willing to accept vaccination in the next flu season in 2021 (38).

In line with our findings, we found an overall low influenza vaccine rates (49.9%) similar to the findings by Alkathlan and colleagues during COVID-19 pandemic (38). In addition, following multivariate logistic regression, our analysis showed a very strong likelihood of older HCWs 35-44 years and above to accept the influenza vaccine in the next flu season, with the likelihood stronger in an increase in age group dependent manner. Also, considering the usefulness of each vaccine prior to acceptance of flu vaccination showed a strong likelihood for HCWs to accept vaccines in the next flu season. However, gender was not a strong enough variable to influence HCWs decision to vaccinate or not. On the contrary, we showed that physicians were most likely to receive influenza vaccination in the next flu season and nurses showed a trend towards a strong likelihood for vaccination. Also, HCWs who did not believe that knowledge on vaccination was necessary for influenza vaccine uptake had a strong likelihood to accept vaccination in the next flu season.

Findings in Saudi Arabia (38) were in accordance with another study carried out in Lebanon during the COVID-19 pandemic in 2020 on 560 Lebanese HCWs who had the belief that good knowledge of vaccination, HCWs that have previously received the influenza vaccine, perception of flu vaccine benefits to decrease hospitalization, and prevention of influenza-COVID-19 co-infection had a positive influence on the attitudes towards influenza vaccination (40).

Notably in our study, the strongest drivers of vaccine uptake by HCWs were confidence in the effectiveness of influenza vaccine (85.1%), and that influenza vaccination was necessary (64.3%). This was supported by strong likelihoods after logistic regression by willingness to receive influenza vaccine. This was in accordance with previous studies in China and Lebanon which reported that the attitudes toward influenza vaccination were the strongest predictor of HCWs' intention, actual acceptance, and recommendation status of influenza vaccination (41, 42). On the contrary, HCWs in studies carried out in Greece and Costa Rica reported that concerns about the effectiveness of flu vaccine was amongst other factors the most common barriers to flu vaccination (43, 44). However, these studies reported low and suboptimal influenza vaccine coverages that has been decreasing in HCWs despite the positive attitudes toward the influenza vaccine.

In addition, constraints turned out to be a key factor considering vaccine hesitancy in HCWs. We showed that, HCWs who did not believe that every day stress had an impact on decision making to vaccinate in the next flu season, had a strong likelihood to accept influenza vaccination. This was in line with a study carried out in Malaysia where more than half (56.2%) of HCWs believed that time constraints was the most common reason for not having the vaccine (45). However, protection of themselves was the most common reason reported for vaccination against influenza infection (73.6%) and 85.3% of respondents had the belief that influenza vaccination was important for disease prevention.

Findings of this study were in support of HCWs' confidence in the effectiveness of influenza vaccines to prevent disease. Also, HCWs perceived vaccination as a collective responsibility and action with a strong likelihood to accept vaccination in the next flu season. Another important factor was that besides vaccination as a collective responsibility, 65.5% of HCWs had the belief that vaccination was essential to protect their co-workers, members of the community or patients with weaker immunity. Following logistic regression, we showed that there was a stronger likelihood for HCWs to receive the flu vaccine in the next flu season. This was in accordance with studies carried out in Oman on 390

HCWs and Greece on 363 HCWs who responded that their main reasons for vaccine acceptance was to protect themself, family, patients, colleagues, and the community at large (46, 43).

This study had some limitations. We might not have exhausted all the important questions for HCWs attitudes, knowledge, and practices on influenza vaccination. We also believe that though we had a justifiable sample size to provide enough statistical power, a larger sampling would probably have strengthened our observation. The third limitation is that this was a cross-sectional survey with data collected at a single time point and there is a possibility that HCWs attitudes about influenza vaccination might change overtime.

5. Conclusions

This study has shown that interventions that enhance knowledge and accessibility of influenza vaccines are warranted to improve vaccination coverage among HCWs. Influenza vaccine coverage was below 50%, demonstrating vaccine coverage that is suboptimal and below expectation. Hence government may look for ways and strategies to encourage HCWs influenza vaccination. Key drivers of vaccine uptake in HCWs were confidence in the effectiveness of influenza vaccine and the collective responsibility and necessity to receive the influenza vaccine even if everyone is vaccinated to protect the vulnerable, old and those with poor immune systems. This reaffirms the importance to build on the confidence of HCWs about flu vaccines and the desire to accept vaccination in future. Key drivers of vaccine hesitancy included age particularly younger HCWs and the desire to consider each vaccine dose before acceptance. For future flu seasons the importance of tailored education programs targeting younger HCWs and more information about the content of flu vaccines would be vital to improve vaccine uptake. This would help alleviate fears and provide avenues to engage communities, assist and address the pertinent issues and build influenza vaccine confidence among HCWs and reassure them about the effectiveness and safety of the seasonal flu vaccines. Finally, we believe that this paper provides the scientific evidence on influenza vaccine acceptance among HCWs in South Africa and broadly the sub-Saharan African region. It further provides better understanding of influenza vaccine hesitancy among HCWs in the time of the COVID-19 pandemic.

Author Contributions: CSW, SMA, and MS co-conceived the project. SMA led the data collection. EBK, ENL, and SC assisted with data collection, drafting the manuscript, and provided intellectual input on all aspects of the project. PdMCK performed all the statistical analyses. RG and AJ provided administrative and technical support in setting up and maintaining the database for data collection. CSW and MS supervised all aspects of the project. EBK, SMA, and PdMCK co-wrote the first draft of the manuscript. All authors read and revised successive versions and approved the final version of the manuscript.

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