



Original Research Article

Covid-19 Awareness, Perception, and Vaccine Hesitancy Among Healthcare Trainees at A Tertiary Health Facility – Lessons for The Future

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ABSTRACT

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Background: Healthcare workers and trainees are at increased risk of contracting Coronavirus infection and constitute priority groups for vaccination. Hesitancy is a major barrier to vaccine uptake, and this has an implication for vaccination programs. AIM: To assess the perception of healthcare trainees on COVID-19 disease, their attitude to the new vaccine, and their willingness to get vaccinated. METHODS: A cross-sectional study of trainees in medicine & surgery, dentistry, physiotherapy, medical laboratory science, and nursing departments was conducted at the University College Hospital, Ibadan. The information included socio-demographic characteristics, knowledge of vaccines, perception, and reluctance to get vaccinated. Descriptive statistics and a Chi-square test were performed; $p \leq 0.05$. Results: Mean age was 22.98±2.48 years. The majority of 163 respondents were medical students (49.10%). Awareness of disease was high; the source of information was social media; 92% of trainees had knowledge of the vaccine and the majority were aware of the intramuscular route of administration. About 57.7% were willing to receive the vaccine. The knowledge of safety increased the willingness to take the vaccine, the perceived risk of contracting infection, and long-term adverse effects. Conclusion: Vaccine hesitancy exists among healthcare trainees despite high awareness of the COVID-19 pandemic, knowledge of available vaccines, and their benefits.

Keywords: COVID-19, COVID-19 Vaccine, Vaccine Hesitancy, COVID-19 Disease, COVID-19 Healthcare Trainees

INTRODUCTION

COVID-19 disease is a pandemic disease of public health importance; characterized by asymptomatic, mild, moderate, or severe diseases with a considerable case fatality especially among the high-risk groups. COVID-19 disease was first identified and described in Wuhan, China at the end of the year 2019 and caused by the novel virus - severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2); an RNA virus in the Coronavirus family of viruses that cause acute respiratory illnesses. ^[1-3]

The risk factors associated with the infection were a history of recent travel to an area with ongoing coronavirus infection, contact with individuals infected with coronavirus, chronic medical conditions such as diabetes mellitus and cancers, healthcare workers in contact with infected people, and contact with infected surfaces.^[4] Healthcare workers and trainees are at increased risk of contracting the infection. Globally, health workers account for about 10% of all detected cases of coronavirus infection^[5,6] Among asymptomatic frontline health workers in Ibadan, Nigeria, Olavanju et al reported that 45% of 133 asymptomatic health workers, who participated in the study were seropositive for SARS-COV-2.^[7] Healthcare trainees constitute an "at-risk" group of individuals because of the risk of exposure being part of the healthcare team. Also, the trainees may be "naïve" and poorly compliant with universal precautions, putting them at risk of infection. It is vital to prevent and control the spread of disease among health workers, trainees, and the general population.

The definitive treatment for COVID-19 is unknown. There are several recommended public health strategies for the control of the spread of the disease including the use of vaccines to achieve herd immunity. COVID-19 vaccines have been developed and approved for emergency use to prevent and control the disease.^[4,8] The currently known COVID-19 vaccines are composed of either whole (inactivated) virus vaccine, nonreplicating viral vector, protein subunit, and messenger RNA (mRNA).^[9-11] The efficacy of these vaccines in terms of disease prevention ranges between 66% and 95% with the highest efficacy recorded with the mRNA types of vaccine. Regardless of vaccine type, all vaccines have been effective in their ability to reduce hospitalization and death. ^[12] After the first dose, the vaccines can provide immunogenicity for at least 119 days and are 94.5% effective in preventing the SARS-CoV-2 infection. The adverse effects of the vaccines include pain, redness or swelling at the injection site, fever, mvalgia, fatigue, headache, muscle pain, nausea, vomiting, itching, chills, joint pain, and thrombosis can also rarely cause anaphylactic shock. [4,13,14] The coverage and efficacy of the COVID-19 vaccine in the prevention and control of disease spread may be affected by vaccine hesitancy. Vaccine hesitancy remains an issue to contend with in various settings. The uptake of the vaccine is not dependent only on the efficacy and safety of the vaccine but also on acceptance by the people.

Vaccine hesitancy is the delay in acceptance or refusal of vaccines despite the availability of vaccine services. ^[2,8] Vaccine hesitancy and misinformation on vaccine safety, storage, and other issues will jeopardize the efforts to achieve wide vaccine coverage and herd immunity in Nigeria and other countries. ^[1,2] Vaccine hesitancy remains a barrier to providing effective herd immunity against highly transmissible infectious diseases.^[1,8] Olomofe et al, reported that 58.2% of

participants were willing to take the COVID-19 vaccine when available in Nigeria; a-fifth of them were unwilling to receive a potential vaccine, which appears to be a consequence of skepticism about the safety of the COVID-19 vaccine. A majority entertained some myths such as potential vaccine being "a mark of the beast" or if the motive of the vaccine is to 'reduce the world's population'. ^[4]

The factors influencing vaccine uptake among healthcare workers include personal risk perception, fear of side effects, access to media, information sources, religious/cultural beliefs, the convenience of getting to a health facility, level of trust for the healthcare system, household wealth, residence and ethnicity.^[4] Other factors identified by Dror et al, were concerns regarding quality control, side effects, efficacy, religious beliefs, and perception of the disease as mild.^[8] In India, a majority (77.27%) wanted the COVID-19 vaccine but they expressed a preference for locally manufactured rather than the foreign vaccine.^[15] Unwillingness to receive the vaccine may pose a challenge to achieving herd immunity and impair disease control. Unwillingness may be due to a lack of awareness, poor perception, wrong information disseminated by the media, fear of potential side effects, doubts regarding the efficacy, issues with the transportation and storage of vaccines. Failure of the healthcare team to access the vaccine services will have a negative impact on disease control.

Although there are various studies about the perception and readiness of healthcare workers to take vaccine in many countries, there is a paucity of data about the perception and willingness of healthcare trainees to receive COVID-19 vaccine. Healthcare trainees are the future healthcare workforce. They are involved directly or indirectly in the care of COVID-19 patients as well as counseling and recommendation of the vaccine to the populace. It is imperative to understand the knowledge, perception and concerns of healthcare trainees on the COVID-19 vaccine.

This study assessed the awareness, knowledge, and perception of healthcare trainees of the university college hospital, Ibadan about the COVID-19 vaccine; and the willingness of the healthcare trainees to receive the COVID-19 vaccine.

METHODOLOGY

Study Design: This study was a cross-sectional survey conducted among healthcare trainees.

Study Setting: The study was conducted at the University College Hospital (UCH), Ibadan, Nigeria among healthcare trainees in various specialties. UCH is a government-owned tertiary health institution; a major

training and referral hospital in South-west, Nigeria and has a dedicated unit for the care of SARS-CoV-2 infected and suspected patients. The study was conducted over 2-weeks period - February, 2021.

Study Participants: The study participants were healthcare trainees in different specialties namely medicine, dentistry, nursing, physiotherapy, and medical laboratory science at the University College Hospital, Ibadan. Eligibility Criteria: These included students in the clinical training years in the various specialties. Eligible consenting trainees were included.

Study sample size determination and sampling procedure: A sample size was calculated using the Leslie Kish formula: $n = Z\alpha p(1-p)/d2$; $Z\alpha = 1.96$, Proportion of medical trainees (p) that are aware of COVID 19 = 50% (0.5%). A sample size of 163 participants was obtained including a 10% attrition. The specialties of study of the healthcare trainees were listed and trainees were selected from the various specialties. A proportional sampling was done based on the distribution of the trainees across the various specialties of interest in the institution to ensure appropriate representation of number of trainees in the various specialties in the study sample. Health care trainees were sampled using a pretested online survey questionnaire using the Google® survey form. The survey link to the Google® form was sent to the class representatives of the selected classes of the various specialties and this was subsequently disseminated to the members of the class via the class social media groups.

Data collection: Data was collected using the study instrument. The study instrument was a pretested semistructured self-administered online survey questionnaire. The validation of the content of the questionnaire was done through a pilot testing of the survey questionnaire. The information obtained included socio-demographic characteristics, years of training, awareness, and knowledge of the COVID-19 vaccine type and composition, perception of vaccines, willingness to be vaccinated, and barriers to vaccination. Data collected was recorded in the online survey software - Google excel sheet. The data was exported and analysed using the IBM SPSS software version (SPSS) 23. Descriptive statistics and bivariate analyses were performed. The level of significance was set at p<0.05.

Ethical Approval: The ethical approval was obtained from the University of Ibadan/University College Hospital, Ibadan ethics review committees (UI/UCH Ethics committee - UI/EC/21/0097). Informed consent

was obtained from all participants and the principles of ethics were maintained during the conduct of the study according to the approved protocol.

Statement of Human and Animal Rights: All procedures in this study were conducted in accordance with the UI/UCH Ethics Committee – (UI/EC/21/0097) approved protocol.

Statement of Informed Consent: All participants in this study gave voluntary informed consent.

RESULTS

One hundred and sixty-three healthcare trainees across five specialties which include medicine & Surgery, dental, medical laboratory science, physiotherapy, and nursing were sampled.

Table 1 shows the sociodemographic characteristics of the respondents. The mean age was 22.98 ± 2.48 years and majority 126 (77.3%) were within the age range of 20-24 years. These were mostly females 57% (93), Christians (85.3%) and single (97.5%). About half (49.1%) of the respondents were medical students, almost one-fifth (19.6%) were nursing students, medical laboratory science (17.8%); dentistry (6.1%), and physiotherapy (7.4%). About 84% of the respondents had spent three to four years in clinical training.

All trainees were aware of Coronavirus infection and COVID-19 disease. Concerning types of COVID-19 vaccine, 92% (150) of the trainees were aware of at least one type of vaccine, and 62.7% knew of the intramuscular route of administration of these vaccines, and 9.8% had incorrect knowledge stating subcutaneous or oral route of administration. About 72(44.2%) were aware of mRNA type of vaccine. Concerning the knowledge of side effects of the COVID-19 vaccines; trainees mentioned pain in the arm (61.3%), fatigue (41.1%), fever and swelling around the injection site (39.3% each). Other side effects mentioned were - sore throat 17(10.4%), difficulty with breathing 12 (7.4%), and death 13 (8.0%). (Table 2)

About 89 (54.6%) of the trainees think they are at risk of Coronavirus infection, and 25.2% had prior contact with persons positive for Coronavirus infection or COVID-19 disease, though only 3.7% (6) of the trainees have tested positive for COVID-19 infection before and 3.7% (6) have been involved directly in the care of COVID-19 positive patients. (Figure 1)

Regarding the perception and attitude towards the COVID-19 vaccine, respondents believe that COVID-19 vaccines can prevent the infection (94.5%) and 80.4% believe that it is safe. About 55% (90) were willing to be tested for COVID-19 at regular intervals; 57.7% are willing to take the vaccine if it is free, but

only 24.8% would not mind the cost if required to pay for the vaccine. Among the trainees, 80% preferred to

Table 1: Socio-Demographic Characteristics of the Respondents

Variables	Frequency (%)			
Mean age (±SD) years	22.98±2.48			
Age (years)				
<20	4 (2.5)			
20-24	126 (77.3)			
≥25	33 (20.2			
Gender				
Female	93 (57.1)			
Male	70 (42.9)			
Religion				
Christianity	139 (85.3)			
Islam	19 (11.7)			
Others	5 (3.1)			
Marital Status				
Married	4 (2.5)			
Single	159 (97.5)			
Specialty of Training				
Medical Laboratory Science	29 (17.8)			
Dentistry	10 (6.1)			
Medicine and Surgery	80 (49.1)			
Nursing	32 (19.6)			
Physiotherapy	12 (7.4)			
Duration of Clinical Training (Years)				
≤ 2	26 (16.0)			
3	92 (56.4)			
4	45 (27.6)			

take the single-dose vaccine and 64.4% would recommend the COVID-19 vaccine to a friend or colleague. (Table 3)

Table 4 shows the factors that may influence willingness to take the COVID-19 vaccine. Of the trainees who thought that the COVID-19 vaccine was not safe, 37.5% said they would not take the vaccine,

Table 2: Knowledge And Awareness Of COVID-19 Vaccine

Variables	Frequency (%)		
Awareness of COVID-19 vaccines			
Knowledge of at least a type of vaccine	150 (92)		
Knowledge of route of administration			
Intramuscular	102 (62.6)		
Subcutaneous	15 (9.2)		
Oral	1 (0.6)		
Don't know	45 (27.6)		
Knowledge of constituents of COVID-19 vaccine	, <i>, , , , , , , , , , , , , , , , , , </i>		
mRNA vaccine	72 (44.2)		
Live attenuated vaccine	47 (28.8)		
Viral Vector vaccine	32 (19.6)		
Protein Subunit vaccine	45 (27.6)		
DNA vaccine	21 (12.9)		
Source of information about COVID-19 vaccine *	, <i>, , , , , , , , , , , , , , , , , , </i>		
Social media	146 (89.6)		
Television/Radio	77 (47.2)		
Friends and Relatives	34 (20.9)		
Journals	38 (23.3)		
Others	3 (1.8)		
*: multiple response variable			

Table 3: Perception of COVID-19 Vaccines

Variables	Frequency (%)	
Perception and attitude towards covid-19 vaccine		
Vaccines can prevent COVID-19 infection	154 (94.5)	
Vaccines are safe	131 (80.4)	
Laboratory errors while manufacturing the vaccines due to speed	58 (35.6)	
Unknown long term adverse effects	92 (56.4)	
Vaccines brought to Nigeria different in constituents	19 (11.7)	
Willingness to be tested for COVID-19 at regular intervals	90 (55.2)	
Willingness to pay for the COVID-19 vaccine	42 (24.8)	
Willingness to receive the COVID-19 vaccine if free	94 (57.7)	
Recommend the vaccine to a friend or colleague	105 (64.4)	
Dose preference		
Single dose	130 (80)	
Double dose	33 (20)	
Knowledge/Perceived side effects of COVID-19 vaccine*		
Pain in the arm	100 (61.3)	
Fatigue	67 (41.1)	
Fever	64 (39.3)	
Swelling	64 ((39.3)	
Headache	58 (36.6)	
Malaise	40 (24.5)	
Not aware of any possible side effect	55 (33.7)	
*- multinle resnanse variable	1	

Variables Willingness to receive COVID- 19 Vaccine			Chi- squared	p- value	
	No (%)	Undecided (%)	Yes (%)	(χ2)	
Safety of the Vaccine				57.938	< 0.001*
No	12 (37.5)	19 (59.4)	1 (3.1)		
Yes	5 (3.8)	33 (25.2)	93 (71.0)		
Perceived risk of COVID-19 infection				11.13	0.004*
No	14 (18.9)	19 (25.7)	41 (55.4)		
Yes	3 (3.4)	33 (37.1)	53 (59.6)		
Unknown long-term adverse effects				18.06	0.001*
Agree	16 (17.4)	33 (35.9)	43 (46.7)		
Disagree	0 (0)	0 (0)	7 (100)		
Undecided	1 (1.6)	19 (29.7)	44 (68.8)		

Table 4: Association between knowledge and willingness to receive the vaccine.

*Fishers exact test



Figure 1: Previous Exposure and Perceived Risk Of COVID-19 Infection



Figure 2: Challenges to Vaccinating Health Workers and Trainees

only one person (3.1%) showed readiness to take the vaccine; a majority (59.4%) were undecided about the vaccine. Seventy-one percent of the trainees who think the vaccine is safe are willing to take the vaccine compared to 3.8% who were unwilling; p<0.001. There Table 4: Association Between Knowledge and Willingness to Receive the Vaccine.

There is a statistically significant association between knowledge of vaccine safety and the willingness to take the vaccine. Among trainees who believed they were not at risk of COVID-19 infection, 55.4% are still willing to take the vaccine, while 18.9% of these will not take the vaccine. Also, about 59.6% of trainees who think they are at risk of contracting COVID-19 infection are willing to take the vaccine, while about 37.1% were still undecided and 3.4% were not willing to take the vaccine, (p - 0.004). There is an association between the perceived risk of COVID-19 infection and the willingness to take the vaccine. Almost half (46.7%) of the 92 trainees who thought the COVID-19 vaccine has some long-term adverse effects were still willing to take the vaccine. Although 35.9% are undecided and 17.4% were unwilling to take the vaccine. About 70% (44) of the trainees who were undecided about possible long-term adverse effects were willing to take the vaccines; (p - 0.001). As shown by the survey, the willingness to take the vaccine does not seem to be affected by the specialty of the trainees (p = 0.094), the number of years spent in clinical training (p-value = 0.315), or perception that vaccine could prevent COVID-19 infection or not (p = 0.257) and the number of doses of the vaccine (p = 0.068).

The challenges of vaccination and coverage are shown in figure 2. These include the inadequate supply of the vaccine (90.2%), challenges of maintaining the cold chain for the vaccine (87.1%), vaccine hesitancy among the people (83.4%), possible complications following the use of the vaccine (80.4%) and prioritizing high-risk groups such as healthcare workers and trainees (75.5%).

DISCUSSION

This study highlighted the awareness, knowledge, perception about the COVID-19 vaccine, and willingness to receive the vaccine among healthcare trainees in various specialties. In this study, there was a high awareness and knowledge of COVID-19 disease and vaccine; less than three-fifths of the trainees were willing to receive the COVID-19 vaccine and a majority will prefer the single-dose vaccine to the double-dose vaccine regimen.

The mean age was 22.98 ± 2.48 years. About half of the participants were medical students and these

represent the largest population of students undergoing clinical training, there were more female respondents in the study. In the training specialties, some of the departments have more female than male trainees; this was reflected in the study sample.

All participants were aware of SARS-CoV-2 infection, COVID-19 disease, and vaccine. This is expected of trainees in the third and fourth year of clinical training; and because the disease is a pandemic with a huge global health burden. The majority of the trainees knew at least one type of COVID-19 vaccine, its constituents, and the correct route of administration. The main source of information among the trainees was the social media. This is similar to the findings of Dayi et al among health workers who reported that a majority got information about COVID-19 from the media television, radio, and newspapers.^[16] The knowledge of the trainees about COVID-19 is similar and may be because the most common source of information was social media which will imply equal access to similar information about COVID-19 among the trainees. Many of the trainees knew the constituents of the vaccine; mRNA was the commonest type known to most of the trainees. This may be a result of a high level of awareness created on the news and social media concerning the mRNA vaccine compared to other types of vaccine.

Some respondents had incorrect knowledge of the route of administration, constituents of the COVID-19 vaccine, and side effects of the COVID-19 vaccine. About a quarter of respondents were not sure of the route of administration. With social media being the most common source of information, some of the trainees may have been exposed to misinformation and misconception including unproven theories thus, distorting the knowledge of COVID-19. Also, the training colleges had been closed to trainees due to the COVID-19 pandemic and lockdown, thus, affecting formal teaching and education of the trainees concerning COVID-19 disease and vaccines. This study was conducted at the onset of the resumption of academic activities after the COVID-19 lockdown restrictions were lifted. The knowledge of trainees on COVID-19 was not affected by exposure to formal classroom lectures or clinical sessions on COVID-19 disease.

Importantly, the fact that nine out of every ten trainees heard of COVID-19 vaccines from social media shows that trainees are abreast of information, however; it is worrisome on the other hand because medical trainees are expected to search for scientific and evidence-based facts from journals rather than relying on social media. The social media comprises of mixed uncensored information being propagated and may be associated with misinformation and misconception. This may affect the willingness to take the vaccines because of misinformation.

More than a quarter of the participants have been exposed to coronavirus infection, 3.7% of trainees have tested positive for COVID-19 infection in the past and a majority believed they were at risk of infection. This is supported by involvement in clinical training and patient care whether the patients are being treated for COVID-19 disease or other medical or surgical conditions. Furthermore, the status of patients may be unknown at the time of first contact irrespective of in-patient or outpatient care and diagnosis. About 3.7% of the healthcare trainees interviewed have tested positive for coronavirus infection in the past, and one in four of the participants have come in contact with persons positive for coronavirus infection is an important finding. According to WHO, healthcare workers account for about 10% of global infections; ^[6] putting healthcare trainees at risk of infection. Also, Olayanju et al reported seropositivity for immunoglobulin G (IgG) among healthcare workers who have never taken the coronavirus test and had no COVID-19-related symptoms.^[7] Seropositivity was higher among healthcare workers in the obstetrics and gynaecology, emergency, and medicine departments that were actively involved in emergency care in the hospital. Healthcare workers in other departments were also seropositive without prior evidence of infection. symptoms, or known exposure.^[7]

A majority of the trainees agreed that the COVID-19 vaccine was effective for the prevention of infection and safe. However, only slightly more than half of the trainees expressed willingness to have COVID-19 tests at regular intervals or to receive the vaccine if available. Qattan et al demonstrated that 50.52% of healthcare workers were willing to receive the COVID-19 vaccine while others will delay until the safety of the vaccine is confirmed. ^[17] While Nzaii et al found COVID-19 vaccine acceptability was low (27.7%) among healthcare workers. ^[18] Willingness to take the vaccine is positively influenced by the belief in vaccine safety and trainees' personal risk perception, that is the risk of infection by the virus in the process of their clinical training. This is following the findings of previous studies reporting that personal risk perception influences the willingness to take the vaccine. [4,19,20] The training specialty of the respondents and the number of years in clinical training did not influence their knowledge and willingness to take COVID-19 vaccines.

The respondents could have drawn confidence in the efficacy of the vaccine from the knowledge of vaccines, results, and evidence from clinical trials supporting the safety and efficacy of the vaccine in preventing infection. The trainees may also have assumed the general knowledge of the protective role of vaccines in disease control and prevention; not necessarily from COVID-19 vaccine use itself. Despite the perceived benefits, many trainees are unwilling to pay for the vaccine if it is unavailable for free. Unwillingness to pay for the vaccine if it is not free may be the fear or anticipation that the vaccine may be expensive. About two-thirds of the respondents would recommend the vaccine to other people. This is greater than the proportion of respondents willing to receive the vaccine.

The possibility of long-term effects is a concern to more than half of the respondents, but this will not prevent them from taking the vaccine. The thought by about one-tenth of the respondents that the vaccine supplied to Nigeria differs from those of other countries could be a result of misinformation from social media, or the fact that there are different brands of the vaccine. The impression of possible laboratory error during rapid production of the vaccines over a few months as expressed by more than a third of the trainees (35.6%) may influence the willingness to take the vaccine. The news of how deadly the virus is and the fear of stigmatization in cases of positive test results may be the reason why only half are willing to have regular COVID-19 screening tests.

The lessons learned from this study is that the healthcare trainees constitute an "at risk group" in epidemics of public health importance such as the SARS-CoV-2 infection, Ebola infection. The trainees may be naïve and new to the variety of clinical symptoms and signs including 'red flags' of contagious diseases. Therefore, trainees may be at increased risk and should be prioritized in the preventive strategies to control the spread infection. Trainees in various specialties may be exposed to high-risk patient at first presentation to the hospital during their clinical or emergency room rotations particularly at a time when the patient's diagnosis is unknown. Hence, education, prompt vaccination and other preventive strategies will prevent the spread of disease to patients, students and other healthcare providers.

The majority of the healthcare trainees obtained information about COVID from social media, and other non-medical sources, therefore efforts should be made to educate the trainees and provide formal teachings, simulations, and drills to improve the knowledge of trainees about the disease. Social media should also be used as a medium to provide correct and accurate knowledge during disease outbreaks to educate, counsel the populace, and minimize misinformation and misconceptions. Health workers and trainees should be educated in the form of seminars, workshops, drills, and scientific meetings about the current interventions for prevailing diseases. Also, a health worker or trainee who is not convinced about the intervention such as a vaccine, may impact negatively on patients and other people within or outside the hospital. Furthermore, about 25% of the respondents were exposed to infected patients, and slightly more than half of the trainees were willing to accept COVID-19 Vaccine. The role of prevention of disease must be consistently emphasized especially the uptake of vaccines in addition to other physical or mechanical interventions for disease control. The strength of this study is that the study population is well-defined, and a proportionate sampling was used to ensure that the study sample was representative of the training specialties at the study site. This allowed the evaluation of a diverse group of healthcare trainees thus, enabling the assessment of awareness of various groups of trainees. The limitations in this study include the small sample size which was limited by the number of trainees that accessed the online survey and the response was slow. Some trainees may not have accessed the survey due to poor, limited, or lack of access to the internet in the period of the study.

CONCLUSION

In conclusion, healthcare trainees were aware of coronavirus infection, and the availability of vaccines to control the spread. However, vaccine hesitancy exists among healthcare trainees. A little more than half of the trainees were willing to take the vaccines and factors affecting the uptake of these vaccines include knowledge of the safety of the vaccine, personal risk perception, and perception of possible long-term adverse effects of the vaccine.

Declaration of Conflicts of Interest: The authors have no conflicts of interest to declare.

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