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Adenovirus and RNA-based COVID-19 vaccines: perceptions and acceptance among healthcare workers

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MHT, MB, JT, ZM, and FS were involved in conception, analyzed the data, and wrote the manuscript. AH, AE, FJ, BS, AR, and NA contributed to the study design; collected, analyzed, and interpreted data; and edited the manuscript. AH, FS, KH, and SS supervised data collection, analyzed data, and edited the manuscript. AA, RH, and AJ interpreted the data and wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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ABSTRACT

Objectives The aim of this study was to compare the perception, confidence, hesitancy, and acceptance rate of various COVID-19 vaccine types among healthcare workers (HCWs) in Saudi Arabia, a nation with MERS-CoV experience.

Design National cross-sectional, pilot-validated questionnaire.

Setting Online, self-administered questionnaire among HCWs.

Participants A total of 2,007 HCWs working in the Kingdom of Saudi Arabia participated; 75.3% completed the survey and were included in the analysis.

Intervention Data were collected through an online survey sent to HCWs during November 1-15, 2020. The main outcome measure was HCW acceptance of COVID-19 candidate vaccines. The associated factors of vaccination acceptance were identified through a logistic regression analysis and via measurement of the level of anxiety, using the generalized anxiety disorder 7 (GAD7) scale.

Results Among the 1512 HCWs who were included, 62.4% were women, 70.3% were between 21 and 40 years of age, and the majority (62.2%) were from tertiary hospitals. In addition, 59.5% reported knowing about at least one vaccine; 24.4% of the participants were sure about their willingness to receive the ChAdOx1 nCoV-19 vaccine, and 20.9% were willing to receive the RNA BNT162b2 vaccine. However, 18.3% reported that they would refuse to receive the Ad5-vectored vaccine, and 17.9% would refuse the Gam-COVID-Vac vaccine. Factors that influenced the differential readiness of HCWs included their perceptions of the vaccine's efficiency in preventing the infection (33%), their personal preferences (29%), and the vaccine's manufacturing country (28.6%).

Conclusions Awareness by HCWs of the several COVID-19 candidate vaccines could improve their perceptions and acceptance of vaccination. Reliable sources on vaccine efficiency could improve vaccine uptake, so healthcare authorities should use reliable information to decrease vaccine hesitancy among frontline healthcare providers.

Strengths and limitations of this study

- among the first studies to compare the perception, confidence, hesitancy, and acceptance rates of various COVID-19 vaccine types among HCWs.

- The press release on the efficacy of the BNT162b2 vaccine coincided with improved HCWs' willingness to vaccinate.

- Being self-reported and survey-based study highlights that observational studies on the HCWs' actual acceptance of various COVID-19 vaccines are warranted in the nearest future.

INTRODUCTION

The COVID-19 pandemic has severely disrupted normal societal and economic activities worldwide and is expected to continue imposing strains and burdens on health systems in most countries. Globally, the COVID-19 pandemic remains out of control.[1] The existing measures to control COVID-19 are detrimental to the global economy[2] and result in significant impairment in physical and psychological well-being.[3] To keep COVID-19 under control requires an effective vaccine. Without COVID-19 vaccination, healthcare workers (HCWs) will likely be at risk of infection and are likely to serve as a reservoir inside health institutes, which would undermine efforts to end the pandemic. According to the World Health Organization (WHO), 56 and 166 candidate vaccines are in clinical and pre-clinical evaluation, respectively, as of December 17, 2020.[4] These include JNJ-78436735, an adenovirus vaccine (Ad26.COV2.S)[5, 6]; mRNA-1273, an mRNA vaccine[7]; AZD1222, an adenovirus vaccine (ChAdOx1 nCoV-19)[8]; BNT162b1, an mRNA vaccine[9]; NVX-CoV2373, a full-length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M[10]; and Ad5-nCoV, an adenovirus vaccine.[11-14] The encouraging news is that several vaccines have been released; many are in phase III clinical trials and show promising effectiveness.[15] As some safe and efficacious vaccines became available, policymakers must ensure successful, large-scale uptake of COVID-19 vaccines to achieve community immunization. However, the success of COVID-19 vaccination programs will largely depend on people's acceptance of the vaccine. A recent global survey suggested that nearly 30% of participants would hesitate to take a COVID-19 vaccine when it is available.[16] A systematic review on the acceptance of a COVID-19 vaccine, based on nationally representative surveys in 20 nations, indicates that the vaccine acceptance rate in most nations would not reach the 67% necessary for achieving population immunity.[17] Mathematic modelling suggested that, if the efficacy of a COVID-19 vaccine was 80%, at least 75% coverage would be needed to extinguish the ongoing

pandemic.[18] Therefore, a timely understanding of community responses to the forthcoming COVID-19 vaccines is important for policymaking and service planning.

Extant literature has explored vaccine acceptance and identified a few demographic and psychosocial correlates, such as gender, age, trust in research, knowledge, and concerns about the novel vaccine, as well as people's judgment and perceptions about the risk of COVID-19.[19-21] Risk of exposure is one of several essential issues that directly shape people's assessments of their vulnerability and risk. Even when using personal protective equipment, healthcare providers and other essential workers experience high-risk exposures to COVID-19 and should be given priority in vaccine allocations. Several studies suggest that being an HCW or being involved in the care of patients with COVID-19 is positively associated with COVID-19 vaccine acceptance.[22-24]

The lessons learned from previous infectious disease pandemics and outbreaks, including SARS, H1N1, MERS-CoV, and Ebola outbreaks, demonstrate the important role that health information has on disease control and vaccine acceptance.[25] Source of health information can affect the manner and frequency of the utilization of such information. The degree to which the information source is trusted can have a remarkable impact on the acceptance of information.[26] If HCWs distrust the source, they will doubt the information about different COVID-19 vaccines, and this doubt will in turn shape the attitudes, perceptions, and potential actions they take toward various COVID-19 vaccines.

The Kingdom of Saudi Arabia (KSA) is one of the top 30 countries with the highest reported COVID-19 cases: The KSA had 360,690 laboratory-confirmed cases and 6101 deaths as of December 19, 2020.[27] Acceptance of a potential COVID-19 vaccine assessed among HCWs in the KSA in a survey of 2007 participants showed an acceptance rate of 70%,[28] which is slightly higher than the acceptance rate found in a public survey among 992 participants from the general population (acceptance rate of 65%).[29] Perception of, confidence in, and hesitancy about various COVID-19 vaccines in the context of emerging viral infections and pandemics and with regard to manufacturing companies and different sources of information are principal factors in assessing vaccine acceptance. To the best of our knowledge, no published surveys specifically target and compare HCW perception, confidence, and hesitancy toward different types of COVID-19 candidate vaccines. Our previous research showed that most (70%) HCWs are willing to receive COVID-19 vaccines once they are available,[28] so we aimed in this study

to compare the perception, confidence, hesitancy, and acceptance rates of various COVID-19 vaccine types among HCWs.

METHODS

Data collection

This study was a national cross-sectional survey among HCWs in Saudi Arabia during the COVID-19 pandemic. Data were collected during November 1–14, 2020. At the time of data collection, at least seven COVID-19 vaccine candidates had been reported in the scientific literature. HCWs were screened for their awareness of any of the seven published vaccines.[28] Participants were invited using a convenience sampling technique. We used several social media platforms and email lists to recruit participants. The survey was a pilot-validated, self-administered questionnaire that was sent to HCWs online through SurveyMonkey©, a platform that allows researchers to deploy and analyze surveys via the internet.[30] The questionnaire was adapted from our previously published study,[31] with modifications and additions related to the potential COVID-19 vaccine.

The questions included the demographic characteristics of respondents (job category, age, sex, years of clinical experience, and work area), and any previous exposure to Middle East respiratory syndrome coronavirus (MERS-CoV) or to patients with COVID-19 (either suspected or confirmed). We assessed the following outcomes related to the seven COVID-19 vaccine candidates that had been reported in the scientific literature: knowledge, perceived awareness, and readiness to receive each type of COVID-19 vaccine candidate. In addition, we assessed factors affecting respondents' readiness to receive various COVID-19 vaccine candidates and the HCW's sources of information about COVID-19 vaccines.

Before participation, the purpose of the study was explained in English at the beginning of the online survey. The respondent was given the opportunity to ask questions via a dedicated email address. The institutional review board at the College of Medicine and King Saud University Medical City approved the study (approval #20/0065/IRB). A waiver for signed consent was obtained because the survey presented no more than a minimal risk to participants and involved no procedures for which written consent is usually required outside the study context. To maximize confidentiality, personal identifiers were not required.

HCWs were screened for their awareness of any of the seven published vaccines. Notably, Pfizer announced during the study that the efficacy of their vaccine in the first interim analysis was more than 90%.[32]

Patient and Public Involvement

While this study did not have a direct patient or public involvement, its aim was directed at the healthcare workers' perceptions about the acceptance of COVID-19 vaccines. However, these HCWs are in the frontline of the pandemic, serving to save the lives of thousands of patients worldwide. Therefore, safeguarding HCWs becomes among healthcare and patients' priorities. No patients were directly involved in this research. The results of the study were published as a preprint that was shared with study participants.

Statistical analysis

Descriptive statistics approaches, with means and standard deviations, were applied to continuous variables, and percentages were used for dichotomous variables. The two-sample *t*-test was used to evaluate continuous scores, and the *Z* test was used to compare proportions.

A multivariable logistic regression model was used to explore associations between the outcome variable of HCW knowledge about the available COVID-19 vaccine candidates and HCW demographic, belief toward vaccine candidates, and level of anxiety. The association between predictors and the outcome was expressed as the odds ratio and 95% confidence interval. SPSS (version 21; IBM Corp) was used for the data analysis, Excel (Microsoft) was used for creating figures and depictions, and statistical significance was set at p=0.050. [33]

RESULTS

A total of 2079 HCWs were invited to participate in the study; 2007 (96.5%) agreed to participate, and 1512 participants (75.3%) were included in the analysis. The participants' sociodemographic characteristics are shown in Table 1.

Women comprised the majority of the population (62.4%), most participants (70.3%) were between 21 and 40 years of age, 68.6% were married—though only 47.3% were living with their families—and 76.2% reported not having any chronic illnesses.

Respondents' working areas were distributed almost evenly across different sectors of health institutions, but the majority were from the public/governmental (47.1%) sectors and tertiary institutions (62.2%). In terms of awareness of potential vaccine candidates reported in the literature, the majority (59.5%) reported knowing about at least one vaccine.

Table 1: Respondents' Sociodemographic and Professional Characteristics (N=1512)		
Characteristic	No.	%
Sex		
Male	568	37.6
Female	944	62.4
Age (years), mean (SD)		37.28 (8.99)
21-30	385	25.5
31-40	677	44.8
41-50	298	19.7
≥50	152	10.1
Marital status		
Single	435	28.8
Married, living with family	715	47.3
Married, living alone	322	21.3
Widowed or divorced	40	2.6
Any chronic illness		
No	1152	76.2
Yes	360	23.8
Clinical role		
Physician	637	42.1
Nurse	757	50.1
Other healthcare provider	118	7.8
Working area		
Intensive care unit: adults and pediatrics	216, 115	14.3, 7.6
Emergency department	152	10.1
General ward	406	26.9
Isolation ward	57	3.8
Outpatient area	319	21.1
Other specialized unit: dialysis, lab, pharmacy, radiology	206	13.6
Hospital administrative	41	2.7
Hospital category		
Private	350	23.1
Governmental	712	47.1
University hospital	450	29.8
Hospital level of care		
Primary healthcare center	210	13.9
Secondary-care hospital	361	23.9
Tertiary hospital	941	62.2

SD: Standard Deviation

The ChAdOx1 nCoV-19 vaccine was the vaccine recognized the most by HCWs (39.3%), followed by the Gam-COVID-Vac vaccine (31.9%) and the RNA BNT162b2 vaccine (30.8%). The least well-known vaccine among HCWs was the mRNA-1273 vaccine (19.9%; Table 2).

HCWs were asked to indicate their readiness to receive each type of COVID-19 vaccine with response categories of never, maybe, or sure (i.e., willing to receive). The vaccine that most HCWs reported they were willing to receive was the AstraZeneca ChAdOx1 nCoV-19 (24.4%), followed by the Pfizer RNA BNT162b2 (20.9%) vaccine. Conversely, HCWs reported that they were most likely to refuse receipt of the CanSino Ad5-vectored (18.3%) and Gamaleya Gam-COVID-Vac (17.9%) vaccines. The respondents reported maybe most often for any vaccine candidate, with maybe responses ranging from 65.1% for the AstraZeneca vaccine to 75.5% for the Moderna mRNA vaccine (Table 2).

Table 2: Perceived Awareness of and Readiness to Receive Various COVID-19 Vaccine Candidates by Healthcare Workers

Vaccine Candidate	No. (%) Knows About Vaccine*	No. (%) Ready to Take Vaccine		
		Never	Maybe	Sure
AstraZeneca (Oxford University: British/Swedish) non-replicating viral vector (chimpanzee adenovirus vectored vaccine (ChAdOx1 nCoV-19)	594 (39.3)	159 (10.5)	984 (65.1)	369 (24.4)
Gamaleya (Russia)-Sputnik V non-replicating viral vector adenovirus (Gam-COVID-Vac)	482 (31.9)	271 (17.9)	1100 (72.8)	141 (9.3)
Pfizer RNA (BNT162b2; USA): nucleoside-modified messenger RNA (modRNA)	466 (30.8)	154 (10.2)	1042 (68.9)	316 (20.9)
Johnson and Johnson (USA; adenovirus type 26 vector; Ad26.COV2-S)	422 (27.9)	154 (10.2)	1108 (73.3)	250 (16.5)
CanSino (China; adenovirus type 5; Ad5-vectored)	397 (26.3)	277 (18.3)	1103 (72.3)	132 (8.7)
Novavax (USA) protein subunit (full-length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M; NVX-CoV2373)	364 (24.1)	166 (11)	1139 (75.3)	208 (13.8)
Moderna RNA (USA; mRNA-1273)	301 (19.9)	170 (11.2)	1142 (75.5)	200 (13.2)

*Percentage expressed of total sample (N=1512 healthcare workers).

In determining the factors that influenced differential readiness of HCWs to receive the vaccine candidates that had been reported in scientific literature, a multiple-response dichotomies analysis showed that respondents' perceptions of the vaccine candidate as more efficient in preventing infection was the most influencing factor (33%) in their decisions, followed by their personal preferences (29%) and the vaccine's manufacturing country (28.6%). The least influential factors were media and social media coverage (12.3%) and trustworthiness (4.2%; Table 3).

Table 3: Factors Affecting Respondents' Readiness to Receive COVID-19 Vaccine Candidates (N=1512)

	No.	%
This COVID vaccine(s) seems more efficient in preventing the infection.	499	33
Personal preference	439	29
Manufacturing country	433	28.6
Possibly fewer adverse effects from this vaccine	417	27.6
Vaccine availability	394	26.1
Company's reputation	395	26.1
Media coverage	186	12.3
Trustworthiness	64	4.2

The HCW's sources of information about COVID-19 vaccines are shown in Table 4. The WHO website was the most utilized source for information (51.1%), followed by social media networks (48.3%), the Saudi Ministry of Health (MOH) website (43.8%), and official press releases (38.3%). The Centers for Disease Control and Prevention website was utilized by only one third of participants (Table 4).

Table 4: Respondents' Sources of Information About COVID-19 Vaccine Types (N=1512)

	No.	%
WHO website	762	51.1
Social networks (e.g., YouTube, Facebook, Twitter, WhatsApp)	719	48.3
MOH website	652	43.8
Official statements or press releases from MOH (e.g., through SMS or newspapers)	570	38.3

Hospital announcements (e.g., roll-ups or newsletters)	543	36.4
Other internet resources	537	36
CDC website	501	33.6

WHO: World Health Organization, MOH: Ministry of Health, SMS: Short Message Service, CDC: Centers for Disease Control and Prevention

A substantial number of HCWs in this study (n=612, 40.5%) reported unawareness of some vaccine candidates reported in scientific literature as of the time of the study. Therefore, as a secondary analysis, the generalized linear multivariate gamma regression analysis was used to explain the predictors of how likely the surveyed HCWs were to be aware of the different scientifically reported vaccine candidates. These results are presented in Table 5 and show that women knew significantly less than men about the different vaccine candidates (p=0.016). Older age correlated significantly and positively with more knowledge (p=0.027). Also, physicians knew significantly more about vaccine candidates than other HCWs did (p=0.001), and the HCWs from primary and secondary health centers knew of significantly fewer COVID-19 vaccine candidates than did HCWs from tertiary medical centers (p=0.002 for primary, p=0.02 for secondary). The participant's belief in the ability of COVID-19 vaccines to stop the pandemic predicted significantly higher knowledge of the available vaccine candidates (p=0.009). HCWs who did not interact with COVID-19–infected family members knew significantly less about the available vaccine candidates (p=0.018). Other specific worry/anxiety levels and beliefs were assessed, as reported in Table 5

Table 5: Generalized Linear Modelling Analysis of the Healthcare Workers' Knowledge of the Available COVID-19 Vaccine Candidates

Parameter	Exponentiated (β) Coefficient	95% CI for Exponentiated (β)		p-value
		Lower	Upper	
(Intercept)	1.936	1.442	2.600	<0.001
Sex=female	0.900	0.826	0.981	0.016
Age (years)	1.005	1.001	1.009	0.027
Clinical role=physician	1.267	1.101	1.458	0.001
Clinical role=nurse and Midwife	0.855	0.747	0.979	0.023
Hospital setup type=primary	0.847	0.763	0.940	0.002

Hospital setup type=secondary	0.904	0.830	0.984	0.020
Hospital sector=private	0.910	0.825	1.003	0.057
Hospital sector= Governmental	0.961	0.884	1.045	0.355
Generalized anxiety, mean score	1.002	0.995	1.010	0.565
Worry level from getting COVID-19 viral infection, mean score	0.961	0.920	1.005	0.080
Worry level from transmitting COVID-19 viral infection to family, mean score	1.029	0.991	1.069	0.133
Believes the vaccine can stop the disease spread	1.073	1.018	1.132	0.009
Believes vaccination prevents COVID-19 complications	1.046	0.994	1.100	0.087
Does not interact with COVID-19–infected family members	0.907	0.836	0.983	0.018
NOTE: Dependent variable was the total number of vaccines the HCW knew about. The exponentiated (β) coefficient was interpreted as a rate.				

Our analysis (Fig 1) showed a significantly higher percentage rate of HCW readiness to receive any COVID-19 vaccine relative to the refusal rate after the Pfizer announcement compared to before it (χ^2[1)]4.56, p=0.032). This result was similar to HCW readiness to receive the BNT162b2 vaccine (Fig 2).

DISCUSSION

Since the beginning of the pandemic, an unprecedented global effort to develop a vaccine has been underway; research and development of different technologies have been applied for different vaccine candidates. The effort resulted in several types of vaccine candidates developed with various technologies, including adenovirus and RNA-based vaccines, all of which are novel and have not been developed for wide clinical use in other infectious diseases. Gaining knowledge of such new vaccines, with the rapid evolution of the development process, may be

challenging: only 40% of study participants were aware of the ChAdOx1 nCoV-19 vaccine,[5-9, 11, 34, 35] and only one third were aware of the BNT162b2, Gam-COVID-Vac, and Ad26.COV2-S vaccines. Only a quarter of participants knew about the remaining vaccines. To our knowledge, data about HCW knowledge of vaccine candidates has not been published elsewhere.

Acceptance about COVID-19 vaccines in general has been studied. In a global survey in 19 countries about the potential acceptance of a COVID-19 vaccine among the public, 71.5% reported they would very or somewhat likely agree to receive a vaccine; respondents from China gave the highest proportion of positive responses (631 [88.6%] of 712 respondents) and the lowest proportion of negative responses (five [0.7%0 of 712) when asked if they would take a proven, safe, and effective vaccine. Respondents from Poland reported the highest proportion of negative responses (182 [27.3%] of 666), whereas Russian respondents gave the lowest proportion of positive responses (373 [54.9%] of 680). Data are available about other diseases with multiple vaccine types as well. In a parental survey on acceptance of an intranasal, live, attenuated influenza vaccine, 81% preferred this version compared with the injectable inactivated influenza vaccine[36]; however no such acceptance rate has been evaluated among HCWs.[37]

It is interesting to note that, of all the HCW respondents asked about taking a COVID-19 vaccine, only 20% or 24% preferred to receive the AstraZeneca or the Pfizer vaccine, respectively. This low response to acceptance of any vaccine in development may indicate variability in the knowledge and understanding about the different vaccines. Vaccine knowledge is an area that needs more study to understand variables contributing to acceptance or rejection of each type of vaccine according to different development platforms used. This understanding would aid policymakers in the development of appropriate educational materials to boost confidence in various vaccine platforms.

Many factors affect the choice to receive vaccines. In this study, the top reason for choosing a vaccine was that the vaccine seems more effective at preventing infection (33%). A previous study found that 50% vaccine efficacy was associated with a 51% rate of acceptance.[38]

The manufacturing country was another reason given for accepting the vaccine (in 28.6% of respondents). This finding is similar to results from a US survey related to hypothetical vaccines. The surveyed individuals had lower acceptance of the vaccine if it originated from a

country outside the United States.[38] Other contributing factors, such as fewer adverse effects, were also reported in this study.[38] Understanding these factors is important to build strategies for vaccine acceptance in any community. Strategies should address concerns, contributing factors, and misconceptions.[39] Trustworthiness was indicated by approximately 4% of the respondents as a factor in accepting a COVID-19 vaccine. It is important to note that trust is an important modifiable element of any successful vaccine campaign. Trustworthiness was strongly associated with acceptance of COVID-19,[40] and this factor was also related to acceptance of other vaccines, such as H1N1, SARS, and MERS vaccines.[25]

The most-reported sources of information for HCWs were the WHO website and social networks (as expected in a pandemic). Previously, Alsubaie et al.[41] reported results from the same HCWs' population, which showed that hospital announcements and MOH official statements were more commonly sought for information about the MERS-CoV national outbreak. Seeking knowledge from reliable sources about the pandemic and vaccinations could significantly impact the HCWs' perceptions of vaccine acceptance. Misinformation about the COVID-19 vaccine was associated with decreased vaccination acceptance among those who would otherwise definitely vaccinate.[42]

Interestingly, HCWs working in tertiary and academic centers were more knowledgeable about various vaccine candidates compared with HCWs working in primary and secondary centers. This result may be explained by more scientific activity and educational campaigns typically associated with teaching hospitals. This increased knowledge was especially common among physicians in our study, like other studies; in a cross-sectional survey conducted in Italy among HCWs to assess their knowledge, attitudes, and practices about vaccinations, physicians and those who had received information about vaccinations from scientific journals, educational activities, or professional associations were more likely to have adequate knowledge.[43] The knowledge differences identified between centers and types of providers highlight the importance of academic activities and keeping up-to-date with the scientific literature during the COVID-19 pandemic.

Remarkably, after the Pfizer and BioNTech announcement about the efficacy rate of BNT162b2, the HCWs in our study demonstrated significantly more willingness to undergo vaccination.[33] This change was despite simultaneous negative news on some COVID-19 vaccination trials, such as the halting of clinical studies with the CoronaVac vaccine by the

Brazilian national sanitary regulator (Anvisa) due to a serious adverse event.[44] Vaccine acceptance is a multifactorial issue, but having positive COVID-19 vaccine trial results circulating in the news and social media for several days after the press release on the efficacy of BNT162b2 could improve the HCWs' willingness to vaccinate.

This study has the limitation of being self-reported and survey-based, so future observational studies on the HCWs actual acceptance of various COVID-19 vaccines is warranted. Another aspect is the national design, that needs further research for external validity in other countries.

CONCLUSION

HCW awareness of the several COVID-19 candidate vaccines could improve perception and acceptance of vaccination. Reliable sources on vaccine efficiency could improve vaccine uptake, and healthcare authorities should utilize these sources to decrease vaccine hesitancy among frontline healthcare providers.

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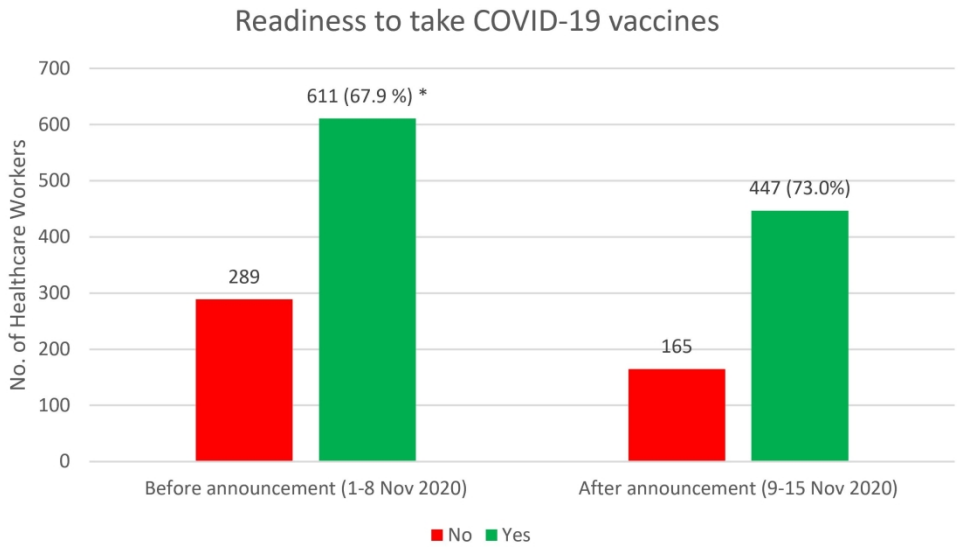
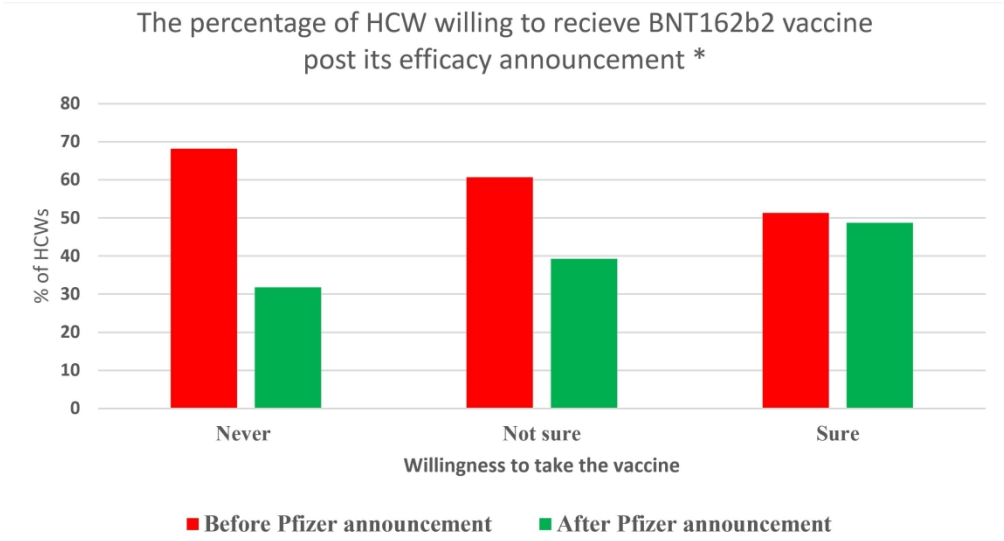
Figure 1: Readiness to take COVID-19 vaccines, as reported before and after the interim report of the efficacy rate of BNT162b2. *p=0.032.

Figure 2: The percentage of healthcare workers (HCWs) willing to receive the BNT162b2 vaccine after its efficacy announcement. *p=0.001.



Readiness to take COVID-19 vaccines, as reported before and after the interim report of the efficacy rate of BNT162b2. *p=0.032.

287x167mm (240 x 240 DPI)



The percentage of healthcare workers (HCWs) willing to receive the BNT162b2 vaccine after its efficacy announcement. *p=0.001.

310x169mm (240 x 240 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	7-8
Outcome data	15*	Report numbers of outcome events or summary measures over time	9

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Adenovirus and RNA-based COVID-19 vaccines' perceptions and acceptance among healthcare workers in Saudi Arabia: A national survey

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Adenovirus and RNA-based COVID-19 vaccines' perceptions and acceptance among healthcare workers in Saudi Arabia: A national survey

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MH.Temsah, M.Barry, J.Al-Tawfiq, Z.Memish, and F.Alsohime were involved in conception, analyzed the data, and wrote the manuscript. A.Alhuzaimi, A.Al-Eyadhy, F.Aljamaan, B.Saddik, A.Alrabiaah, and N.Alamro contributed to the study design; collected, analyzed, and interpreted data; and edited the manuscript. A.Alhuzaimi, F.Al-Shahrani, K.Alhasan, A.Alrabiaah, A.Alaraj, A.Alhaboob and S.Alsubaie supervised data collection, analyzed data, and edited the manuscript. A.Al-Eyadhy, R.Halwani, and A.Jamal interpreted the data and wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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ABSTRACT

Objectives The aim of this study was to compare the perception, confidence, hesitancy, and acceptance rate of various COVID-19 vaccine types among healthcare workers (HCWs) in Saudi Arabia, a nation with MERS-CoV experience.

Design National cross-sectional, pilot-validated questionnaire.

Setting Online, self-administered questionnaire among HCWs.

Participants A total of 2,007 HCWs working in the Kingdom of Saudi Arabia participated; 1512 (75.3%) participants completed the survey and were included in the analysis.

Intervention Data were collected through an online survey sent to HCWs during November 1-15, 2020. The main outcome measure was HCW acceptance of COVID-19 candidate vaccines. The associated factors of vaccination acceptance were identified through a logistic regression analysis and via measurement of the level of anxiety, using the generalized anxiety disorder 7 (GAD7) scale.

Results Among the 1512 HCWs who were included, 62.4% were women, 70.3% were between 21 and 40 years of age, and the majority (62.2%) were from tertiary hospitals. In addition, 59.5% reported knowing about at least one vaccine; 24.4% of the participants were sure about their willingness to receive the ChAdOx1 nCoV-19 vaccine, and 20.9% were willing to receive the RNA BNT162b2 vaccine. However, 18.3% reported that they would refuse to receive the Ad5-vectored vaccine, and 17.9% would refuse the Gam-COVID-Vac vaccine. Factors that influenced the differential readiness of HCWs included their perceptions of the vaccine's efficiency in preventing the infection (33%), their personal preferences (29%), and the vaccine's manufacturing country (28.6%).

Conclusions Awareness by HCWs of the several COVID-19 candidate vaccines could improve their perceptions and acceptance of vaccination. Reliable sources on vaccine efficiency could improve vaccine uptake, so healthcare authorities should use reliable information to decrease vaccine hesitancy among frontline healthcare providers.

Strengths and limitations of this study

- The research is among the first studies to explore the perception, confidence, hesitancy, and acceptance rates of various COVID-19 vaccine types among HCWs.

- This is a national, cross-sectional survey among healthcare workers.

- The press release on the efficacy of the BNT162b2 vaccine coincided with ongoing data collection about the HCWs' willingness to vaccinate.

- Being a self-reported and survey-based study highlights that observational studies on the HCWs' actual acceptance of various COVID-19 vaccines are warranted in the nearest future.

- The convenience sample could limit the generalizability; therefore, further research is warranted.

INTRODUCTION

The COVID-19 pandemic has severely disrupted normal societal and economic activities worldwide and is expected to continue imposing strains and burden on health systems in most of countries. Globally, the COVID-19 pandemic remains out of control.[1] The existing measures to control COVID-19 are detrimental to the global economy [2] and result in significant impairment in physical and psychological wellbeing.[3] To keep COVID-19 under control there is a strong need for an effective vaccine. Without COVID-19 vaccination, health care workers (HCWs) will likely be at risk and are likely to serve as reservoir inside health institutes, which would undermine efforts to end the pandemic. According to the World Health Organization (WHO), there are 56 and 166 candidate vaccines in clinical and pre-clinical evaluation by December 17, 2020.[4] These include JNJ-78436735 an adenovirus vaccine (Ad26.COV2.S), [5, 6]mRNA-1273 an mRNA vaccine,[7] AZD1222 an adenovirus vaccine (ChAdOx1 nCoV-19),[8] BNT162b1an mRNA vaccine,[9] NVX-CoV2373 a full-length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M,[10] Ad5-nCoV an adenovirus vaccine.[11-14] Encouraging news is that several vaccines had been released and many are in phase 3 clinical trials and showing promising effectiveness.[15] As some safe and efficacious vaccines became available, policy makers need to ensure a successful large-scale uptake of COVID-19 vaccines to achieve community immunization. However, the success of COVID-19 vaccination programs will largely depend on people's acceptance of the vaccine. A recent global survey suggested that nearly 30% of participants would be hesitated to take a COVID-19 vaccine when it is available.[16] A systematic review on acceptance of a COVID-19 vaccine based on nationally representative

surveys in 20 nations indicates that vaccine acceptance rate in most nations would not reach 67% that is necessary for achieving population immunity.[17] Mathematic modelling suggested that if a COVID-19 vaccine efficacy was 80%, the coverage must achieve at least 75% to extinguish the ongoing pandemic.[18] Therefore, a timely understanding of community responses to the forthcoming COVID-19 vaccines would be important for policy making and service planning.

Extant literature has explored vaccine acceptance and identified a few demographic and psychosocial correlates such as gender, age, trust in research, knowledge, and concerns about the novel vaccine, as well as people's judgment and perceptions regarding risk of COVID-19.[19-21] Risk exposure to the disease is one of several essential issues that directly shape people's assessment to their vulnerability and risk. Even being weaponed with personal protective equipment, healthcare providers and other essential workers are considered to have high risk exposures to COVID-19 and given priority in vaccine allocations. Several studies suggest that being a healthcare worker or being involved in the care of COVID-19 patients is positively associated with COVID-19 vaccine acceptance.[22-24]

The lessons learned from previous infectious disease pandemics and outbreaks, including SARS, H1N1, MERS-CoV and Ebola demonstrate the important role that health information has on disease control and vaccine acceptance.[25] Source of health information can affect the manner and frequency of the utilization of such information. The degree to which the information source is trusted can have a remarkable impact on the acceptance of information.[26] If HCWs distrust the source, they will doubt the information regarding different COVID 19 vaccines, and this doubt will in turn shape their attitudes, perceptions, and potential actions they take toward various COVID 19 vaccines.

The Kingdom of Saudi Arabia (KSA) is one of the top thirty countries with the highest reported COVID-19 cases: 360,690 laboratory confirmed cases and 6101 deaths as of December 19, 2020.[27] Acceptance of a potential COVID-19 vaccine assessed among HCWs in KSA in a survey of 2007 participants showed an acceptance rate of 70%,[28] which is slightly higher than the acceptance rate found in public survey among 992 participants of general population (acceptance rate of 65%).[29] Perception, confidence, and hesitancy for various COVID 19 vaccines in the context of emerging viral infections and pandemics and manufacturing company and the different sources of information are principal factors in assessing vaccine acceptance of various

types. To the best of our knowledge, none of published surveys specifically targeted and compared HCWs perception, confidence, and hesitancy toward different types of COVID 19 candidate vaccines. While our previous research showed that most (70%) HCWs are willing to receive COVID-19 vaccines once available,[28] we aimed in this study to compare the perception, confidence, hesitancy, and acceptance rate of various COVID 19 vaccines types among HCWs.

METHODS

Data Collection

This study was a national cross-sectional survey among healthcare workers (HCWs) in Saudi Arabia during COVID-19 pandemic. Data were collected during 4-14, November 2020. At the time of data collection, at least seven COVID-19 vaccine candidates had been reported in the scientific literature. HCWs were screened for their awareness of any of the seven published vaccines[28]. Participants were invited using a convenience sampling technique. We used several social media platforms and email lists to recruit participants for direct invitation. The survey was a pilot-validated, self-administered questionnaire that was sent to HCWs online through SurveyMonkey©, a platform that allows researchers to deploy and analyze surveys via the internet.[30] The English questionnaire (as invited participants were multinational and all were English speakers) (Appendix 1) [31] with modifications and additions related to the potential COVID-19 vaccine.

The questions included the demographic characteristics of respondents (job category, age, sex, years of clinical experience, and work area), and any previous exposure to Middle East respiratory syndrome coronavirus (MERS-CoV) or to patients with COVID-19 (either suspected or confirmed). We assessed the following outcomes related to the seven COVID-19 vaccine candidates that had been reported in the scientific literature: knowledge, perceived awareness, and readiness to receive each type of COVID-19 vaccine candidate. In addition, we assessed factors affecting respondents' readiness to receive various COVID-19 vaccine candidates and the HCW's sources of information about COVID-19 vaccines.

Before participation, the purpose of the study was explained in English at the beginning of the online survey. The respondent was given the opportunity to ask questions via a dedicated email address. The institutional review board at the College of Medicine and King Saud University Medical City approved the study (approval #20/0065/IRB). A waiver for signed consent was obtained because the survey presented no more than a minimal risk to participants and involved no procedures for which written consent is usually required outside the study context. To maximize confidentiality, personal identifiers were not required.

HCWs were screened for their awareness of any of the seven published vaccines. Notably, Pfizer announced during the study that the efficacy of their vaccine in the first interim analysis was more than 90%.[32]

Patient and Public Involvement

While this study did not have a direct patient or public involvement, its aim was directed at the healthcare workers' perceptions about the acceptance of COVID-19 vaccines. However, these HCWs are in the frontline of the pandemic, serving to save the lives of thousands of patients worldwide. Therefore, safeguarding HCWs becomes among healthcare and patients' priorities. No patients were directly involved in this research. The results of the study were published as a preprint that was shared with study participants.

Statistical analysis

Descriptive statistics approaches, with means and standard deviations, were applied to continuous variables, and percentages were used for dichotomous variables. The two-sample *t*-test was used to evaluate continuous scores, and the *Z* test was used to compare proportions.

A multivariable logistic regression model was used to explore associations between the outcome variable of HCW knowledge about the available COVID-19 vaccine candidates and HCW demographic, belief toward vaccine candidates, and level of anxiety. The association between predictors and the outcome was expressed as the odds ratio and 95% confidence interval. SPSS (version 21; IBM Corp) was used for the data analysis, Excel (Microsoft) was used for creating figures and depictions, and statistical significance was set at p=0.050. [33]

RESULTS

A total of 2007 HCWs agreed to participate, and 1512 participants (75.3%) completed the survey and were included in the analysis. Almost quarter of respondents did not complete the survey and were excluded from analysis. The participants' sociodemographic characteristics are shown in Table 1.

Women comprised most of the population (62.4%), most participants (70.3%) were between 21 and 40 years of age, 68.6% were married—though only 47.3% were living with their families—and 76.2% reported not having any chronic illnesses.
Respondents' working areas were distributed almost evenly across different sectors of health institutions, but the majority were from the public/governmental (47.1%) sectors and tertiary institutions (62.2%). In terms of awareness of potential vaccine candidates reported in the literature, the majority (59.5%) reported knowing about at least one vaccine.

Table 1: Respondents' Sociodemographic and Professional Characteristics (N=1512)

Characteristic	N (%)
Sex	
Male	568 (37.6)
Female	944 (62.4)
Age (years), mean (SD)	37.28 (8.99)
21-30	385 (25.5)
31-40	677 (44.8)
41-50	298 (19.7)
≥50	152 (10.1)
Marital status	
Single	435 (28.8)
Married, living with family	715 (47.3)
Married, living alone	322 (21.3)

Widowed or divorced	40 (2.6)
Any chronic illness	
No	1152 (76.2)
Yes	360 (23.8)
Clinical role	
Physician	637 (42.1)
Nurse	757 (50.1)
Other healthcare provider *	118 (7.8)
Working area	
Intensive care unit: adults and pediatrics	331 (21.9)
Emergency department	152 (10.1)
General ward	406 (26.9)
Isolation ward	57 (3.8)
Outpatient area	319 (21.1)
Other specialized units: dialysis, lab, pharmacy, radiology	206 (13.6)
Hospital administrative	41 (2.7)
Hospital category	
Private	350 (23.1)
Governmental	712 (47.1)
University hospital	450 (29.8)
Hospital level of care	
Primary healthcare center	210 (13.9)
Secondary-care hospital	361 (23.9)
Tertiary hospital	941 (62.2)

SD: Standard Deviation

** other healthcare provider include Technicians, Respiratory Therapists and Pharmacists*

The ChAdOx1 nCoV-19 vaccine was the vaccine recognized the most by HCWs (39.3%), followed by the Gam-COVID-Vac vaccine (31.9%) and the RNA BNT162b2 vaccine (30.8%). The least well-known vaccine among HCWs was the mRNA-1273 vaccine (19.9%; Table 2).

HCWs were asked to indicate their readiness to receive each type of COVID-19 vaccine with response categories of "never, maybe, or sure" (i.e., willing to receive). The respondents reported "maybe" in (65.1%) for the (AstraZeneca) vaccine and up to (75.5%) for the (Moderna), while they were "sure" to receive the vaccine if it was (CanSino) in (9.3%) but up to (24.4)% if the (AstraZeneca) one, on the other hand they answered "never receive" for the (Johnson and Johnson) or (Pfizer) vaccines in (10.2%) but up to (18.3) for the (CanSino) (Table 2).

Table 2: Perceived Awareness of and Readiness to Receive Various COVID-19 Vaccine Candidates by Healthcare Workers

Vaccine Candidate	No. (%) Knows About Vaccine*	No. (%) willingness to Take the Vaccine		
		Never	Maybe	Sure
AstraZeneca (Oxford University: British/Swedish) non-replicating viral vector (chimpanzee adenovirus vectored vaccine (ChAdOx1 nCoV-19)	594 (39.3)	159 (10.5)	984 (65.1)	369 (24.4)
Gamaleya (Russia)-Sputnik V non-replicating viral vector adenovirus (Gam-COVID-Vac)	482 (31.9)	271 (17.9)	1100 (72.8)	141 (9.3)
Pfizer RNA (BNT162b2; USA): nucleoside-modified messenger RNA (modRNA)	466 (30.8)	154 (10.2)	1042 (68.9)	316 (20.9)
Johnson and Johnson (USA; adenovirus type 26 vector; Ad26.COV2-S)	422 (27.9)	154 (10.2)	1108 (73.3)	250 (16.5)
CanSino (China; adenovirus type 5; Ad5-vectored)	397 (26.3)	277 (18.3)	1103 (72.3)	132 (8.7)
Novavax (USA) protein subunit (full-length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M; NVX-CoV2373)	364 (24.1)	166 (11)	1139 (75.3)	208 (13.8)

Moderna RNA (USA; mRNA-1273)	301 (19.9)	170 (11.2)	1142 (75.5)	200 (13.2)

*Percentage expressed of total sample (N=1512 healthcare workers).

In determining factors influencing differential readiness of HCWs to receive vaccine candidates, a multiple-response dichotomies analysis showed that respondents' perceptions of the vaccine candidate as being more efficient in preventing infection was the most influencing factor (33%) in their decisions, followed by their personal preferences (29%) and the vaccine's manufacturing country (28.6%). The least influential factors were media and social media coverage (12.3%) and trustworthiness (4.2%; Table 3).

Table 3: Factors Affecting Respondents' Readiness to Receive COVID-19 Vaccine Candidates (N=1512)

	N (%)
This COVID vaccine(s) seems more efficient in preventing the infection.	499 (33)
Personal preference	439 (29)
Manufacturing country	433 (28.6)
Possibly fewer adverse effects from this vaccine	417 (27.6)
Vaccine availability	394 (26.1)
Company's reputation	395 (26.1)
Media coverage	186 (12.3)
Trustworthiness	64 (4.2)

The HCW's sources of information about COVID-19 vaccines are shown in Table 4. The WHO website was the most utilized source for information (51.1%), followed by social media networks (48.3%), the Saudi Ministry of Health (MOH) website (43.8%), and official press releases (38.3%). The Centers for Disease Control and Prevention website was utilized by only one third of participants (Table 4).

Table 4: Respondents' Sources of Information About COVID-19 Vaccine Types (N=1490)

	N.(%)
WHO website	762 (51.1)
Social networks (e.g., YouTube, Facebook, Twitter, WhatsApp)	719 (48.3)
MOH website	652 (43.8)
Official statements or press releases from MOH (e.g., through SMS or newspapers)	570 (38.3)
Hospital announcements (e.g., roll-ups or newsletters)	543 (36.4)
Other internet resources	537 (36.0)
CDC website	501 (33.6)

WHO: World Health Organization, MOH: Ministry of Health, SMS: Short Message Service, CDC: Centers for Disease Control and Prevention

A substantial number of HCWs in this study (n=612, 40.5%) reported unawareness of some vaccine candidates reported in scientific literature as of the time of the study. Therefore, as a secondary analysis, the generalized linear multivariate gamma regression analysis was used to explain the predictors of how likely the surveyed HCWs were to be aware of the different scientifically reported vaccine candidates. These results are presented in Table 5 and show that women knew significantly less than men about the different vaccine candidates (p=0.016). Older age correlated significantly and positively with more knowledge (p=0.027). Also, physicians knew significantly more about vaccine candidates than other HCWs did (p=0.001), and the HCWs from primary and secondary health centers knew of significantly fewer COVID-19 vaccine candidates than did HCWs from tertiary medical centers (p=0.002 for primary, p=0.02 for secondary). The participant's belief in the ability of COVID-19 vaccines to stop the pandemic predicted significantly higher knowledge of the available vaccine candidates (p=0.009). HCWs who did not interact with COVID-19–infected family members knew significantly less about the available vaccine candidates (p=0.018). Other specific worry/anxiety levels and beliefs were assessed, as reported in Table 5.

Table 5: Generalized Linear Modelling Analysis of the Healthcare Workers' Knowledge of the Available COVID-19 Vaccine Candidates

Parameter	Exponentiated (β) Coefficient	95% CI for Exponentiated (β)		p-value
		Lower	Upper	
(Intercept)	1.936	1.442	2.600	<0.001
Sex=female	0.900	0.826	0.981	0.016
Age (years)	1.005	1.001	1.009	0.027
Clinical role=physician	1.267	1.101	1.458	0.001
Clinical role=nurse and Midwife	0.855	0.747	0.979	0.023
Hospital setup type=primary	0.847	0.763	0.940	0.002

Hospital setup type=secondary	0.904	0.830	0.984	0.020
Hospital sector=private	0.910	0.825	1.003	0.057
Hospital sector= Governmental	0.961	0.884	1.045	0.355
Generalized anxiety, mean score	1.002	0.995	1.010	0.565
Worry level from getting COVID-19 viral infection, mean score	0.961	0.920	1.005	0.080
Worry level from transmitting COVID-19 viral infection to family, mean score	1.029	0.991	1.069	0.133
Believes the vaccine can stop the disease spread	1.073	1.018	1.132	0.009
Believes vaccination prevents COVID-19 complications	1.046	0.994	1.100	0.087
Does not interact with COVID-19–infected family members	0.907	0.836	0.983	0.018
NOTE: Dependent variable was the total number of vaccines the HCW knew about. The exponentiated (β) coefficient was interpreted as a rate.				

Our analysis (Fig 1) showed a significantly higher percentage rate of HCW readiness to receive any COVID-19 vaccine relative to the refusal rate after the Pfizer announcement compared to before it (χ^2[1)]4.56, p=0.032). In addition, the percentage of HCWs accepting to take the BNT162b2 vaccine increased from 18% to 25.1% and proportion of those who stated they will never take the BNT162b2 vaccine dropped from 12% to 8.1% following Pfizer's announcement (Fig 2).

DISCUSSION

Since the beginning of the pandemic, an unprecedented global effort to develop a vaccine has been underway; research and development of different technologies have been applied for different vaccine candidates. The effort resulted in several types of vaccine candidates developed with various technologies, including adenovirus and RNA-based vaccines, all of which are novel and have not been developed for wide clinical use in other infectious diseases. Gaining knowledge of such new vaccines, with the rapid evolution of the development process, may be challenging: only 40% of study participants were aware of the ChAdOx1 nCoV-19 vaccine,[5-9, 11, 34, 35] and only one third were aware of the BNT162b2, Gam-COVID-Vac, and Ad26.COV2-S vaccines. Only a quarter of participants knew about the remaining vaccines. To our knowledge, data about HCW knowledge of vaccine candidates has not been published elsewhere.

The acceptance rate of COVID-19 vaccines is variable. In a global survey in 19 countries about the potential acceptance of a COVID-19 vaccine among the public, 71.5% reported they would very or somewhat likely agree to receive a vaccine; respondents from China gave the highest proportion of positive responses (631 [88.6%] of 712 respondents) and the lowest proportion of negative responses (five [0.7%0 of 712) when asked if they would take a proven, safe, and effective vaccine. Respondents from Poland reported the highest proportion of negative responses (182 [27.3%] of 666), whereas Russian respondents gave the lowest proportion of positive responses (373 [54.9%] of 680). Data are available about other diseases with multiple vaccine types as well. In a parental survey on acceptance of an intranasal, live, attenuated influenza vaccine, 81% preferred this version compared with the injectable inactivated influenza

vaccine.[36] During the H1N1 pandemic, 50 of 161 healthcare workers (31.1%) were willing to take the 2009 H1N1 vaccine[37]. In a cross-sectional survey conducted in Riyadh in 2019 on influenza vaccine uptake, results showed an acceptance rate of 71% with hesitancy attributed to concerns on adverse events in 50% of participants [38]. It was also noted that people in the Middle East generally have low acceptance rate of COVID-19 vaccines and such acceptance was 23-66% [29, 39, 40]. However, no such acceptance rate has been evaluated among HCWs. [41]

It is interesting to note that, of all the HCW respondents asked about taking a COVID-19 vaccine, only 20% or 24% preferred to receive the AstraZeneca or the Pfizer vaccine, respectively. This low response to acceptance of any vaccine in development may indicate variability in the knowledge and understanding about the different vaccines. Vaccine knowledge is an area that needs more study to understand variables contributing to acceptance or rejection of each type of vaccine according to different development platforms used. This understanding would aid policymakers in the development of appropriate educational materials to boost confidence in various vaccine platforms.

Many factors affect the choice to receive vaccines. In this study, the top reason for choosing a vaccine was that the vaccine seems more effective at preventing infection (33%). A previous study found that 50% vaccine efficacy was associated with a 51% rate of acceptance[42]

The manufacturing country was another reason given for accepting the vaccine (in 28.6% of respondents). This finding is similar to results from a US survey related to hypothetical vaccines. The surveyed individuals had lower acceptance of the vaccine if it originated from a country outside the United States.[42] Other contributing factors, such as fewer adverse effects, were also reported in this study.[42] Understanding these factors is important to build strategies for vaccine acceptance in any community. Strategies should address concerns, contributing factors, and misconceptions.[43] Trustworthiness was indicated by approximately 4% of the respondents as a factor in accepting a COVID-19 vaccine. This is quite different when compared to the general population in the United Sates, in which trust, and perceptions of local COVID-19 vaccination norms were the strongest predictors of COVID-19 vaccine acceptance[44]. The difference might be the fact that our study included only HCWs who may have better understanding of the disease

and the vaccination. It is important to note that trust is an important modifiable element of any successful vaccine campaign. Trustworthiness was strongly associated with acceptance of a COVID-19 vaccine,[45] and this factor was also related to acceptance of other vaccines, such as H1N1, SARS, and MERS-CoV vaccines. [25]

The most-reported sources of information for HCWs were the WHO website and social networks (as expected in a pandemic). Previously, Alsubaie et al. [46] reported results from the same HCWs' population, which showed that hospital announcements and MOH official statements were more commonly sought for information about the MERS-CoV national outbreak. In the case of the general public, the source of knowledge and information about COVID-19 was official government social media and Twitter [47]. And another study showed 85.8% of the public in Saudi Arabia used the internet and social media for information regarding COVID-19. In a study from the US, 45-66% of HCWs used social media as a source of information [48, 49]. These findings suggest that HCWs in Saudi Arabia use social networking sites differently than their US counterparts, which is important for other studies that look at social media and knowledge. Seeking knowledge from reliable sources about the pandemic and vaccinations could significantly impact the HCWs' perceptions of vaccine acceptance [50]. Misinformation about the COVID-19 vaccine was associated with decreased vaccination acceptance among those who would otherwise definitely vaccinate. [51]

It is interesting to note the differences in knowledge about vaccines by level of training. Physicians knew significantly more about vaccine candidates than other HCWs did (p=0.001) (Table 5). Similarly, in a study from the USA, general COVID-19 knowledge among physicians was higher than other HCW, but non-physicians who work in healthcare did not have greater knowledge than public [49]. Noteworthy, HCWs working in tertiary and academic centers were more knowledgeable about various vaccine candidates compared with HCWs working in primary and secondary centers. This result may be explained by more scientific activity and educational campaigns typically associated with teaching hospitals. This increased knowledge was especially common among physicians in our study, like other studies; in a cross-sectional survey conducted in Italy among HCWs to assess their knowledge, attitudes, and practices about

vaccinations, physicians and those who had received information about vaccinations from scientific journals, educational activities, or professional associations were more likely to have adequate knowledge.[52] The knowledge differences identified between centers and types of providers highlight the importance of academic activities and keeping up-to-date with the scientific literature during the COVID-19 pandemic.

Remarkably, after the Pfizer and BioNTech announcement about the efficacy rate of BNT162b2, the HCWs in our study demonstrated significantly more willingness to undergo vaccination.[32] This change was despite simultaneous negative news on some COVID-19 vaccination trials, such as the halting of clinical studies with the CoronaVac vaccine by the Brazilian national sanitary regulator (Anvisa) due to a serious adverse event.[53] Vaccine acceptance is a multifactorial issue, but having positive COVID-19 vaccine trial results circulating in the news and social media for several days after the press release on the efficacy of BNT162b2 could improve the HCWs' willingness to vaccinate.

This study has the limitation of being self-reported and survey-based, so future observational studies on the HCWs actual acceptance of various COVID-19 vaccines is warranted. As a cross-sectional survey promoted on social media, it is not possible to calculate a response rate, and results may not be generalizable over time, therefore, further research is warranted. Another aspect is the national design, that needs further research for external validity in other countries.

CONCLUSION

HCW awareness of the several COVID-19 candidate vaccines could improve perception and acceptance of vaccination. Reliable sources on vaccine efficiency could improve vaccine uptake, and healthcare authorities should utilize these sources to decrease vaccine hesitancy among frontline healthcare providers.

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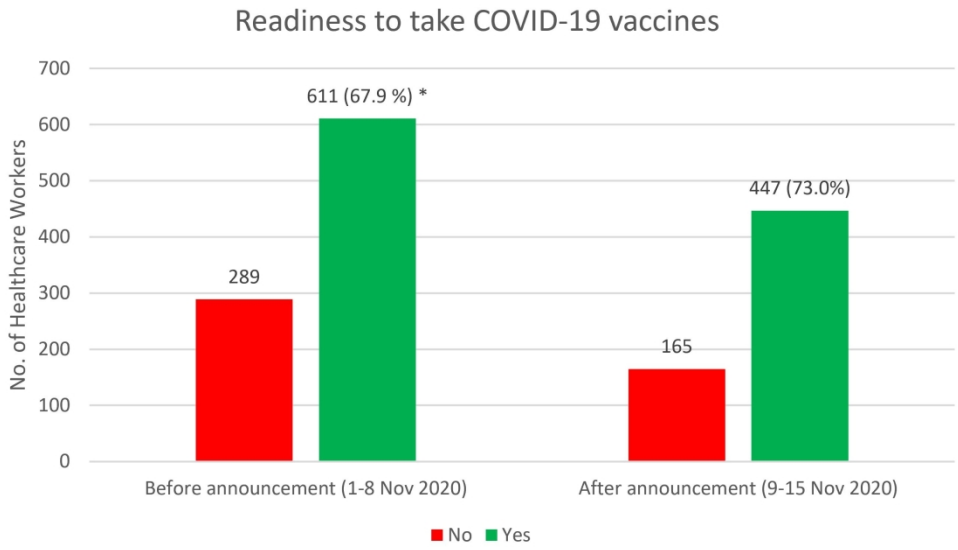
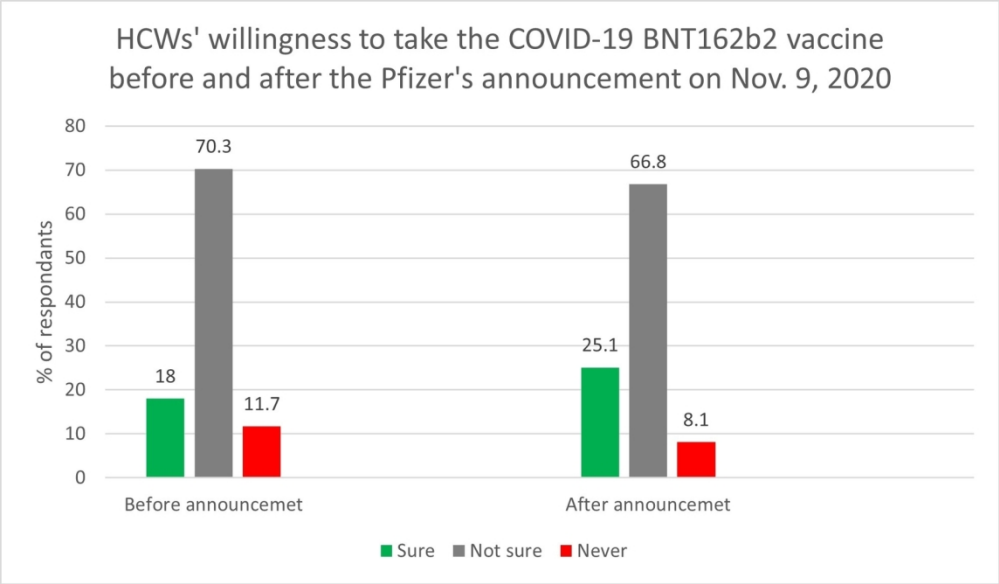
Figure 1: Readiness to take COVID-19 vaccines, as reported before and after the interim report of the efficacy rate of BNT162b2. *p=0.032.

Figure 2: The percentage of healthcare workers (HCWs) willing to receive the BNT162b2 vaccine after its efficacy announcement.



Readiness to take COVID-19 vaccines, as reported before and after the interim report of the efficacy rate of BNT162b2. *p=0.032.

287x167mm (240 x 240 DPI)



The percentage of healthcare workers (HCWs) willing to receive the BNT162b2 vaccine after its efficacy announcement.

152x88mm (300 x 300 DPI)

COVID-19 Vacciantion perceptions of HCWs

* 1. **Greetings dear healthcare provider,**

We would like you to imagine a situation where a number of vaccines for COVID-19 have been developed. These vaccines have undergone all required testing and have received regulatory approval for use in humans from the health authorities in Saudi and in other countries. Vaccination has also been recommended by the World Health Organisation (WHO).

Kindly take 5 minutes to answer, keeping in mind that all your answers are confidential. This will also give you more insight into several COVID vaccines that are currently in Phase 3 trial.

The study was approved by the Institutional Review Board at the College of Medicine, King Saud University (approval # 20/0065/IRB).

Thank You!

Dr. Hani Temsah, Dr. Mazin Barry
mtemsah@ksu.edu.sa

- I am a healthcare worker in Saudi Arabia, and I **ACCEPT** to participate in this Survey
- I do **NOT accept** to participate in this Survey

* 2. Region:

- Riyadh region
- Makkah region
- Madinah region
- Qassim region
- Eastern Region
- Asir
- Tabuk
- Hail
- The Northern Border region
- Jazan
- Najran
- Al Baha
- Al Jouf

COVID-19 Vacciantion perceptions of HCWs

Please Choose Your Answers then Press "Next"

* 3. You are

- Consultant
- Assistant consultant
- Resident
- Nurse
- RT
- Other (please specify)

* 4. What is your age?

Age in years:

* 5. What is your gender?

- Female
- Male

* 6. Are you now married, widowed, divorced, separated, or have you never been married?

- Married and living with children
- Married but living alone
- Widowed
- Divorced
- Never married

* 7. At what Hospital area do you work usually most of the time?

- Pediatric ICU
- Adult ICU
- Pedia ER
- Adult ER
- Isolation ward
- General ward
- OPD
- Other (please specify)

8. Do you have a chronic medical condition?
(like Hypertension, DM, chronic kidney disease, Heart disease, Asthma, COPD, Cancer, Immunocompromised state, SCD, Obesity)

- No
- Yes (please specify)

* 9. Your hospital setting and type of practice?

	Hospital/healthcare center Type	Practice Level
Hospital Setting:		

* 10. Have you been previously in contact with Corona (proven or suspected COVID) patients?
(Please choose all that apply)

- Yes: With COVID-Infected Patient
- Yes: With COVID-positive family member or friend
- Yes: With MERS-CoV Patient
- No: No contact at all

* 11. Have you been infected with laboratory-confirmed COVID-19 yourself?

- Yes
- No

COVID-19 Vacciantion perceptions of HCWs

* 12. Did you take the influenzas vaccine during the last 2 years?

- Yes
- No

* 13. If an approved MERS-CoV vaccine became available in Saudi Arabia this year, would you take it yourself?

- Yes
- No

* 14. If an approved COVID vaccine became available in Saudi Arabia this year, would you take it yourself?

- Yes
- No

* 15. If a COVID vaccine became available when you will take it?

- Get one as soon as possible
- Delay getting it for few months
- Never get one

COVID-19 Vacciantion perceptions of HCWs

16. You choose not to get the COVID Vaccine:
What are your reasons for not taking the vaccine?
(Choose what apply)

- [ ] Inadequate data about the safety of a new vaccine
- [ ] I am against vaccine in general (or I avoid medications whenever possible)
- [ ] Vaccine administration is painful or inconvenient
- [ ] I already had COVID infection
- [ ] A concern of adverse effects of the vaccine
- [ ] A concern of acquiring Covid19 from the vaccine
- [ ] A concern of vaccine being ineffective
- [ ] Prior adverse reaction to the vaccine
- [ ] I perceive myself not at high risk to acquire Covid19 infection
- [ ] I perceive myself not at high risk to develop complications if I get infected with Covid19 infection
- [ ] Other (please specify)

COVID-19 Vacciantion perceptions of HCWs

COVID Vaccine

* 17. If a COVID vaccine is announced this year in 2020, would your first thoughts be:

- ◯ It is a scientific achievement to find a vaccine that fast
- ◯ It was probably rushed without enough testing
- ◯ Other (please specify)

* 18. COVID vaccine is the most likely way to stop this pandemic.

- ◯ Strongly agree
- ◯ Agree
- ◯ Neither agree nor disagree
- ◯ Disagree
- ◯ Strongly disagree

* 19. Once the vaccine is available and approved; it would be safe.

- ◯ Strongly agree
- ◯ Agree
- ◯ Neither agree nor disagree
- ◯ Disagree
- ◯ Strongly disagree

* 20. The best way to avoid the complications of COVID is by being vaccinated

- ◯ Strongly agree
- ◯ Agree
- ◯ Neither agree nor disagree
- ◯ Disagree
- ◯ Strongly disagree

* 21. From the following COVID vaccines in phase 3 trials, which do you know?

	I do not know this vaccine	I know about this vaccine
AstraZeneca: (OxfordUniversity: British/Swedish) Non-Replicating Viral Vector (chimpanzee adenovirus vectored vaccine (ChAdOx1 nCoV-19)	○	○
Johnson and Johnson (USA): (adenovirus type 26 vector Ad26.COV2-S)	○	○
Pfizer RNA (BNT162b2 (USA): nucleoside-modified messenger RNA modRNA)	○	○
Novavax (USA): protein subunit (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M)	○	○
Moderna RNA (USA): mRNA-1273	○	○
CanSino (China) (Adenovirus type 5)	○	○
Gamaleya (Russia): Sputnik V non replicating viral vector Adenovirus	○	○

* 22. From the following COVID vaccines in phase 3 trials, how likely would you accept each one:

	I will never accept to take	Not sure	Surely I will accept
AstraZeneca: (OxfordUniversity: British/Swedish) Non-Replicating Viral Vector (chimpanzee adenovirus vectored vaccine (ChAdOx1 nCoV-19)	○	○	○
Johnson and Johnson (USA): (adenovirus type 26 vector Ad26.COV2-S)	○	○	○
Pfizer RNA (BNT162b2 (USA): nucleoside-modified messenger RNA modRNA)	○	○	○
Novavax (USA): protein subunit (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M)	○	○	○
Moderna RNA (USA): mRNA-1273	○	○	○
CanSino (China) (Adenovirus type 5)	○	○	○
Gamaleya (Russia): Sputnik V non replicating viral vector Adenovirus	○	○	○

* 23. What factors affected your choice your answer to the above question?

- ☐ This COVID vaccine(s) seem more efficient on preventing the infection
- ☐ Vaccine availability
- ☐ Company's reputation
- ☐ Manufacturing country
- ☐ Possibliy lessor side effects from this vaccine
- ☐ from the Media coverage
- ☐ Personal preferance
- ☐ Other (please specify)

COVID-19 Vacciantion perceptions of HCWs

Changes after Corona (MERS)

Please Choose Your Answers then Press "Next"

* 24. What is/are your usual source(s) of information about COVID vaccine? (Check all that apply)

- [ ] Hospital announcements (e.g. roll-ups or newsletters)
- [ ] Official statements or press release from MOH (e.g. through SMS or newspapers)
- [ ] MOH website
- [ ] WHO website
- [ ] CDC Website
- [ ] Other internet resources
- [ ] Social Networks (like YouTube, Facebook, Twitter, WhatsApp)

COVID-19 Vacciantion perceptions of HCWs

* 25. On a scale from 1 to 5, please rate how much worry you experienced over the past 2 weeks about contracting COVID19 Infection yourself:

1- Not worried at all	2- Little worried	3- Somewhat worried	4- Very worried	5- Extremely worried
○	○	○	○	○

* 26. On a scale from 1 to 5, please rate how much worry you experienced over the past 2 weeks about transmitting the COVID19 Infection to your family:

1- Not worried at all	2- Little worried	3- Somewhat worried	4- Very worried	5- Extremely worried
○	○	○	○	○

* 27. Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	○	○	○	○
Not being able to stop or control worrying	○	○	○	○
Worrying too much about different things	○	○	○	○
Trouble relaxing	○	○	○	○
Being so restless that it is hard to sit still	○	○	○	○
Becoming easily annoyed or irritable	○	○	○	○
Feeling afraid as if something awful might happen	○	○	○	○

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	7-8
Outcome data	15*	Report numbers of outcome events or summary measures over time	9

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7-9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.