PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Adenovirus and RNA-based COVID-19 vaccines' perceptions and acceptance among healthcare workers in Saudi Arabia: A national survey
AUTHORS	Temsah, Mohamad-Hani; Barry, Mazin; Aljamaan, Fadi; Alhuzaimi, Abdullah; Al-Eyadhy, Ayman; Saddik, Basema; Alrabiaah, Abdulkarim; Alsohime, Fahad; Alhaboob, Ali; Alhasan, Khalid; Alaraj, Ali; Halwani, Rabih; Alamro, Nurah; Al-Shahrani, Fatimah S; Jamal, Amr; Alsubaie, Sarah; Memish, Ziad; Al-Tawfiq, Jaffar

VERSION 1 – REVIEW

REVIEWER	Sallam, Malik The University of Jordan
REVIEW RETURNED	12-Feb-2021

GENERAL COMMENTS	In the current study, Mohamad-Hani Temsah et al. investigated a timely and important topic, namely COVID-19 vaccine hesitancy among health-care workers (HCWs) in Saudi Arabia, which is one of the largest countries in the Middle East. The authors investigated the attitude of HCWs towards different vaccine formulas (adenovirus-based vs. RNA-based vaccines) using a survey of more than 1500 participants. Three points specifically show the significance of this study; (1) A few studies in the Middle East and North Africa showed the high prevalence of vaccine hesitancy in the region among the general public and the healthcare workers, with more studies needed to confirm these findings (https://www.medrxiv.org/content/10.1101/2021.01.11.21249324v1); (https://www.mdpi.com/2076-393X/9/1/42), (2) the discussions in different media platforms regarding reluctance to get COVID-19 vaccines for some type (particularly for RNA-based vaccines) shows that importance of further analysis of such an attitude, and (3) the frontline position of healthcare workers in the fight against this unprecedented pandemic and the importance of assessing their attitude towards vaccination to prevent the disease. Thus, I recommend accepting the manuscript following the clarification of a few issues by the authors: 1. It appears that the language of the questionnaire was English, but the authors are advised to state that clearly 2. The authors mentioned that 2007 individuals agreed to participate, and 1512 individuals were included in final analysis. The authors are recommended to explain the reason behind excluding 495 submitted responses from final analysis 3. In Table 1, can you please provide a clarification in the footnote of the table for what "Other healthcare provider" entails specifically? 4. The authors are recommended to submit the survey as a supplementary file to allow a clear view of the items used in the

	study 5. Figure 2 needs further clarification, since it appears that it shows the proportions for each single response (e.g. for the Sure answer it appears that the response did not show a significant change before and after the announcement) 6. The authors can include additional references addressing vaccine hesitancy in the Middle East region

REVIEWER	Lennon, Robert P Penn State College of Medicine, Family and Community Medicine
REVIEW RETURNED	04-Mar-2021

GENERAL COMMENTS	This is an outstanding paper, and an important contribution. The minor revision is to amend your methods statement and limitations to reflect that because you used social media to promote your survey, you cannot identify the response rate. That is not a problem for publication - the work is valuable and novel. For clarity, please put quotations around survey items in the text (see details below.) Other considerations, and specifics re: above are listed below for consideration. Very well done, a pleasure to read, and a timely contribution as we seek to understand and overcome healthcare worker vaccine hesitancy. Comments, BMJ HCW vaccine confidence Reference 26 is from 2011. It may be worth commenting that this phenomenon has been seen in COVID-19 vaccine hesitancy. https://doi.org/10.1101/2020.12.11.20235838 Results line 39-42 You state that this was a convenience sample promoted on social media, but also state that 2079 HCW were invited. Usually with snowball techniques promoting on social media, you can't know for certain how many HCW were "invited" because many could have seen it on social media even if not directly invited. This prevents you from giving a response rate – you know that 2007 HCW responded, but you can't say that's 96.5%, because you don't know how many HCW actually had the opportunity to complete the survey. Unless you know for certain that no HCW answered the survey without singular invitation, this should be reworded to reflect this. "A total of 2007 HCWs agreed to participate, and 1512 participants (75.3%) completed the survey and were included in the analysis." For snowball sampling like this, it is OK that you don't know true response rate; the completion rate serves as a proxy, and the demographics of respondents demonstrate where generalizability will be stronger or weaker. Table 1 – you might tighten this; you can report a single column with the heading "N (%)" or "No. (%)" and combine columns 2 and 3. You can also shorten the width of column 1; if you halve the width, you'll have two lines that double up, but it will be much easier to read, because there will be much less "white space" between the variable and the number. Same for Table 3, 4 Page 11 line 10-22. Put specific survey items in single or double quotes for clarity. I.e., "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)."

	Use of “Sure”. If you used “sure” in the survey, it is appropriate to use it. The challenge with “sure” in English is that it’s meaning is “certain”, but in common usage it is a non-committal answer. I.e., if asked, “Do you want to go to the movies”, an answer of “Sure” means “I would go, but I’d be ok not going.” If “Sure” was used in your survey, not a problem, but going forward, please consider using “Certain.” Page 13, line 19; was gender different by weight of representation? If far more nurses are women than men, and far more respondents were nurses than doctors, then the fact that doctors knew more than nurses may be behind the apparent gender difference. If your sample size is robust enough, it is worth looking at gender splits within subcategories (age, level of training, etc.) rather than on the whole sample to avoid this confounder. Page 14, line 34. You have double-tabbed the first indentation. Page 16, lines 9-16: it is incredible that only 4% of respondents indicated that trust was a factor in accepting a COVID-19 vaccine. This is quite different when compared to the US (general population), in which trust and perceptions of local COVID-19 vaccination norms were the strongest predictors of COVID-19 vaccine acceptance. doi: https://doi.org/10.1101/2020.12.11.20235838. It may be worth commenting on why trust may be less of an issue in your population; is it that HCW understand vaccine development, and so have greater confidence in them? Or is it that citizens of Saudi Arabia have more confidence in their systems (i.e., Government) compared to places like the US, where trust in government and healthcare agencies is low and getting lower. https://www.kff.org/coronavirus-covid-19/report/kff-health-tracking-poll-september-2020/ Page 16, line 14, you have, “. . . with acceptance of COVID-19, . . .” consider, “. . . with acceptance of a COVID-19 vaccine, . . .” Page 16 lines 17-19. This is remarkable, and different than HCW information sources reported during COVID-19 in US HCW. DOI: 10.1177/0890117120982416 (Compare your Table 4 to that study’s Table 2). It is worth commenting on this difference, particularly in light of the link between information sources and knowledge that you review (Alsubaie’s work.) The difference suggests that HCW 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. (Assumptions that social media use for information leads to poor information may not generalize to Saudi Arabia, where HCW use social media and have high knowledge.) Page 16, lines 31-43. It may be interesting to compare knowledge about vaccines by level of training – doctor versus nurse versus other healthcare worker. You mention this in results, page 13, lines 21-23. In the US, general COVID-19 knowledge among physicians has been higher than other HCW, but non-physicians who work in healthcare did not have greater knowledge than general public. DOI: 10.1177/0890117120982416 Page 17, limitations. After the first sentence of limitations, you can add, “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." Other things to consider in a revision are listed below.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Malik Sallam, The University of Jordan

Comments to the Author:

In the current study, Mohamad-Hani Temsah et al. investigated a timely and important topic, namely COVID-19 vaccine hesitancy among health-care workers (HCWs) in Saudi Arabia, which is one of the largest countries in the Middle East. The authors investigated the attitude of HCWs towards different vaccine formulas (adenovirus-based vs. RNA-based vaccines) using a survey of more than 1500 participants.

Three points specifically show the significance of this study; (1) A few studies in the Middle East and North Africa showed the high prevalence of vaccine hesitancy in the region among the general public and the healthcare workers, with more studies needed to confirm these findings (https://www.medrxiv.org/content/10.1101/2021.01.11.21249324v1); (https://www.mdpi.com/2076-393X/9/1/42)Mazin/Fatimah, (2) the discussions in different media platforms regarding reluctance to get COVID-19 vaccines for some type (particularly for RNA-based vaccines) shows that importance of further analysis of such an attitude, and (3) the frontline position of healthcare workers in the fight against this unprecedented pandemic and the importance of assessing their attitude towards vaccination to prevent the disease.

Thus, I recommend accepting the manuscript following the clarification of a few issues by the authors:

1. It appears that the language of the questionnaire was English, but the authors are advised to state that clearly Hani

Reply: Thanks for your valuable suggestion, added in the revised manuscript for clarity.

2. The authors mentioned that 2007 individuals agreed to participate, and 1512 individuals were included in final analysis. The authors are recommended to explain the reason behind excluding 495 submitted responses from final analysis

Reply: Thank you for question. The 495 did not complete the survey and their survey's responses were very deficient and were not fit for analysis. We added the following statement in the results to explain "Almost quarter of respondents did not complete the survey, and therefore were excluded from analysis."

3. In Table 1, can you please provide a clarification in the footnote of the table for what "Other healthcare provider" entails specifically?

Reply: Thanks for you suggestion, the details in the footnote were added.

4. The authors are recommended to submit the survey as a supplementary file to allow a clear view of the items used in the study Hani

Reply: Thanks, added as Appendix 1.

5. Figure 2 needs further clarification, since it appears that it shows the proportions for each single response (e.g. for the Sure answer it appears that the response did not show a significant change before and after the announcement):

Reply: Thank you for your valid suggestion. We adjusted figure 2 to represent the change of HCW decision toward taking the BNT162b vaccine before and after the Pfizer announcement. In addition, we added the following statement to the result section to comment about the findings " 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 announcement (Fig 2)"

6. The authors can include additional references addressing vaccine hesitancy in the Middle East region:

Reply: Thank you for the suggestion and we had included additional references:

"During the H1N1 pandemic, 50 of 161 healthcare workers (31.1%) were willing to take the 2009 H1N1 vaccine (Al-Tawfiq JA. Willingness of health care workers of various nationalities to accept H1N1 (2009) pandemic influenza A vaccination. Ann Saudi Med. Jan-Feb 2012;32(1):64-7. doi: 10.5144/0256-4947.2012.64).).In a cross-sectional survey conducted in Riyadh in 2019 on influenza vaccine, results showed an acceptance rate of 71% with hesitancy atributed to concerns on adverse events in 50% of participants. 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%. (Sallam, M.; Dababseh, D.; Eid, H.; Al-Mahzoum, K.; Al-Haidar, A.; Taim, D.; Yaseen, A.; Ababneh, N.A.; Bakri, F.G.; Mahafzah, A. High rates of COVID-19 vaccine hesitancy and its association with conspiracy beliefs: A study in Jordan and Kuwait among other Arab countries. Vaccines 2021, 9, 42) (Salali, G.D.; Uysal, M.S. COVID-19 vaccine hesitancy is associated with beliefs on the origin of the novel coronavirus in the UK and Turkey. Psychol. Med. 2020, 1–3.) (Al-Mohaithef, M.; Padhi, B.K. Determinants of COVID-19 Vaccine Acceptance in Saudi Arabia: A Web-Based National Survey. J. Multidiscip. Healthc. 2020, 13, 1657–1663)."

Reviewer: 2

Dr. Robert P Lennon, Penn State College of Medicine

Comments to the Author:

This is an outstanding paper, and an important contribution.

The minor revision is to amend your methods statement and limitations to reflect that because you used social media to promote your survey, you cannot identify the response rate. That is not a problem for publication - the work is valuable and novel. For clarity, please put quotations around survey items in the text (see details below.)

Reply: Thanks for your comments and review, all suggestions were addressed as below.

Other considerations, and specifics re: above are listed below for consideration. Very well done, a pleasure to read, and a timely contribution as we seek to understand and overcome healthcare worker vaccine hesitancy.

Comments, BMJ HCW vaccine confidence

Reference 26 is from 2011. It may be worth commenting that this phenomenon has been seen in COVID-19 vaccine hesitancy. https://doi.org/10.1101/2020.12.11.20235838 Mazin/Fatimah

Reply: Thanks for your comments and this was added as well.

Results line 39-42

You state that this was a convenience sample promoted on social media, but also state that 2079 HCW were invited. Usually with snowball techniques promoting on social media, you can't know for certain how many HCW were "invited" because many could have seen it on social media even if not directly invited. This prevents you from giving a response rate – you know that 2007 HCW responded, but you can't say that's 96.5%, because you don't know how many HCW actually had the opportunity to complete the survey. Unless you know for certain that no HCW answered the survey without singular invitation, this should be reworded to reflect this. "A total of 2007 HCWs agreed to participate, and 1512 participants (75.3%) completed the survey and were included in the analysis." For snowball sampling like this, it is OK that you don't know true response rate; the completion rate serves as a proxy, and the demographics of respondents demonstrate where generalizability will be stronger or weaker.

Reply: Thank you for your valuable feedback. Although we sent this survey to 2079 HCWs using their email , social media accounts (such as WhatsApp) but it is possible that the survey propagated to a bigger sample. We agree with reviewer the response rate is inaccurate. Therefore, we changed the stated results as advised by reviewer.

Table 1 – you might tighten this; you can report a single column with the heading "N (%)" or "No. (%)" and combine columns 2 and 3. You can also shorten the width of column 1; if you halve the width, you'll have two lines that double up, but it will be much easier to read, because there will be much less "white space" between the variable and the number. Same for Table 3, 4

Reply: Thank you for your valuable input. The tables were adjusted as advised.

Page 11 line 10-22. Put specific survey items in single or double quotes for clarity. I.e., "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)."

Reply: Thanks, added for clarity of the paragraph as per your valuable suggestion.

Use of "Sure". If you used "sure" in the survey, it is appropriate to use it. The challenge with "sure" in English is that it's meaning is "certain", but in common usage it is a non-committal answer. I.e., if asked, "Do you want to go to the movies", an answer of "Sure" means "I would go, but I'd be ok not going." If "Sure" was used in your survey, not a problem, but going forward, please consider using "Certain."

Reply: Thank you for your comment. We asked as "sure" in the survey (Appendix 1) to examine the acceptance approach among the professional HCWs, and we do believe it reflects their actual certainty level.

Page 13, line 19; was gender different by weight of representation? If far more nurses are women than men, and far more respondents were nurses than doctors, then the fact that doctors knew more than nurses may be behind the apparent gender difference. If your sample size is robust enough, it is

worth looking at gender splits within subcategories (age, level of training, etc.) rather than on the whole sample to avoid this confounder.

Reply: Most of nurses were female and most of physicians were males. However, in our generalized linear regression model we tested the interaction effect of gender and job on the main outcome and effect was not significant. Therefore, to avoid adding complexity in the analysis model the interaction effect was dismissed.

Page 14, line 34. You have double-tabbed the first indentation. Hani

Reply: Thanks for the notion, and this was corrected.

Page 16, lines 9-16: it is incredible that only 4% of respondents indicated that trust was a factor in accepting a COVID-19 vaccine. This is quite different when compared to the US (general population), in which trust and perceptions of local COVID-19 vaccination norms were the strongest predictors of COVID-19 vaccine acceptance. doi: https://doi.org/10.1101/2020.12.11.20235838. It may be worth commenting on why trust may be less of an issue in your population; is it that HCW understand vaccine development, and so have greater confidence in them? Or is it that citizens of Saudi Arabia have more confidence in their systems (i.e., Government) compared to places like the US, where trust in government and healthcare agencies is low and getting lower. https://www.kff.org/coronavirus-covid-19/report/kff-health-tracking-poll-september-2020/

Reply: thank you for the comments and we amended the discussion with these points and references:

"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. The difference might be the fact that our study included only HCWs who may have better understanding of the disease and the vaccination."

Page 16, line 14, you have, ". . . with acceptance of COVID-19, . . ." consider, ". . . with acceptance of a COVID-19 vaccine, . . ."

Reply: thank you. This was corrected.

Page 16 lines 17-19. This is remarkable, and different than HCW information sources reported during COVID-19 in US HCW. DOI: 10.1177/0890117120982416 (Compare your Table 4 to that study's Table 2). It is worth commenting on this difference, particularly in light of the link between information sources and knowledge that you review (Alsubaie's work.) The difference suggests that HCW 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. (Assumptions that social media use for information leads to poor information may not generalize to Saudi Arabia, where HCW use social media and have high knowledge.)

Reply: Thank you for the suggestion. We amended the discussion as follows:

In the case of the general public, the source of knowledge and information about COVID-19 was official government social media and Twitter. 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. These findings suggest that HCW 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.

Page 16, lines 31-43. It may be interesting to compare knowledge about vaccines by level of training – doctor versus nurse versus other healthcare worker. You mention this in results, page 13, lines 21-23. In the US, general COVID-19 knowledge among physicians has been higher than other HCW, but non-physicians who work in healthcare did not have greater knowledge than general public. DOI: 10.1177/0890117120982416

Reply: Thank you for the valuable suggestions. We added the following in the discussion:

"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). 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."

Page 17, limitations. After the first sentence of limitations, you can add, "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."

Reply: Thanks for the valuable advice. We added: "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."

Other things to consider in a revision are listed below.

VERSION 2 – REVIEW

REVIEWER	Sallam, Malik The University of Jordan
REVIEW RETURNED	16-May-2021

GENERAL COMMENTS	Thanks for addressing all the previous points raised during the first round of peer-review

REVIEWER	Lennon, Robert P Penn State College of Medicine, Family and Community Medicine
REVIEW RETURNED	10-May-2021

GENERAL COMMENTS	Very well done. In the version I see, the references in the Introduction are roman numeral, inline with text; starting in Methods they are superscript - may help editors to make them uniform. Page 8, line 7, "Even being weaponed . . . ". The nearest English equivalent is armed, "Even being armed . . .", however, I recommend avoiding militaristic terminology, and changing to, "Even being equipped . . ." Page 8, line 32. Most numbers larger than 999 are given without a comma, i.e., "6101"; here you use a comma, "360,690". Unless editors prefer this for very large numbers, recommend consistency. Again, very well done, and an important contribution. Thank you!