PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Why do people consent to receiving SARS-CoV2 vaccinations? A Representative Survey in Germany</th>
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</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Walach, Harald; Ofner, Michael; Ruof, Viviane; Herbig, Markus; Klement, Rainer</td>
</tr>
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</table>

VERSION 1 – REVIEW

| REVIEWER | Nash, Denis  
|          | City University of New York System, Epidemiology and Biostatistics  
|          | I have a research grant from Pfizer to study the influence of vaccination on long COVID. |
| REVIEW RETURNED | 09-Mar-2022 |

GENERAL COMMENTS

This cross sectional study attempted to assess reasons for vaccination and vaccine hesitancy in an online sample of 1000 people from a 30 thousand person panel of German residents.

The article includes many statements and claims that are either not relevant to the study at hand (the introduction) or not supported by the data collected and analyzed (discussion and conclusions). And there are some inaccurate and misleading statements about SARS-CoV-2 vaccine efficacy and side effects. Such statements are not supported by the totality of the scientific literature.

The introduction includes several paragraphs with detailed information about the molecular behavior and immunology of mRNA vaccines that are not germane to the research question of vaccine hesitancy and methodology. This section should be focused on the vast global literature, including all over Europe, on SARS-CoV-2 vaccine behaviors, including vaccine hesitancy.

There are statements in the introduction regarding the lack of efficacy/effectiveness of SARS-CoV-2 mRNA vaccines against severe disease and death against variants and over time. These claims are immaculate and misleading. The authors clearly have not taken a comprehensive view of the literature.

The authors conclusions that vaccine hesitancy/resistance ‘can only be overcome by careful and active long-term efficacy and safety monitoring’ are not supported by the data that they have analyzed. Moreover, their conclusion and discussion does not account for the fact that even the most definitive and conclusive evidence on safety and efficacy will be countered and distorted by disinformation efforts and campaigns, which is a major and interesting omission.

| REVIEWER | Kampf, Günter |

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GENERAL COMMENTS

Introduction, lines 6 - 13: The authors describe different motivations for vaccination. They may consider to distinguish between a medical indication (e.g. prevention of severe or fatal disease) and a social indication (participation in social life) which per se should not be an indication for a medical treatment.

Introduction, line 15: „safety problems“ is not a suitable term. Please be more specific / scientific.

Introduction, line 17: „Vaccination“ is not approved, „vaccines“ are approved. In addition: none of the vaccines is „approved“, they are all „conditionally approved“. Please use the correct wording.

Introduction, line 17: Please provide at least one example of a red hand letter per vaccine and the reason for its publication including the appropriate references.

Introduction, line 25: To my knowledge the spike protein is not an ingredient of any mRNA vaccine. Please review and revise.

Introduction, line 40: was LNP detected in the organs or was LNP AND mRNA detected? To my knowledge it was only LNP. Please review and revise, if it requires correction.

Introduction, general: I consider the various aspects on the pathophysiology of side effects not necessary to be explained in detail. It could be shortened substantially as the topic is motivations in favor and against vaccination.

Method, line 31: What is the rationale to describe the survey as „representative“?

Tables 2 and 3: Please align the reasons consistently with a decreasing percentage in the first rank.

Table 4 is difficult to read. I suggest to present only the positive and negative effects (all with only YES answers) whereas the other topics may well be described in words. Difficult to understand that more of the vaccinated are convinced to protect others than themselves.

Table 5: I find it difficult to have different scales in a table. Please revise to have only one scale, the other information may be described in words.

Table 6: Abbreviations must be explained.

Discussion, lines 37 – 46: consider to use new data until December 31, 2021.

Discussion, line 50 – 51: The reference describes symptomatic cases, not all cases. Please review and revise.

Discussion, under-reporting: You may consider to add a meta-analysis as an additional reference (10.2165/00002018-200629050-00003).

Observation, lines 53-58: please us a more appropriate wording (propaganda noise pro vaccination).

Observation, lines 60 – 8: This is not correct. The VE is usually described for symptomatic cases, it may also be described for severe cases (e.g. emergency admission, ICU treatment) and it may be described for fatal cases. Epidemiological data from Germany and the UK indicate a protective effect for severe and fatal cases. The effect is waning with the omicron variant. Please revise.

Discussion: I am missing the value of a former COVID-19 disease leading to natural immunity which has been shown to be at least as effective as vaccination. This should be added as some unvaccinated participants mentioned this as a reason.
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<td>I would rather underplay the representativeness of the study. The participants may have been a rather specific population of half-professional respondents, and there are some indices that they might differ from the general population. The authors discuss the fact that the participants reported an unusually high percentage of vaccine complications, which would correspond to an under-reporting factor (URF) of 100. This is a very high estimate, but because exact estimation of the URF is very difficult, I can accept that even URF=100 is possible. There are, however, other numbers that appear to be very high, e.g., 21.5% of the unvaccinated have ever been infected with SARS-CoV-2, and 17% (i.e., almost 80% of the infected!) have had Covid, while we know that many Covid infections usually get asymptomatic. Moreover, 2.2% of the unvaccinated (i.e., every tenth of the infected) had to be hospitalized.</td>
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<td>While the group of the unvaccinated is rather small, the group of the vaccinated is large enough to perform an additional analysis: What are the differences between those who were vaccinated because of the fear of the disease and those who were vaccinated because of social pressure? The two motives are so much different that the corresponding persons can hardly be regarded as one homogenous group. Were there differences in age, gender, education level?</td>
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"marginal absolute risk reduction of 0.025% only". The statement is unclear without specification, e.g., risk reduction against what: asymptomatic infection, mild illness, severe illness, etc. Furthermore, a problem of ARR is that there is no standard of "good" or "poor" numbers. Generally in rare diseases (and severe Covid is a rare disease), ARR under 1% is not an exception. If the authors insist to mention this point, I would recommend a comparison with natural immunity against Covid whose ARR is distinctly higher as compared with the ARR after vaccination (e.g., Sheehan MM, et al. Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study; Kim P, et al. Duration of Severe Acute Respiratory Syndrome Coronavirus 2 Natural Immunity and Protection Against the Delta Variant: A Retrospective Cohort Study; Gazit S, et al. Comparing SARS-CoV-2 natural immunity to vaccine-induced immunity: reinfections versus breakthrough infections; Altarawneh H, et al. Protection afforded by prior infection against SARS-CoV-2 reinfection with the Omicron variant).

Similarly, unclear is the sentence in line 50-51: "This has been shown to be true for the delta variant…" What is "this": cytokine storm or antibody dependent enhancement? They are not synonymous. Has ADE been shown in vivo or in vitro? But the main question is, whether such matters should be discussed in the present article altogether, since they are only weakly related to the major topic. More relevant for the discussion are the data of other (partially similar) interviews, e.g., Schabus & Eigl, https://osf.io/35sa6.

As already said, these critical points do not change my generally very positive view on the paper. I hope the text can be improved and presented to the readership of the journal.

VERSIO 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Denis Nash, City University of New York System
Comments to the Author:
This cross sectional study attempted to assess reasons for vaccination and vaccine hesitancy in an online sample of 1000 people from a 30 thousand person panel of German residents.

The article includes many statements and claims that are either not relevant to the study at hand (the introduction) or not supported by the data collected and analyzed (discussion and conclusions).

*****************************************************************************

************ We changed the introduction and discussion substantially. Specifically, we dropped all references to the molecular issues *******
*****************************************************************************

And there are some inaccurate and misleading statements about SARS-cov-2 vaccine efficacy and side effects. Such statements are not supported by the totality of the scientific literature.

*****************************************************************************

************ We beg to disagree, but we dropped some of the statements anyway. If we are talking about safety issues, then it is not important to take into account all studies, but those that are most
pertinent to safety issues. It could be the case that 20 studies support safety, while one very good study is devastating and killing any safety claim. This has been the case with Pandemrix, for instance. Hence, it is neither scientifically sound nor necessary to use all information, but only the pertinent one, and this we have done. *****************************************

The introduction includes several paragraphs with detailed information about the molecular behavior and immunology of mRNA vaccines that are not germane to the research question of vaccine hesitancy and methodology. This section should be focused on the vast global literature, including all over Europe, on SARS-CoV-2 vaccine behaviors, including vaccine hesitancy.

*********** We dropped these paragraphs and have included more literature on vaccine hesitancy ************************************+

There are statements in the introduction regarding the lack of efficacy/effectiveness of SARS-CoV-2 mRNA vaccines against severe disease and death against variants and over time. These claims are immaculate and misleading. The authors clearly have not taken a comprehensive view of the literature.

*********** We dropped those statements ********************************

The authors conclusions that vaccine hesitancy/resistance 'can only be overcome by careful and active long-term efficacy and safety monitoring' are not supported by the data that they have analyzed. Moreover, their conclusion and discussion does not account for the fact that even the most definitive and conclusive evidence on safety and efficacy will be countered and distorted by disinformation efforts and campaigns, which is a major and interesting omission.

*********** We have dropped this. We would say that the statement that the "most definite and conclusive evidence on safety and efficacy will be countered and distorted by disinformation" is in fact a kind of conspiracy claim that presupposes that people are too stupid to read the scientific data and that political campaign groups will not be converted by data. This might be true. But it has not been proven, as no conclusive evidence exists. Hence, we think that this point needs not to be taken into account ****************************************

Reviewer: 2
Prof. Günter Kampf, Universität Greifswald

******* Thanks for a very diligent reading and commenting *******

Comments to the Author:
Introduction, lines 6 - 13: The authors describe different motivations for vaccination. They may consider to distinguish between a medical indication (e.g. prevention of severe or fatal disease) and a social indication (participation in social life) which per se should not be an indication for a medical treatment.

*********** we included this distinction ***********

Introduction, line 15: „safety problems“ is not a suitable term. Please be more specific / scientific.

*********** We have dropped these paragraphs in the intro; so the comment seems no longer relevant ***********

Introduction, line 17: „Vaccination“ is not approved, „vaccines“ are approved. In addition: none of the vaccines is „approved“, they are all „conditionally approved“. Please use the correct wording.
Introduction, line 17: Please provide at least one example of a red hand letter per vaccine and the reason for its publication including the appropriate references.
Introduction, line 25: To my knowledge the spike protein is not an ingredient of any mRNA vaccine. Please review and revise.
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Introduction, general: I consider the various aspects on the pathophysiology of side effects not necessary to be explained in detail. It could be shortened substantially as the topic is motivations in favor and against vaccination.

************ Thank you. We have dropped these paragraphs ************

Method, line 31: What is the rationale to describe the survey as „representative“?

************ We added information as to the variables that we used to achieve representativity

Tables 2 and 3: Please align the reasons consistently with a decreasing percentage in the first rank.

************ done *********************************

Table 4 is difficult to read. I suggest to present only the positive and negative effects (all with only YES answers) whereas the other topics may well be described in words.

************ We would like to leave it as it is, as describing figures in Words, is always less clear and less efficient than in tables

Difficult to understand that more of the vaccinated are convinced to protect others than themselves.

************ True, but these are the data; we refer to it in the Discussion

Table 5: I find it difficult to have different scales in a table. Please revise to have only one scale, the other information may be described in words.

************ In principle, this is true. But here we are talking about the frequency distribution of the items that form our Corona Orthodoxy Score with which we work further on. And these are the items in its format. Therefore, we would like to keep it as it is. It would not be helpful to describe part of the table in figures and the rest in words. ************

Table 6: Abbreviations must be explained.

************ done *********************************

Discussion, lines 37 – 46: consider to use new data until December 31, 2021.

************ We have included the most recent data of the RKI and a new reference to the RKI study ************

Discussion, line 50 – 51: The reference describes symptomatic cases, not all cases. Please review and revise.

************ done *********************************
Discussion, under-reporting: You may consider to add a meta-analysis as an additional reference (10.2165/00002018-200629050-00003).

************************ included ************************

Observation, lines 53-58: please us a more appropriate wording (propaganda noise pro vaccination).

************************ Well, we actually thought this was an accurate description, but changed it anyway ************************

Observation, lines 60 – 8: This is not correct. The VE is usually described for symptomatic cases, it may also be described for severe cases (e.g. emergency admission, ICU treatment) and it may be described for fatal cases. Epidemiological data from Germany and the UK indicate a protective effect for severe and fatal cases. The effect is waning with the omicron variant. Please revise.

************************ done and introduced some references ************************+

Discussion: I am missing the value of a former COVID-19 disease leading to natural immunity which has been shown to be at least as effective as vaccination. This should be added as some unvaccinated participants mentioned this as a reason.

************************ done ************************

Reviewer: 3
Dr. Boris Kotchoubey, Univ Tubingen
Comments to the Author:
The authors report highly interesting data about motivations of people who decide to be or not to be vaccinated against Covid-19 with novel, genetic-based substances. I am convinced that these data are of great importance for the readers and should be published. However, I am not very happy with the present version for the following reasons.

I would rather underplay the representativeness of the study. The participants may have been a rather specific population of half-professional respondents, and there are some indices that they might differ from the general population. The authors discuss the fact that the participants reported an unusually high percentage of vaccine complications, which would correspond to an under-reporting factor (URF) of 100. This is a very high estimate, but because exact estimation of the URF is very difficult, I can accept that even URF=100 is possible. There are, however, other numbers that appear to be very high, e.g., 21.5% of the unvaccinated have ever been infected with SARS-Cov-2, and 17% (i.e., almost 80% of the infected!) have had Covid, while we know that many Covid infections usually get asymptomatic. Moreover, 2.2% of the unvaccinated (i.e., every tenth of the infected) had to be hospitalized.

***********************************************************************
************* We have considered this and added several phrases qualifying the potential problems in various places ***************
***********************************************************************

Of course, I am fully aware of the fact that a discordance between the sample numbers and the official numbers of German statistics might result not only from the lack of representativeness but also from the unreliability of the official data, but this point can be discussed separately.

While the group of the unvaccinated is rather small, the group of the vaccinated is large enough to perform an additional analysis: What are the differences between those who were
vaccinated because of the fear of the disease and those who were vaccinated because of social pressure? The two motives are so much different that the corresponding persons can hardly be regarded as one homogenous group. Were there differences in age, gender, education level?

*************** Thanks for this suggestion. We have done another exploratory analysis which we now report ****************************

Another point deserving discussion is an apparent contradiction in reasons given by the vaccinated. On the one hand, many reported fear of Covid-19 as the main reason to be vaccinated, even though, as indicated by other data, they were to some degree aware of possible adverse events. On the other hand, twice as many respondents believe that the vaccine protects from infecting OTHERS than those who believe that it can protect THEMSELVES from being infected. This combination of results is strange.

************* This is indeed strange, and we have now pointed this out separately ****************************

A first glance hypothesis appears to be that many vaccinated individuals are zealous altruists whose fear to damage others' health is stronger than their fear to damage the own health, and who are even ready to sacrifice the own health in order to protect their fellow men. Another explanation, which I believe is more plausible, is that they are rather a socially adjusted group whose conformist behavior manifested itself in both readiness to accept the vaccine and their responses to interview items.

********* We took this up and added this ****************************

Another issue is that the Introduction appears to be much too general. It discusses many biological-molecular aspects of the vaccination, which are not the point of the article. In doing this, the authors leave several passages unclear to the reader, e.g., line 58: “marginal absolute risk reduction of 0.025% only”. The statement is unclear without specification, e.g., risk reduction against what: asymptomatic infection, mild illness, severe illness, etc. Furthermore, a problem of ARR is that there is no standard of “good” or “poor” numbers. Generally in rare diseases (and severe Covid is a rare disease), ARR under 1% is not an exception. If the authors insist to mention this point, I would recommend a comparison with natural immunity against Covid whose ARR is distinctly higher as compared with the ARR after vaccination (e.g., Sheehan MM, et al. Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study; Kim P, et al. Duration of Severe Acute Respiratory Syndrome Coronavirus 2 Natural Immunity and Protection Against the Delta Variant: A Retrospective Cohort Study; Gazit S, et al. Comparing SARS-CoV-2 natural immunity to vaccine-induced immunity: reinfections versus breakthrough infections; Altarawneh H, et al. Protection afforded by prior infection against SARS-CoV-2 reinfection with the Omicron variant).

********** We dropped all those passages due to other reviewers' suggestions ****************************

Similarly, unclear is the sentence in line 50-51: „This has been shown to be true for the delta variant...” What is “this”: cytokine storm or antibody dependent enhancement? They are not synonymous. Has ADE been shown in vivo or in vitro? But the main question is, whether such matters should be discussed in the present article altogether, since they are only weakly related to the major topic. More relevant for the discussion are the data of other (partially similar) interviews, e.g., Schabus & Eigl, https://osf.io/35sa6.

********** This passage has been dropped now ****************************

As already said, these critical points do not change my generally very positive view on the paper. I hope the text can be improved and presented to the readership of the journal.
VERSION 2 – REVIEW

REVIEWER | Kampf, Günter  
| Universitä Greifswald  
REVIEW RETURNED | 20-May-2022  

GENERAL COMMENTS | Many thanks for the careful revision. Only one aspect remains. In the new Table 4 the ranking of last line should be changed (decreasing percentage).

REVIEWER | Kotchoubey, Boris  
| Univ Tubingen  
REVIEW RETURNED | 24-May-2022  

GENERAL COMMENTS | Generally, the MS has been considerably improved as compared with the first version. The authors performed additional analyses and now report more data shedding light on the issue of the motivation of people deciding to get or not to get vaccinating. The only remaining issue is that I am not quite happy with the clarity of English. As I am not a native speaker either, I would not overplay this issue but, unfortunately, I am afraid that a few statements can just be misunderstood. For example, in the middle of p. 17 we read "Slightly more of those vaccinated, namely 5.8% described their health status after vaccination worse than before, while 4% said it was better". In the same paragraph, below: "Roughly 30% of our respondents felt better after the vaccination." This is bemusing, the reader wonders whether 4% or 30% felt better. When the authors clarify such positions, the MS can be accepted for publication WITHOUT an additional review.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2  
Prof. Günter Kampf, Universität Greifswald  
Comments to the Author:  
Many thanks for the careful revision. Only one aspect remains. In the new Table 4 the ranking of last line should be changed (decreasing percentage).

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Reviewer: 3  
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Generally, the MS has been considerably improved as compared with the first version. The authors performed additional analyses and now report more data shedding light on the issue of the motivation of people deciding to get or not to get vaccinating. The only remaining issue is that I am not quite happy with the clarity of English. As I am not a native speaker either, I would not overplay this issue but, unfortunately, I am afraid that a few statements can just be misunderstood. For example, in the middle of p. 17 we read "Slightly more of those vaccinated, namely 5.8% described their health status after vaccination worse than before, while 4% said it was better". In the same paragraph, below: "Roughly 30% of our respondents felt better after the vaccination."
This is bemusing, the reader wonders whether 4% or 30% felt better. When the authors clarify such positions, the MS can be accepted for publication WITHOUT an additional review.

************ done; we changed the wording and clarified that these figures were about different questions ************