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# Covid-19 vaccines: where are the data? - The BMJ

7-9 minutes

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Through press releases, three pharmaceutical companies recently announced the interim, positive results of their covid-19 vaccine candidates clinical trials. Firstly, Pfizer/BioNTech presented the initial results for their mRNA based BNT162b2 vaccine, which showed that it was 90% effective in preventing covid-19. [1] The vaccine was tested on 43,538 participants and, so far, there have been 94 confirmed cases. [2] They will submit to the US Food and Drug Administration (FDA) for approval when the safety profile has reached a pre-determined milestone. In the meantime, Pfizer has continued to market the vaccine.

Secondly, the Data Safety Monitoring Board, appointed by the National Institutes of Health (NIH) for the phase III study of the MODERNA mRNA-1273 vaccine candidate against covid-19, confirmed its trial met the statistical criteria pre-specified in the study protocol, with a vaccine efficacy of 94.5%. [3,4]

Thirdly, the University of Oxford and AstraZeneca, announced that their adenovirus-based vaccine ChAdOx1 nCoV-2019 was safe and also, in the preliminary findings of a peer-reviewed phase II/III trial, as triggering a seemingly encouraging immune response in older age groups included in the trial. [5] In a subsequent press

release, they reported that in the phase III trial of about 20,000 participants, the vaccine was around 70% efficacious. This week it has also transpired that some of the participants were, in error, given a first dose which was half of what was intended. These participants were all under the age of 55. Doubts have now been raised about how Oxford and Astra Zeneca have handled the release of their preliminary results, given the dosing error and what that could mean for the efficacy of the vaccine.

All these data for the different vaccines are potentially very promising, but none of the phase III trials have been published in peer reviewed journals or analysed by age group, gender and case description (asymptomatic, mild, severe), virus transmissibility after immunisation, or duration of protection.

As public health professionals, we believe that the results of clinical trials, whether interim or final, should be subject to an appropriate systematic process, and then published in peer-reviewed professional journals. Reporting the covid-19 vaccine trial results in press releases before publication in journals is neither good scientific practice nor does it help to build public trust in vaccines. If trial data for covid-19 candidate vaccines are prematurely announced, this may threaten the integrity and credibility of the trials. This could distort what should be a rigorous peer review process. [7] We believe that data and conclusions should not be released as credible before the scientific community can judge the validity of those claims by assessing a complete account of what was done. [8]

The process of reporting on the clinical trials and the concurrent marketing of the covid-19 vaccines also raises concerns about the basis on which the many candidate vaccines at advanced stages

of development can be assessed. Since companies are asking governments to place orders at an early stage, this raises a question about the minimum amount of data that companies should release publicly during the marketing process. [9]

It is crucial that the World Health Organisation, as a credible neutral body, should appoint a group of experts to compile an updated list of the current status of the clinical trials and to specify how to communicate the results. We believe that this should be within the WHO framework of The Access to COVID-19 Tools (ACT) Accelerator initiative. [10] This overview should identify all aspects of the vaccine production and the trial methodology. For example, production methods should specify all the ingredients including antigens, adjuvants, stabilisers, antibiotics and preservatives.

Companies should be encouraged to publish a paper with their trial design, methods and results in a peer-reviewed journal. And given that we should strive to publish these papers as rapidly as possible, journals should prioritise them, and ensure rigour and timeliness in their peer-review process.

The scientific publication should at least include the following:

- detailed study design
- method of recruiting participants
- sample size in total and by study arm.
- main characteristics of the study population including age, gender, ethnicity, health status and other key variables.
- detailed features of the vaccine
- storage requirements

- dose
- route of administration and schedule
- trial duration
- total accrual time
- loss to follow-up, as specified in the standard protocols for clinical trials investigating vaccines. [11]

  Safety and efficacy evaluation should identify the primary and secondary endpoints. Results need to be presented systematically, with precise statistical analyses and specification of the overall efficacy and sub-group efficacy (with confidence intervals), and adverse effects analyses by age group and sex. The authors also need to discuss the strengths and limitations of the trial. [12] There are other relevant questions that the company should discuss, such as the possible impact of carrying out the trial in a limited time. In addition, the authors must present the current understanding of the following:

- estimates of how long after immunisation it takes to be protected
- the estimated duration of protection
- whether vaccination will prevent transmission
- to what extent violations of the cold-chain affect the efficacy of the vaccine
- could there be atypical disease in vaccinated subjects.

  Governments, public health professionals and society as a whole must support fair and equitable access for every country. To help with the logistical and practical aspects of making this happen, all the information from the clinical trials must have incontrovertible

credibility. [13] In summary, with covid-19 vaccines there are reasons to be hopeful, but we need to address the concerns. [14] We strongly advocate for the need to define a standard protocol on what data must be released before a company starts to market its vaccine. This should be complemented with guidelines on how to compare the benefits of each new vaccine as it becomes available. We believe the WHO is best suited to coordinate such a process.

***Jose M Martin-Moreno*** *is professor of preventive medicine and public health at the Medical School and INCLIVA-Clinical Hospital, University of Valencia, Spain, and Honours' committee chair, Association of Schools of Public Health in the European region.*

***John Middleton*** *is honorary professor of public health, Wolverhampton University, and president of the Association of Schools of Public Health in the European region.*

***Mohamud Sheek-Hussein*** *is associate professor, Institute of Public Health, College of Medicine & Health Sciences, UAE University, Al-Ain, UAE.*

***Manfred S Green*** *is professor of epidemiology and public health, and head of the International MPH Program, School of Public Health, University of Haifa, Israel.*

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