The Development and Distribution of the COVID-19 Vaccine

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Recommended Reading from the Rutgers University Robert Wood Johnson Medical School Pulmonary and Critical Care Fellows; Sugeet Jagpal, M.D., Associate Program Director

Gbesemete D, *et al.* Exploring the Acceptability of Controlled Human Infection with SARSCoV-2—A Public Consultation. *BMC Med* (1)

Reviewed by Brian Chinai

Although some vaccine trial designs can take more than a decade to complete, the urgency of the pandemic has led researchers to consider controlled human infection studies (CHIs) (1–3). CHIs involve giving a strain of an infectious agent to selected volunteers to better understand disease processes and to aid the development of vaccines. Although the implementation of coronavirus disease (COVID-19) CHIs can potentially lead to answers regarding safety and efficacy, the ethical acceptability of this study design requires careful review.

In *BMC Medicine*, Gbesemete and colleagues conducted a focus group–based qualitative study incorporating 57 individuals to assess attitudes toward CHIs and acceptable prerequisites for enrollment (1). Overall, the focus groups were positive about CHIs and their potential benefits. Concerns included the lack of known efficacious treatment for planned intentional infection, personal anxiety about infection, psychological impact of isolation and quarantine, and the potential for transmission to loved ones. An important consideration included the communication of risk to potential volunteers and avoiding undue bias with financial compensation. Each of these issues will need to be carefully considered. The authors ultimately state that ongoing public consultation is key to performing a COVID-19 CHI.

After extensive debate, it has been determined that risk may be acceptable without an effective treatment, given that the chances of significant illness are quite low in certain subsets of the population that can be targeted for trial enrollment (1, 2, 4). In addition, attention is needed when considering recruitment of subjects in high-incidence areas where healthcare centers may be otherwise overburdened, potentially decreasing the ability of the research participant to get medical care if needed (4).

Because of its publication early in the course of the pandemic, this study does not consider the long-term sequelae of COVID-19, nor does it reflect the current state of vaccine availability. However, given the uncertainty regarding the long-term efficacy of the vaccines, CHIs will likely play a large role in further vaccine development in the future. Therefore, from a societal lens, justice would support COVID-19 CHIs, as they would allow for the fastest implementation of a tested vaccine to the largest number of individuals. The overall consensus is that CHIs are ethical, and it will be essential to gain public acceptance of this trial design and have ongoing public consultations such as the one done in this study throughout the process of running a CHI. ■

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Raifman MA and Raifman JR. Disparities in the Population at Risk of Severe Illness from COVID-19 by Race/Ethnicity and Income. *Am J Prev Med* (5)

Reviewed by Renuka Rajagopal

Healthcare disparities should inform resource allocation, particularly preventative care such as masking, feasibility of social distancing, feasibility of quarantine, and vaccine distribution during a pandemic. Raifman and Raifman discuss the increased risk of severe illness of COVID-19 in Black, American Indian, and Asian populations (5). The National Academy of Sciences, Engineering, and Medicine (NASEM) and the World Health Organization have called for a vaccination policy that mitigates the social and health disparities that result in the increased risk of severe illness noted in the previously mentioned populations.

NASEM has issued a framework for vaccine distribution, stating that vaccines should be rolled out in sequential phases and allocated according to priority groups (6). The CDC recommends using the NASEM framework as well as intentionally identifying vulnerable groups for prioritization. Attempts to identify vulnerable groups involves using indices that primarily combine economic and social factors, an area rife with controversy because of ambiguity and lack of consensus. The CDC recommends the social vulnerability index (SVI) to identify geographic areas that can be prioritized. The SVI includes several domains: social, language, racial, household composition, and access to transport. To use the SVI effectively, the relative contribution of each of the factors still needs to be determined. Previous epidemiological data demonstrate that vulnerable populations also have reduced vaccination access (7). Budgeting of the vaccine attempts to bridge this immunization gap (7).

Allocation based on SVI is very different from allocation based on age alone. Raifman and Raifman point out that lower-income households are at higher risk despite being younger than age 65 years, one of the currently used priority criteria (5). This brings to our attention that objective data based on the effects of COVID-19 in vulnerable populations should be used to guide vaccine distribution, and using criteria such as age alone paradoxically may widen disparities, as higher socioeconomic groups have longer lifespans. Public health agencies can mitigate the social and racial injustice by being thoughtful and data driven in vaccine distribution, and it is important for us as physicians to be aware of these public health endeavors so that we can endorse and explain them to all our patients. ■

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Dror AA, *et al.* Vaccine Hesitancy: The Next Challenge in the Fight against COVID-19. *Eur J Epidemiol* (8)

Reviewed by Joseph J. Lee

In addition to understanding clinical trial design choices and the factors that are part of fair allocation of vaccine, it is important for physicians to also understand vaccine hesitancy to participate in shared decision-making conversations with our patients and the public. Vaccine hesitancy is defined as a delay in acceptance or refusal of vaccination despite availability and access to vaccination services. In the following review, we describe the survey-based study by Dror and colleagues that sought to identify drivers for vaccine hesitancy (8).

Dror and colleagues surveyed 1,941 Israeli medical staff and members of the general population and found that self-preservation is a major motivator for vaccine acceptance (8). Self-preservation included economic concerns with return to work, avoidance of unemployment and sick time, and concerns for one's own health and well-being (8). This finding is supported by additional work, such as the survey by Malik and colleagues of 672 participants in the United States, which found that those who would accept the vaccine had a higher self-risk perception score (9). Self-preservation was also a motivating factor in 13,426 participants across 19 countries in a global survey (10).

Although it was not a direct question in these studies, high mortality and high cases per million population in any geographic region were both positive predictive variables for accepting a COVID-19 vaccine (9). Unfortunately, despite higher mortality rates, Black communities, lower socioeconomic class, and lower education levels all indicated more vaccine hesitancy than comparison groups in the United States (9). The communities with higher vaccine hesitancy had concerns for quality control, side effects, and associated COVID-19 illness.

Dror and colleagues also report that healthcare worker status, compared with the general population, surprisingly did not have a positive predictive value of acceptance (8). However, further analysis showed that healthcare workers with higher self-perceived risk, such as those working in COVID-19 units, had higher predictive values of acceptance (8). It is important for physicians to be aware of the level of nuance in vaccine decision making. Conversations with populations with higher rates of vaccine hesitancy need to be approached carefully and thoughtfully, and understanding the drivers for hesitancy elucidated by this article can help physicians with these conversations. ■

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