



# Meet the Challenges of Mass Vaccination against COVID-19

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## Abstract

As coronavirus disease 2019 (COVID-19) vaccines continue to be reviewed and approved by regulatory bodies for emergency use, mass vaccination against COVID-19 is on the horizon. This will significantly reduce the incidence and mortality of COVID-19. However, the unintended consequences of mass vaccination and their associated challenges could be urgent and severe. To effectively prepare for and meet these challenges, we propose three guiding principles and share cautionary perspectives on the mass vaccination against COVID-19. These opinions could help shape policy-making and the implementation of the mass vaccination.

Three coronavirus disease 2019 (COVID-19) vaccines have been reported to show >90% efficacy.<sup>1–3</sup> Two vaccines against COVID-19 have been approved for emergency use in the USA, and one vaccine has been approved in the UK.<sup>4–8</sup> The frameworks for the optimal allocation of COVID-19 vaccines have been well planned, and should satisfactorily address allocation issues.<sup>9,10</sup> However, the unintended consequences of mass vaccination and their associated challenges might be urgent and severe. They should be carefully prepared for and prevented. Here, we propose three guiding principles and share a cautionary perspective on mass vaccination.

Three principles are recommended for the effective conduct of mass vaccination against COVID-19, which include accountability, transparency, and immediacy. Accountability is required for effective governance, quality control, and root-cause analysis, which could identify the causes of any adverse events associated with the vaccination; transparency is required to reduce misinformation, build trust among stakeholders and increase vaccination rates; immediacy is required because of the rapidly changing vaccine development landscape (e.g., 9 days between the interim and final reports for a vaccine's efficacy),<sup>11</sup> and the rapidly increasing number of COVID-19 cases.

## A proposed action plan to meet the challenges of mass vaccination

First, actively monitor the efficacy and safety of the new vaccines

at local sites. As noted previously,<sup>12,13</sup> vaccine safety cannot be thoroughly assessed easily. In addition, stringent storage requirements mean that the vaccines are susceptible to degradation.<sup>13</sup> Given the unprecedented number of vaccinations required in a short time, local healthcare providers or authorities should keep track of or regular contact with vaccinated individuals about the vaccine's efficacy and safety. In addition, it is recommended that regular and appropriate communications among vaccine administration sites, regulators, and local health authorities. This will help to resolve any issue associated with a vaccine batch and lot numbers, which could be timely notified and systematically corrected.

Second, timely publish the full and in-depth data from the vaccine trials. As the regulatory bodies review the vaccine manufacturers' application for approval, the public and healthcare providers require this trial data, and regular updates on the additional trial results and postmarketing data (i.e., phase 4 trial), to make more informed decisions for the vaccination and laboratory tests.

Third, maintain the implementation of nonpharmaceutical interventions. Vaccine production might take 12–24 months to reach full capacity.<sup>14</sup> An additional 28 days might be required to complete the vaccination protocol for some vaccines.<sup>1,2</sup> Moreover, approximately 25% of the public would refuse the vaccination when it is available,<sup>15–17</sup> which is close to or lower than the vaccination rate (75–90%) required for herd immunity<sup>14</sup> and might cause delayed or unsuccessful herd immunity. Therefore, the development of herd immunity will probably require 13–25 months if successful at all, during which nonpharmaceutical interventions are required to control COVID-19. In addition, 5–10% of the vaccinated will not be protected as the trial data show.<sup>1,2,11</sup> Before understanding who will not be protected by the vaccine(s), nonpharmaceutical interventions probably should be implemented to protect this 5–10% of the vaccinated.

Fourth, prepare for a drug shortage owing to the mass production of COVID-19 vaccines. We anticipate that many manufacturing facilities will be rightfully allocated to mass vaccine production. Subsequently, these facilities cannot be used for their originally planned drug production, which could lead to a shortage of certain drugs. Pharmacies and healthcare providers should prepare for the possible shortage and seek alternative drugs for the continued care

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**Abbreviations:** COVID-19, coronavirus disease 2019; IgG, Immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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of the patients. However, no data or formal communication have been released for this. Therefore, we call for drug manufacturers to timely release the related information, and to optimize the allocation process; therefore, alternative drugs will be available.

Fifth, interpret the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serology results with caution. The ChAdOx1 nCoV-19 vaccine is effective in generating anti-spike SARS-CoV-2 Immunoglobulin G (IgG) in 90% of vaccinated individuals,<sup>1</sup> which could lead to positive results in the SARS-CoV-2 IgG test. However, unless the postvaccination IgG level is assessed in every vaccinated individual (not considering the test's false positivity), we cannot reliably distinguish a positive SARS-CoV-2 IgG result owing to vaccination versus the infection in a vaccinated individual that does not generate IgG and would not be protected. In addition, no data is currently available regarding the protective level of IgG. Therefore, caution must be used to interpret SARS-CoV-2 serology results regarding infection status, and the molecular testing of the SARS-CoV-2 virus in nasopharyngeal specimens should be used to examine infection status.

Sixth, be aware of the ineffectiveness of the vaccines. The vaccinated individuals might not have the required SARS-CoV-2 antibodies for several reasons: during the antibody generation window period (28 days for ChAdOx1 nCoV-19),<sup>1</sup> lack of efficacy (5–10% of the trial population),<sup>1–3</sup> possible decline in antibodies (12–18 months postvaccination),<sup>14</sup> and virus mutations.<sup>18</sup> Therefore, the vaccinated individuals will probably be protected against COVID-19, but could still be infected. Further, the immunogenicity data from the other two vaccine trials remain largely unknown.<sup>2,3</sup> Therefore, it is difficult to predict the possibility of infection in the individuals who have received these vaccines. Therefore, vaccinated individuals should remain cautious and maintain the use of nonpharmaceutical interventions.

Finally, maintain sufficient resources for COVID-19 patients, such as healthcare providers, medical equipment, and medical supplies. The mass vaccination could help control the COVID-19 pandemic, but there are already approximately 75 million COVID-19 cases in the world.<sup>19</sup> Therefore, it is probably warranted that the required resources for COVID-19 patients should be provided to reduce the COVID-19 mortality rate, in particular, when a large number of resources are allocated for mass vaccination.

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## Conflict of interest

ZC is an employee and owns stocks of Bristol Myers Squibb, Co. The spouse of LZ is an employee and owns stocks of Bristol Myers Squibb, Co.

## Author contributions

The two authors conceptualized, wrote, and edited the manuscript.

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