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Perspective

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Making sound public health policy decisions for COVID-19 vaccination

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As we surpass a year into the global pandemic triggered by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an efficacious vaccine has been our best bet for the mitigation of coronavirus disease 2019 (COVID-19). As early as the decipherment of the SARS-CoV-2 genome in January 2020,[1] the worldwide research has revolved around the development of vaccines yielding several promising options in hand. The next diligent step for universal control of the pandemic is to instigate a successful immunization program throughout the globe, which would hinge on the resolution of an array of challenges related to bulk manufacture, quality control, supply coordination, equitable distribution, compliance of dose and schedule, public health communication, implementation pace, record keeping, surveillance of coverage, safety and vaccine effectiveness and the continuation of non-pharmaceutical intervening practices. These meticulous yet vincible field challenges can be addressed by making sound public health policy decisions based on the comprehensive standards for vaccine distribution and dedicated monitoring of vaccine coverage and efficacy from the factory to the public doorsteps, i.e. the real-world battlefield (Figure 1). The in-field logistics of COVID-19 vaccine distribution, coverage and efficacy, including the roadblocks and resolution plans, have been delineated in the present discourse.

As per the estimates of the coalition of epidemic preparedness innovations (CEPI), the annual global vaccine manufacturing capacity ranges from 2 to 4 billion doses and, the manufacture of enough vaccines can be accomplished upto 2023–2024.[2] Although the manufacturing has been scaled up *via* initiation of parallel production at phase 2 or 3 as per the safety and efficacy data at hand and, by the strategic partnerships between several vaccine manufacturing firms; it needs to be emphasized that the quality should not be compromised at any stage as it can have a profound effect on the safety as well efficacy of COVID-19 vaccines. The vaccine quality compliance with the international standards of GxPs, the term which encompasses Good Clinical Practice, Good Manufacturing Practice and Good Laboratory Practice must be ensured.[3] The national regulatory authorities' stringency is also crucial and should be supplemented with the World Health Organization (WHO) pre-qualification approval, which in turn would entail consistent safety and efficacy throughout the globe wherever the vaccines are deployed.

The individual countries and organizations such as United Nations International Children's Emergency Fund (UNICEF) must ensure procurement arrangements based on accurate forecasting of demand and budget. Accordingly, vaccine manufacturing firms can maintain long-term supply with fair pricing while dealing with occasional fluctuations in demand and supply caused by quality control issues in the bulk product, cold-chain breakdown in delivery, imperfect prediction of demand, etc. Inspite of efforts to escalate the manufacturing capacity, the current *status quo* is that the global COVID-19 vaccine demand outruns the supply chains. With limited vaccines available amid the novel pandemic, the decisions about the allocation must be taken to balance the two primary goals targeted by vaccines, i.e. direct protection of vaccinated individuals from SARS-CoV-2 infection and severe disease and; decreased transmission providing indirect protection to unvaccinated ones through herd immunity.[4] Thus, the immunization approach may involve high-risk groups, i.e. people who are aged or have certain comorbidities and thus are at higher risk of severe disease or; the high-transmission groups, i.e. young people who are more likely to transmit SARS-CoV-2. Considering the initial vaccine shortage, an efficient prioritization strategy needs to be developed, segregating the different target groups by balancing the science and ethics; with a plan of expanded vaccination in the future, once the worldwide vaccine deficiency has been overcome.

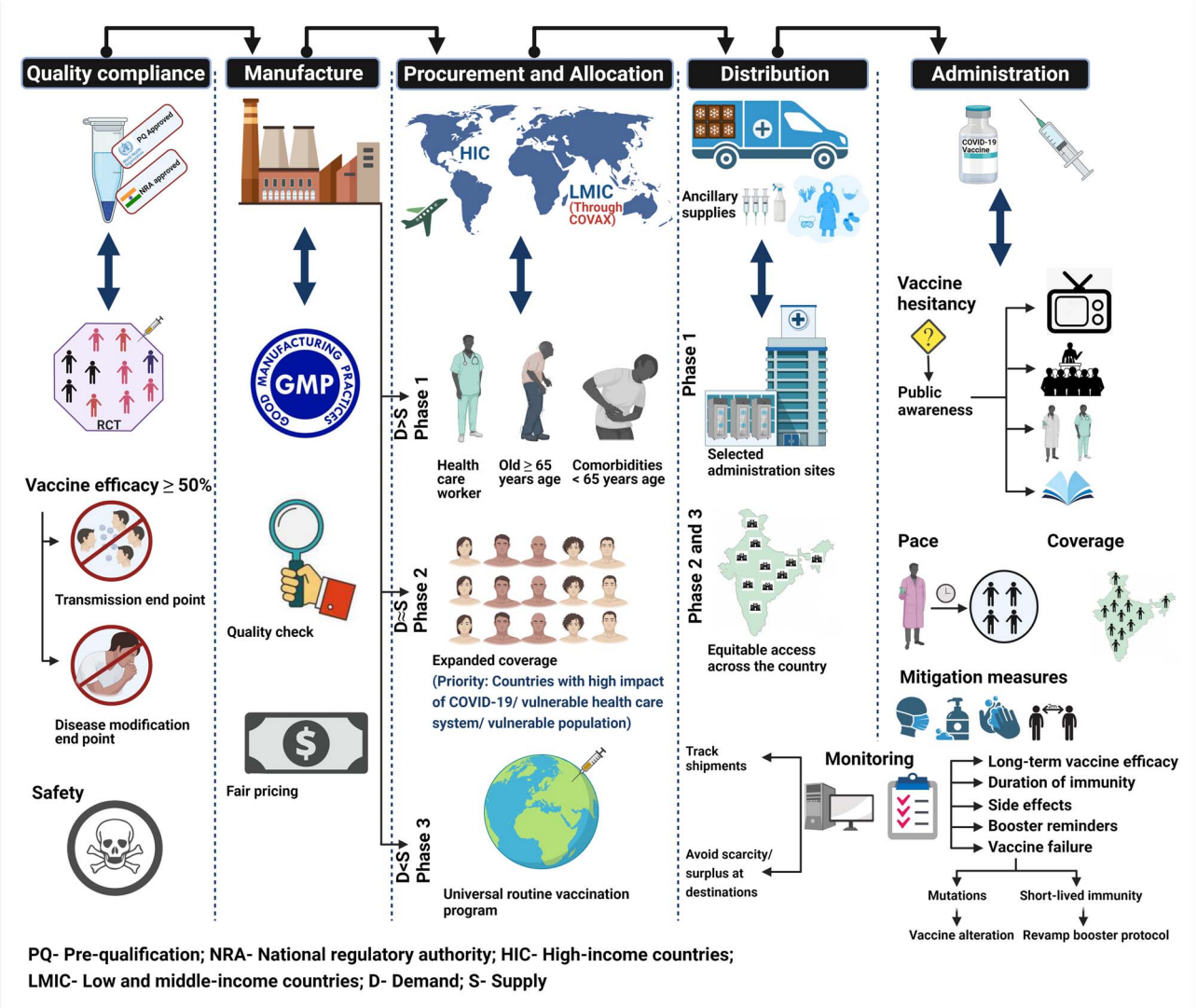

Figure 1. A comprehensive outline of the in-field logistics of COVID-19 vaccination.

As per the WHO Strategic Advisory Group of Experts on Immunization, the priority groups have been outlined, and phase-wise allocation has been recommended.[5] The prioritized groups include the health care workers and frontline responders, followed by people > 65 years old and people < 65 years old but suffering from underlying health conditions, putting them at a higher risk of severe disease and death. Many of the low and middle-income countries have become part of the COVID-19 vaccines global access (COVAX) facility so that procurement and equitable vaccine distribution can be ensured, covering 20% of their national populations in phase one. COVAX is especially relevant to cover the COVID-19 vaccine access gap due to bulk pre-order by high-income countries. It has been deduced from a modeling study that exclusive acquiring of the initial 2 billion doses by high-income countries regardless of vaccine equity could lead to doubling of deaths due to COVID-19.[6]

The second phase should expand the vaccine distribution and coverage as per the funds and dose availability. In case of persisting supply limitations, the countries with a high impact of COVID-19 as per the epidemiological data or those with vulnerable populations and health care systems should be prioritized. It could be expected that by the third phase of immunization, there would be a substantial supply throughout the globe, and universally available COVID-19 vaccines might be integrated into the routine vaccination programs. Once the implementation phases have been outlined, the challenges related to storage and distribution need to be addressed. The distribution plan must ensure the timely and controlled vaccine delivery from the manufacturing point up to all possible immunization endpoints while taking into account various factors such as the safety of the product, coordination of stakeholders, public acceptance and uptake and maximum coverage.

Many of the vaccines developed against COVID-19, especially the messenger RNA (mRNA) vaccines, have ultra cold-chain requirements (−70°C) during storage and transport, and such facilities may be lacking in some low to middle-income countries, which would greatly hamper the storage life and efficacy of vaccines. In such countries, vaccines requiring refrigerated storage at 2–8°C may be opted; but it should be ensured that refrigerators are specialized to maintain a consistent

temperature. The importance of efficient vaccine packaging in durable glass vials that can withstand extreme temperatures and global transportation risks should also be highlighted. Ancillary supplies such as syringes, needles, alcohol and personal protective equipment kits for healthcare staff should be secured in adequate quantity.

The efficient coordination of manufacturers, shipments and government agencies at the central, state and regional levels is an enormous challenge to ensure proper distribution within a country. It is essential to have centralized monitoring of vaccine distribution to properly track shipments and avoid scarcity or surplus in the intended destinations. Inconsistencies in the internet services and data storage infrastructure need to be overcome in the concerned countries so that the digital and technological pipelines can be efficiently streamlined.[7] Administration sites should be selected in the first phase to optimize the storage of vaccines as well as the ease of access for the target population and then expanded to include pharmacies, hospitals, community health centres, etc. to ensure equitable access across the country involving maximum healthcare professionals in rural and remote areas as well. The concealed factors such as political influences and vaccine hoarding should be strictly controlled.

Widespread public confidence in the approved vaccine products is essential to overcome the vaccine hesitancy due to the thought-provoking short span of vaccine development i.e. less than a year against the historic trend of more than a decade, apart from the concerns over the novelty of mRNA approach and misinformation circulated by anti-vaccination groups on unregulated social media.[8] Strategies must be enforced to motivate large masses for both initial and booster shots of the COVID-19 vaccine keeping in view the ethical standards as well as the need to overcome concerns over the safety and efficacy of vaccines so that high coverage can be achieved. Health care professionals and policymakers should communicate up-to-date and transparent information to the public through different means such as media, civil society organizations, social influencers, etc. The information provided should clarify the benefits and risks of COVID-19 vaccination apart from the details of eligibility, access points, registration process and post-vaccination care.[9] Reasonable costs and reimbursements are also vital to sustaining immunization within communities. Following the vaccine administration, immunization records need to be maintained religiously to monitor long-term vaccine efficacy, duration of vaccine-acquired immunity, side effects, vaccine failure and reminders for booster doses. Tracking of the vaccine failure is especially pertinent to identify immunologically relevant viral mutations as well as the undeciphered duration of immunity, which would serve as guidance for the need for vaccine alterations and revamped booster protocols. The record-keeping should be assisted with highly efficient software tools to ensure confidentiality and prevent data loss and spoofing.

The successful mitigation of the COVID-19 pandemic relies on the vaccination, not the vaccine. As per the Food and Drug Administration, a COVID-19 vaccine can be deduced to be effective if it has a minimum efficacy threshold of atleast 50% with a primary efficacy endpoint of transmission or disease modification.[10] The vaccine efficacy refers to the reduction in the risk of infection in the vaccinated individuals relative to that of the unvaccinated ones measured in Phase III randomized controlled trials. However, the real-world effectiveness depends on the interplay of vaccine efficacy and downstream implementation, including the vaccination pace and coverage. The manufacturing capacity and distribution logistics determine the pace, i.e. the percentage of population vaccinated on a given day, whereas the coverage, i.e. the percentage of ultimately vaccinated population, depends on the public willingness and vaccine availability.[11] Pace and coverage are complementary measures i.e. adequacy of one of them cannot compensate for another's insufficiency. The slow pace of vaccination can cause more COVID-19 cases and associated deaths apart from the risk of a longer epidemic; thus, high vaccine uptake is essential, which can be achieved through the increased manufacturing apart from the rapid and efficient transport, storage and distribution monitoring.

Since the herd immunity to SARS-CoV-2 is achievable only *via* vaccination, instead of the natural infection; the global efforts should be focused on implementing a vaccination program with a highly efficacious vaccine with efforts to achieve as high coverage as possible. Vaccines with even a high efficacy of 90% require 66% coverage to achieve herd immunity, while on the other end of the spectrum, the efficacy of 60% requires a practically impossible coverage of 100%.[12] Thus, the strategies should focus on higher efficacy vaccine and fast pace even if the population coverage is less because of the initial vaccine shortage and exclusion of children from the immunization protocols due to lack of trial data.

Apart from the factual considerations on the pace, coverage and efficacy, the final barricade to be overcome for an effective immunization program is controlling epidemic growth. The effective reproductive number of the virus (R_t) should be minimized at the time of vaccine deployment. Even a vaccine with high efficacy implemented with adequate pace and coverage will not substantially impact the epidemic control if the disease is highly infectious.[11] The major reductions in R_t are achievable through the continued public adherence to non-pharmaceutical interventions such as the use of proper facial masks, frequent hand washing, social distancing, provision of effective ventilation, etc.

The scientific and technological advances accentuated by the global cooperation in the wake of the COVID-19 pandemic have led to the fast-track development of an array of efficacious vaccines. However, the challenge which lies ahead is the control of real-world divergence of vaccine efficacy due to factors underlying the manufacture, storage, distribution and implementation. Thus, the ultimate triumph of vaccination program relies on the upscaled production, efficient framework of distribution logistics, escalation of implementation parameters including pace and coverage, compliance with the non-pharmaceutical mitigation measures in conjunction with the monitoring of infield efficacy, side effects and instances of vaccine failure which would serve as guidance for the adaptation of current vaccines and booster protocols in the future.

Authors' contributions

P.R. did the ideation, conceptualization, data curation, writing original draft, reviewing and editing. O.P.C. executed the

conceptualization, writing original draft, reviewing and editing. I.S. did the reviewing and editing.

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