Preparing the Global Immunization Cold Chain for COVID-19 Vaccines

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Abstract: With the recent announcement that COVID-19 vaccines are entering wide scale production, it is time to start preparing for global immunization campaigns so that everyone on earth is protected. There are multiple challenges to the global roll out of COVID-19 vaccines as this will be, by far, the largest vaccine introduction in history. In this essay, we focus on the infrastructure challenge in keeping the vaccines at a safe temperature from arrival into a country until used for vaccinations. The vaccine cold chain infrastructure is well developed in almost all countries for routine immunization, but risks being overwhelmed by COVID-19 vaccines due to the number of vaccine doses that are required to reach the entire adult population. We describe the existing approach for the vaccine cold chain in developing countries and analyse how it is likely to be impacted by COVID-19 vaccines. Country vaccine programs are generally managed by Ministries of Health, and have a hierarchy of storage from cold rooms at the national vaccine store down to the vaccine refrigerators at peripheral health facilities. Substantial capacity will need to be added to accommodate vaccines used in national COVID-19 immunization campaigns and planning for the campaigns needs to take place early to ensure infrastructure is in place. We conclude the essay with a discussion of the overall challenges and identify specific areas that require attention from global vaccine and engineering communities.

Index Terms: COVID-19 vaccine, Immunization Cold Chain

1. Introduction

Recently, there has been a lot of very good news on the development of COVID-19 vaccines. Multiple organizations have announced results of vaccine trials that showed very high levels of protection and approvals are being sought in many countries with plans to immediately go into mass production. Within the next couple of years, billions of doses of vaccines should be available. For example, India alone expects to receive 400-500 million doses in the next year [1]. To control the global pandemic it is essential that the immunization efforts are also global. There are a host of challenges in the global introduction of COVID-19 vaccines such as financing the acquisition of vaccines, allocating the vaccines to countries, ensuring the vaccines are safe, and creating public awareness. We focus on the challenge of storing vaccines at safe temperatures as they progress through a country's logistics system. Our attention is primarily on developing countries, especially those that receive support from Gavi, the Vaccine Alliance. The COVID-19 vaccine introduction will take place on a scale never seen before. The closest world wide mobilization is probably the Polio vaccine campaigns of the 1980s and 1990s. Vaccines need to be kept at a low temperature to ensure their potency with the requirements depending on the formulation of the vaccine. The challenge countries will face is that the volume of the vaccine required is so great that it cannot be accommodated in the existing cold rooms, vaccine refrigerators, and vaccine freezers (which we collectively refer to as the *vaccine cold chain*). The basic explanation for this is that the initial COVID-19 vaccine campaign will target a significant fraction of the population (such as the adult population) while the existing cold chain was designed for routine vaccines which primarily targets infants. One way to look at the storage challenge is to count the number of doses of vaccines needed. The routine vaccine schedule (depending on the country) consists of about 12-16 doses of vaccine for children under one (which are 2% of the population world wide and 3% in Africa). The COVID-19 vaccine is likely to require two doses, and may target the adult population (which is 74% of the population worldwide and 59% in Africa). Assuming that doses of all vaccines have the same volume, this suggests that the vaccine volume for country wide immunization against COVID-19 will be three times that of the routine vaccines in African countries, and five times that worldwide. We now give some background on how we expect COVID-19 campaigns to be run and address the cold chain in more detail, and conclude with a discussion of challenges to be addressed.

2. Methods

At the national level, vaccination takes the form of routine immunization or widespread immunization campaigns. Routine immunizations are administered to young children following a predetermined schedule based on age. Immunization campaigns often occur in response to an outbreak and large quantities of a single vaccine must be manufactured, distributed and administered across a target population. In response to the current pandemic, the cold chain for COVID-19 vaccines will start as a focused effort, resembling ongoing immunization campaigns, such as those for Measles. Measles campaigns in low-resource nations have mobilized large groups of health workers and have vaccinated 2 billion children since 2001 by employing unique solutions in different areas. For example, vulnerable populations have been reached in Kenya by going door-to-door and indigenous communities in the Philippines have been vaccinated in the dead of night, using car headlights to see [2], [3]. National immunization plans for the COVID-19 campaign must include equity-based strategies to finance and distribute the new vaccinations in low-resource countries [4]. Even if the COVID-19 vaccine can be stored at refrigeration temperature, the existent cold chains only have the storage capacity to enable immunization of infants. This capacity “risks being vastly insufficient as we try to rapidly vaccinate the entire population for COVID-19” [1]. The number of doses required must be estimated in each country, giving health officials enough information to facilitate equitable immunization coverage at the national and district levels by designing cold chains with specific temperature and storage requirements in mind [1], [5]. Given the insufficient research period, the duration of immunity from vaccination is unknown and there are concerns as to how the disease and vaccination strategies may evolve over time. It is possible that the COVID-19 vaccine could become a part of a routine immunization schedule including booster doses for the elderly.

When determine a vaccines storage, chief considerations are the storage temperature and volume requirements per dose. As of this writing Pfizer/BioNTech, Moderna, and AstraZeneca/Oxford have announced vaccines that are gaining approval for early or limited use. Press reports suggest that there will be additional options soon (as many as 13 are in phase three trials in the United States) [6]. The Pfizer/BioNTech vaccine has created temperature-monitored, GPS-tracked coolers for distribution of their vaccine that must be stored ultracold at -70℃. Each cooler, surrounded by 50 pounds of dry ice pellets, contains 4,875 doses split into 2mm glass vials, each containing five doses. Upon delivery, the vaccine must be transferred to ultralow temperature freezers or the dry ice surrounding the container must be replenished every five days. The two doses are administered three weeks apart. This poses a problem for developing countries as both ultra-cold refrigeration units and dry ice are not easily available (DRC and Uganda have a small number of ultra-cold units for Ebola vaccines). Each vial needs to be diluted to obtain five doses from the 2 mm vial, and once diluted, the vaccines only last for 6 hours. Further, the container cannot be opened more than twice daily, and the contents must be used within 15 days [7]. The Moderna vaccine must be stored frozen at a standard freezer temperature of -20℃ and keeps for up to a month at conventional refrigeration temperatures. The vaccine is ready to use out of the container

Fig. 1. Vaccine freezers for ultralow temperature storage at a national vaccine store

and the two doses are administered four weeks apart [8]. These factors cause it to be a viable option for rural or under resourced areas that may not have access to specialized freezers [7]. The AstraZeneca Oxford vaccine can be stored at refrigeration temperatures for up to 6 months. The two doses are administered four weeks apart. This vaccine relies entirely on conventional refrigerators and is thus the most suited for low-resource countries.

The development of the vaccine cold chain through the Expanded Program on Immunization [9] has been a significant global effort. The major global health organizations, such as WHO, UNICEF and GAVI have had a major role, along with donor organizations, NGOs and country MOHs. The standard approach in most developing countries is to have immunization as a public health program managed by the MOH. With global support, countries have set up vaccine cold-chains along a common model with a hierarchy of storage facilities. There will be walk-in cold rooms at the national vaccine store where vaccines are received in the country. Below that level, there are a series of regional and district vaccine stores which may use either cold rooms or large vaccine refrigerators. From the vaccine stores, vaccines are distributed to storage at health facilities (hospitals, health centers, dispensaries) to support immunization activities including outreach sessions. Vaccine storage equipment is standardized with an approved list of equipment managed by WHO [4]. Since much of the equipment is supplied by global organizations, standards are enforced. Power is an important consideration for cold chain equipment since vaccine storage is required in areas that either have frequent outages in grid electricity or are entirely off-grid. Backup generators are used for major vaccine stores. A very significant innovation was the development of Ice Lined Refrigerators which provide a layer of ice to keep vaccines cool when power is lost. Gas and kerosene refrigerators have been important in the past, but there is now an effort to phase them out. For off-grid settings, solar direct drive refrigerators are now the preferred alternative. The question faced by countries is how to build the cold chain with assignment of equipment to facilities and organizing the distribution chain. The amount of equipment required is generally linear in population with thousands to tens of thousands of refrigerators required for a country. Based on our experience in Africa, a country of 40 million people will have approximately 4500 vaccine refrigerators. There is a well developed methodology for computing vaccine volume requirements for facilities [10] based on catchment population, the vaccine schedule, delivery frequency, wastage and reserve requirements. Campaigns have somewhat different requirements as vaccines arrive all at once and potentially are not stored at peripheral facilities. To understand the overall cold chain status a countrywide cold chain equipment inventory is needed. This allows an assessment of gaps in capacity of the cold chain as well as information on the quality of equipment and energy sources. When parameters for COVID-19 vaccines are known, it will be possible to estimate the amount of new storage equipment needed, but looking at current equipment inventory data, conservative estimates suggest that at certain levels of the supply chain, such as the district level, the amount of refrigerators will need to at least double.

3. Discussion

Global immunization for COVID-19 is probably a year or two out. It is likely to be conducted in phases with a staggered introduction to countries as has been done for other vaccines. The existing cold chain is not going to be adequate so it is essential that planning and investments need to start now. The first step is to assess the existing vaccine cold chains and strengthen them at the key points. It is estimated that fewer than half of developing countries even have cold chain equipment inventories so there is a significant information gap. Modelling of the country supply chain based on country data can identify different opportunities for optimizing storage as supply chain techniques provide mechanisms for trade offs in deliveries and static storage. There is need to identify what upgrades to the cold chain are necessary, including novel approaches such as mobile vaccine warehouses. Integration of planning of vaccine campaigns with the management of storage space is important in achieving efficient utilization storage and in preventing wastage of vaccines. To support all of this, it is essential that both vaccine program managers and vaccine logisticians have access to powerful digital tools for planning and tracking immunization campaigns.

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