London Work, Travel, Convene Coalition

Vaccines: Pathway to Immunity is Littered with Obstacles

By Dr Rodrigo Rodriguez-Fernandez, Global Medical Director, International SOS

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"Responding to COVID-19 is like conducting a train while laying the tracks.

Every day we learn new things about the virus, the vaccines, and how they interact with the human body. But there is also a lot that we know and that we have learnt so far."

Dr Rodrigo Rodriguez-Fernandez, Global Medical Director, International SOS







Rapid testing 2024

Rapid testing will be the next major

Hopefully by 2024, we will have a good









357_m 2021

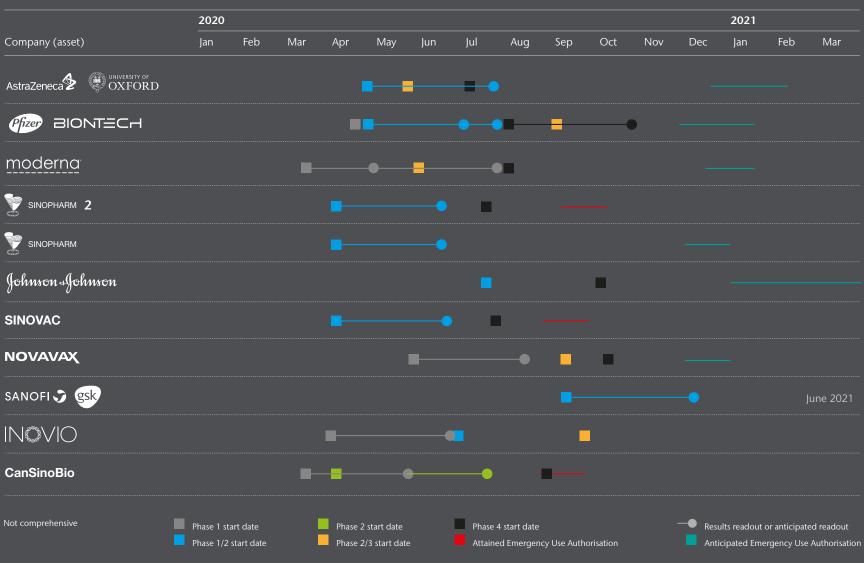
Decrease transmission 0.96%

purchased 357 million vaccines, and the first

All known current vaccines are non-sterilising, so the virus can still be potentially contracted and transmitted **post-vaccination**. We are still understanding how

Vaccine pipeline

Announced clinical-trial timelines for COVID19-vaccine candidates



Vaccine pipeline

At the time of writing, the UK Government had purchased 357 million vaccines; 800,000 had been shipped, and the vaccine roll out programme started in December. Other vaccines are in development, with imminent emergency use authorisation.

The UK was proud to be the first to approve the vaccine. However, this initial step doesn't reflect the rollout to the general population. While the UK might have launched its vaccine in December, the number of people vaccinated is still low.

So how quickly will it take to roll out the vaccine in each country? The German government has predicted it will take well into 2022 to get everyone vaccinated.

Even a well-oiled machine takes a long time to vaccinate an entire population, and there are significant logistical hurdles in production, transportation and the need to administer booster doses for most leading candidates.

There are too many variables to give a realistic date on a vaccination end-game. Factors that come into play include public willingness and the number of healthcare workers and centres performing vaccinations.

A large supply of the same or several vaccines will not necessarily equate to a faster roll out if the manpower and supply chain logistics are not there. Certain groups will be prioritised, and each country decides this. In the UK, we have high-risk vulnerabilities like those being treated for HIV and cancer, then nursing homes, NHS, essential workers and the general public.



How do the vaccines compare?



Different vaccines, with varying levels of effectiveness, will become available at different times.

When comparing the COVID-19 vaccines, there is a huge variance in cost and storage requirements, and it is anticipated that countries and hospitals will struggle with supply chain logistics.

What is similar across the different vaccines is the dosing regimen and the vaccines' effectiveness. While the key vaccines in development are around 95% effective, the Oxford-Astra-Zeneca vaccine currently has an outlier 62-90% result, depending on the dosing scheme. This is because of an accidental finding where an unintended half dose was administered. When affected participants had no complaints or side effects, like pain in the arm, doctors realised the error. What the mistake revealed was that giving the half dose produced better results than the original protocol. The reasoning is this mimics a real infection, but whether this plays out in reality remains to be seen. There are those that say that the lower dose was intentional, however, it is not clear.

Is the speed of vaccine development a safety concern?

Vaccine development usually occurs at a glacial pace; process development and preclinical toxicology studies last two to four years, followed by three phases of clinical trial, each lasting between one and three years. Regulatory review then requires a couple of years before large scale production and distribution.

The COVID-19 vaccine development has necessitated a huge overlap in different parts of this process. The three clinical trial phases were conducted simultaneously. This is not too uncommon in epidemiology; there are statistical models for other interventions that overlap, but it had never been seen in the vaccine R&D world at this scale.

Another shortcut was the red tape bureaucracy. The UK decided to look at different studies and approve on a rolling basis throughout the year. Much of the technology already existed from an infrastructure perspective, and from a scientific perspective, COVID-19 is part of the wider coronavirus family. It is very different to HIV, for example, which is unlike any other virus.

Corporate organisations have a role to play

Our attitude to the vaccine will have a significant role to play in its distribution and efficacy. It is expected that the role of pro- and anti-vaccine groups will have a major influence on vaccination rollout. Whilst initial data shows mild side effects of the vaccine – pain in the arm, slight headache – there is a risk that individuals do not return for their second dose if they had a minor adverse effect to their first dose. This is an important consideration for messaging and positioning of the vaccine – and something where there is a key role for corporate employers. From a business perspective, we can influence this messaging in our internal communications and company approach. In the UK, whilst the vaccines are currently under lock and key and for government-procured and arranged distribution – companies should consider providing vaccinations as soon as the vaccine is available to the private sector.

Vaccines: who has bought what, and who will be left out?

There is already competition between countries to acquire adequate vaccines through pre-purchase contracts with manufacturers, limiting the availability of the vaccine in low-middle income countries. Additionally, we will see a lot of geopolitical practice in play with vaccine distribution. Figure 2 illustrates the huge disparity in terms of who has bought what. The commitments that vaccine manufacturers have made to certain governments have been on the basis of future agreements for purchasing. It is a very complex negotiation process. However, the lower and middle-income countries don't have that bargaining power, and they haven't secured the doses.

Perhaps unsurprisingly, higher-income countries will enjoy clear access to vaccines, while it might take two or three years to distribute these to certain parts of Africa and Asia.

This is something that China and the UN are trying to change independently. The UN has put together the initiative – Covax, to secure procurement for countries that can't afford vaccines. China, through soft power, is trying to give the vaccine for free in countries in Africa where it has current or future interests.

The world will go from a pandemic where every country in the world has the virus to an endemic where we have pockets of the virus circulating. Similar to Malaria – there is no sign of it in the UK, but go to Africa, Central America or Indonesia, and it is still circulating there.

The vaccines are destined for a handful of countries, but whilst it also would appear India (fig 3) is well stocked – the number per capita radically changes the positions of many countries.

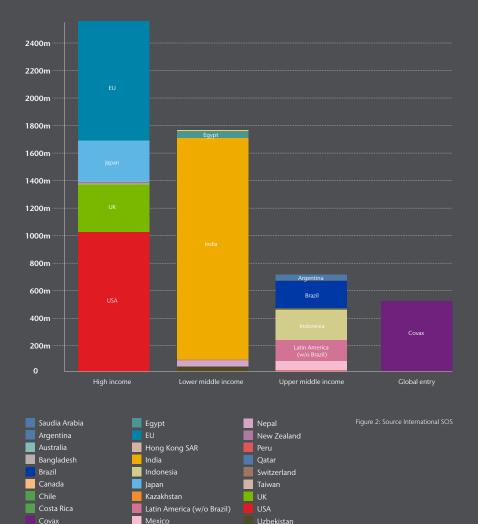
In figure 4, India's position has shifted because of its population of over 1.35 billion people, whereas other countries like Canada and the US have procured a far larger number of doses per capita.

At this point in time, representation will constantly change, and there will be many soft power political moves in play. But this is why the timeline for global herd immunity is so difficult to predict.

Total confirmed vaccine doses procured by country income level

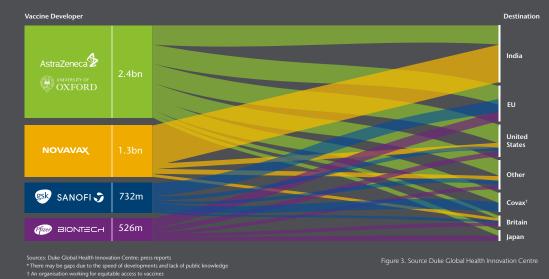
Ecuador

Morocco

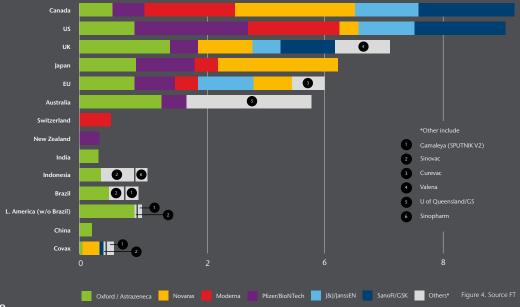


Vietnam

Five billion vaccine orders



Which countries have built the biggest vaccine portfolios?



Herd immunity can be a misleading term

No vaccine is expected to provide enough protection to stop COVID-19 from spreading between people completely, and herd immunity is unlikely to be achieved in 2021.

So what do we have to do to return to normal, and are 'herd immunity' and the vaccine the best routes to get there? There are different ways to achieve immunity. The world is currently looking towards the vaccine; however, we don't know how long immunity will last.

There are two types of immunity: conferred immunity from the COVID-19 vaccine or previous vaccinations and natural immunity from COVID-19 infection or other coronavirus infections.

International SOS is currently researching antibody duration, and its initial studies indicate antibodies last around three or four months. However, the firm has recently learnt that the vaccines activate

something called T-cell immunity. While T-cells can't be measured through antibodies, they seem to last significantly longer. Currently, the most data available is for a year, and after 12 months, patients with natural immunity and acquired immunity still seem to have circulating levels of protective antibodies.

Herd immunity is a term widely used, but it can be misleading because this state is rarely achieved. The last time a virus was eradicated was smallpox. Thanks to the success of vaccination, the last natural outbreak of smallpox in the United States occurred in 1949. In 1980, the World Health Assembly declared smallpox eliminated, and no cases of naturally occurring smallpox have happened since. This took years to complete and the door-to-door vaccination of around 500 million houses in India. It was a completely different scenario from what we see here.



The pathway to immunity

	55%	60%	65%	70%	75%	80%	85%	90%	95%	100%
100%	55.00%	60.00%	65.00%	70.00%	75.00%	80.00%	85.00%	90.00%	95.00%	100.00%
95%	52.25%	57.00%	61.75%	66.50%	71.25%	76.00%	80.75%	85.50%	90.25%	95.00%
90%	49.50%	54.00%	58.50%	63.00%	67.50%	55.00%	76.50%	81.00%	85.50%	90.00%
85%	46.75%	51.00%	55.25%	59.50%	63.75%	55.00%	72.25%	76.50%	80.75%	85.00%
80%	44.00%	48.00%	52.00%	56.00%	60.00%	55.00%	68.00%	72.00%	76.00%	80.00%
75%	41.25%	45.00%	48.75%	52.50%	56.25%	55.00%	63.75%	67.50%	71.25%	75.00%
70%	38.50%	42.00%	45.50%	49.00%	52.50%	55.00%	59.50%	63.00%	66.50%	70.00%
65%	35.75%	39.00%	42.25%	45.50%	48.75%	52.00%	55.25%	58.50%	61.75%	65.00%
60%	33.00%	36.00%	39.00%	42.00%	45.00%	48.00%	51.00%	54.00%	57.00%	60.00%
55%	30.25%	33.00%	35.75%	38.50%	41.25%	44.00%	46.75%	49.50%	52.25%	55.00%

Explainer: The numbers displayed in the coloured area are the percentage of immune people in the population.

Colour

No herd immunity

Possible herd immuni

Likely herd immun

Figure 5: Source International SC



The pathway to immunity

The pathway to immunity (fig 5) is possible but will be littered with obstacles. Consider other vaccines: the world has tried for years to eradicate certain diseases with little success. Polio is a good example. The vaccine has been around since 1955, and some regions still can't eradicate it. Uptake in certain countries per year is pretty low for a number of reasons. For example, Pakistan is still in the 90s (%). So even when vaccines are really cheap and readily available, we still can't get past low to mid 90s (%).

Receiving the vaccine is not the silver bullet to normality

It's important to make the distinction between sterilising and non-sterilising vaccines. With a sterilising vaccine – the patient has a jab, and they are immune, they won't develop the disease. However, all 'current' COVID-19 vaccines are non-sterilising. This means when someone has the recommended dose of the vaccine, they develop antibodies and activate T-cells, and when they encounter COVID-19, they may still become infected but will be asymptomatic.

The salient point is that this person might still have the virus in their nose and oropharynx replicating. If they sneeze, then they can still potentially transmit the virus. This has essential and perhaps under-discussed consequences: they still have to wear a mask.

They still have to socially distance. We hope that the vaccines elicit such a response that the replication of the virus is so small that asymptomatic transmission goes from what it is typically, to zero and won't be enough to transmit. This is what we have seen with HIV. Patients on regular medication have low circulating levels of the virus, and therefore transmission is less likely.

When it comes to self-isolation, a factor that is limiting many people from working, the government is waiting on two things to see if self-isolation time can reduce. Firstly, how much viral shedding occurs after someone has been vaccinated, and secondly, how quickly it can make mass testing widely available.

Conclusion

From a company and societal perspective, it is very unlikely we will return to normal even when the vaccine is rolled out entirely in the UK. As it is such a central hub for the rest of the world, there will be a constant threat of people entering into the UK and reintroducing community transmission of the virus. We have to manage expectations that being vaccinated does not mean anyone can take their mask off. Relaxing these measures will take a lot more than that.

Essentially two parameters need to reach a certain point before the global population can feel more comfortable. One is vaccine efficacy, which at 95% is higher than originally expected and not the issue at play. The other, coverage, is more challenging but no less crucial. Achieving over 60% coverage in the UK, let alone across the world, will be extremely difficult for a number of reasons: procurement, logistics and whether people actually want to get vaccinated.

Whilst the vaccine's rapid development and distribution is good news for the world - the vaccine is just one of our lines of defence against the virus, and we must recognise that no single intervention will stop the spread. The next major development step to normality is rapid testing – and this will be a crucial focus for 2021 and beyond. Until then, we have to manage expectations that there is still some way to go.



Q&A

Considerations for corporate organisations and office workers

"If the UK achieves 'herd immunity,' will we still need to have social distancing and mask-wearing in offices?"

Yes. From an infection control perspective, even if someone has the vaccine, there is still the risk of transmitting COVID-19. However, rapid testing could lead to opening an office with no masks or social distancing. It will be a combination of how many people are immune, updated studies on seroprevalence*, and our ability to carry out mass testing – these will all determine the government's confidence level.

"If I am vaccinated, how will I know if I am carrying COVID-19 and will I be tested?"

If you are vaccinated and are possibly a carrier, it is very likely you will not know you're infected Carrier status is something we are looking at but still have a lot to learn. What is certain is that you won't know you are shedding the virus as the vaccine will likely stop you from developing any signs of symptoms. The only way to know if you have been infected is via testing.

We will see infrastructure develop around airports and office spaces where there is rapid testing regardless of whether you have been vaccinated. What we will do with those individuals depends on how we see immunity progressing. If we see that carriers are still shedding x amount of particles, we will say everyone still needs to wear a mask. If we see that only three particles shed, then this is not enough to infect. This is still relatively unknown, and rapid testing will be the velvet rope at the gate of the door that allows people in and out.

"When private vaccines become available, should organisations play a role in ensuring their staff are vaccinated and introduce vaccination programmes themselves?"

Large organisations have an enormous power in creating the right messaging for employees that they should get vaccinated, and have an ability and duty of care to provide certain health services such as vaccinations if and when available

In October 2020, we saw companies take up flu jabs, and there is an expectation for organisations to do this with COVID-19. It is beneficial to us for our employees to be vaccinated – healthy, well, and working. Companies should consider providing vaccinations as soon as the government releases the availability to the private sector.

^{*} Seroprevalence: the level of a pathogen in a population, as measured in blood serum.

What is the London Work, Travel, Convene Coalition?

The London Work, Travel, Convene Coalition launched in September 2020. It brings together large employers in the City and Canary Wharf to share key learnings and insights related to planning and operations, to assess impact and measurement of efforts and to evaluate the latest technologies. The coalition's aim is to develop a set of guidelines to help navigate the challenges businesses face as society re-opens throughout the recovery phase of the COVID-19 pandemic.

Founding members of the coalition include, Accenture, Ashurst, Aviva, Clyde & Co, JLL, Legal & General and others. Member roles range from Chief Operating Officer, Director of People Services, Director of Employee Experience, and Future Workplace Director.

Other coalitions worldwide include Chicago and New York, Dublin, and Singapore.

If you would like to find out more about the coalition, please contact The London Work, Travel & Convene Coalition Team [LondonWTC@aon.co.uk]

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