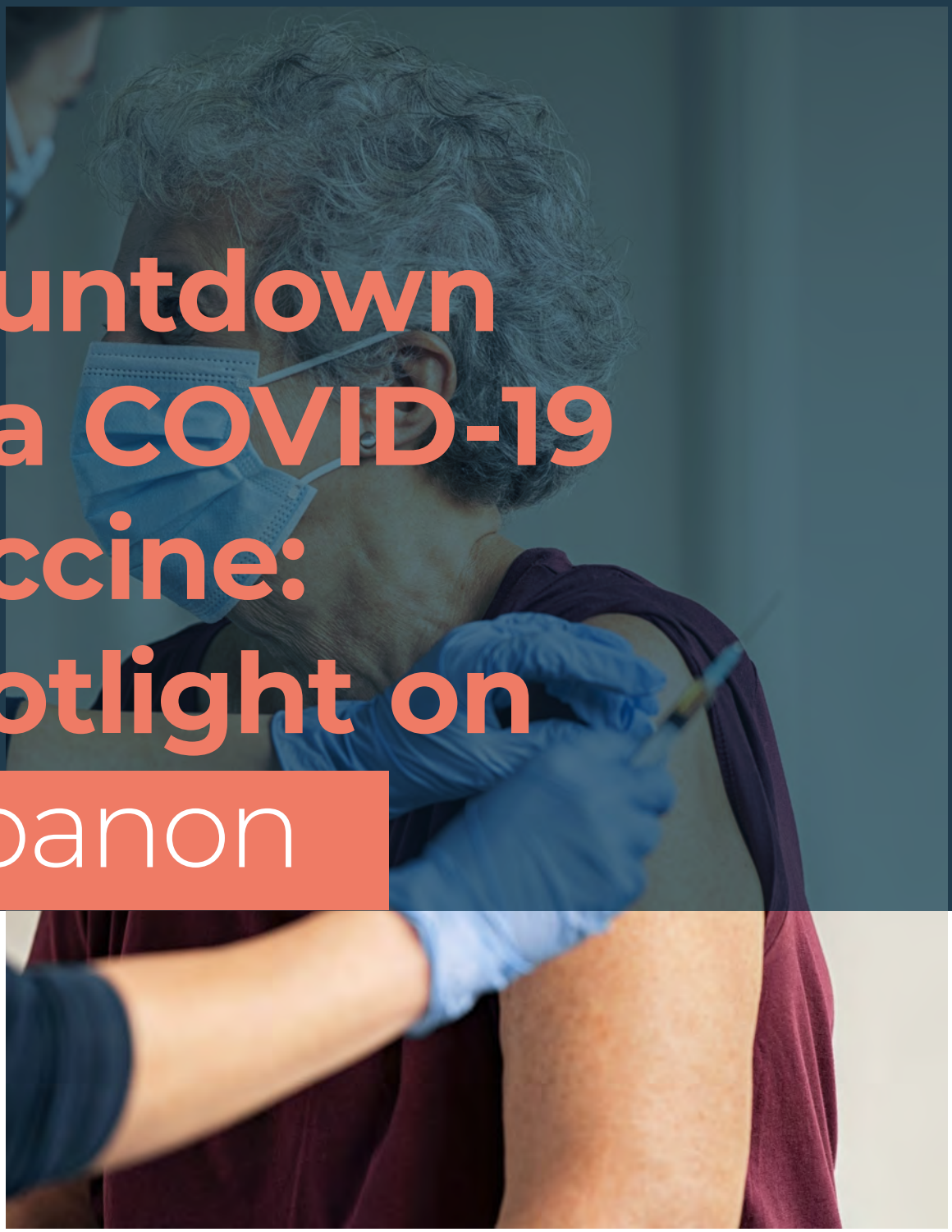
Evidence Summary



Countdown to a COVID-19 Vaccine: Spotlight on Lebanon

K2P COVID-19 Series

Knowledge to Policy Center K2P

1866 AUB American University of Beirut الجامعة الأميركية في بيروت

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Key Messages

As the COVID-19 pandemic evolves, its substantial toll on health and the economy continues to unfold. The pandemic has challenged and overstretched health systems beyond capacities and the response to the pandemic has required difficult and unprecedented decisions. Pharmacological and non-pharmacological interventions have had limited success in curtailing the spread of the virus and natural herd immunity has proven to be precarious. With all of this in hand, a vaccine appeared to be the only solution to curb the pandemic and the most promising means of restoring some semblance of normalcy to our lives.

This document intends to describe the journey to a COVID-19 vaccine from the expedited production process to distribution at the country level, passing through public acceptance and ethical disputes. This document also provides an overview of considerations for COVID-19 vaccine deployment in Lebanon.

SELECTION PROCESS

A comprehensive search of the literature was undertaken to identify articles -systematic reviews and single studies- focusing on the topic of COVID-19 vaccines. Search strategy consisted of reviewing the following databases: Medline/ Pubmed (MeSH term: Coronavirus Infections and Viral Vaccines; keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), IMEMR (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), ProQuest Health Management (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), Health Evidence (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), Health Systems Evidence (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), WHO global health library (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), Cochrane Library (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine), and Embase (keywords: COVID-19 vaccine, coronavirus vaccine, and SARS-COV-2 vaccine). In addition, data retrieved from grey literature websites including WHO, MOPH, FDA, CDC, Gavi, and others were included. Last search was done on January 5, 2021. Only articles published in English and with a focus on humans were included. Articles with purely clinical scope, such as those assessing the mode of action of a vaccine, were excluded. Articles were segregated into themes (the need for a vaccine, vaccine development process, country preparedness and regulation, public perception, ethical considerations, and the Lebanese context) and presented accordingly in the document. Handsearching was consequently performed with two objectives: 1) search for supporting data and 2) conduct fine searches for the retrieved themes. As a result of this methodology, 108 articles were eventually included in this Evidence Summary.

The Imperative Need for a Vaccine

Several factors have rendered a COVID-19 vaccine the only opportunity to control the pandemic and a necessity for limiting the adverse consequences of the infection on health, health systems, and the economy.

High Disease Burden

As the COVID-19 pandemic evolves, substantial toll on health and the economy continues to unfold. As of January 4th, 2021, there have been almost 84 million cases of COVID-19 and over 1.8 million deaths due to the disease worldwide, reported to the World Health Organization. In Lebanon, on January 4th 2021, the cumulative number of COVID-19 cases was 192,136 cases since the advent of the epidemic in the country on February 21, 2020, with 1499 total recorded deaths recorded to date.

Limited Success of Pharmacological Interventions

No cure has been identified for COVID-19 to date. Interventions including Remdesivir, steroids, convalescent plasma, anti-malarials, IL-6 inhibitors and other biological treatments and small molecules have been used in practice with varying clinical responses.

Challenged Implementation of Non-pharmacological Interventions

Non-pharmacological interventions (including travel restrictions, isolation and quarantine, physical distancing, use of face masks, and hand hygiene) have been the mainstay of the response to COVID-19 and the only resort to flatten the epidemiologic curve. Despite the proven success of non-pharmacological interventions, implementation is challenged by impediments related to feasibility, acceptability, and compliance in many settings.

High Virus Infectivity

COVID-19 is a global concern because of its high infectivity and transmission capacity with a reproduction rate of around 3 and epidemic doubling time of about 3-7 days. A new COVID-19 variant that was recently discovered in London on November 2020 and is predicted to be around 70% more rapidly transmissible than previously circulating strains of COVID-19.

Difficult to Attain and Costly Herd Immunity

It is estimated that herd immunity to COVID-19 will be achieved when around 67% of the population develops immunity to the virus either naturally through infection or with the help of a vaccine, after which the incidence of the infection will start to decline.

Relying on natural infection to achieve herd immunity is associated with 1) uncertainty regarding the duration of the acquired immunity; 2) strain on the health system due to increased number of cases requiring hospitalization and intensive care; and most importantly 3) high cost in terms of human lives lost. As a result, an effective vaccine presents the safest way for achieving herd immunity.

The Path to COVID-19 Vaccine

Progressing at Pandemic Pace through Trials

Typically, vaccine development is a long and complex process, often lasting 10-15 years. During a pandemic, the development process may be atypical or expedited. Governmental agencies, international counterparts, academia, nonprofit organizations and pharmaceutical companies developed a coordinated strategy for prioritizing and speeding the development of the most promising treatments and vaccines for COVID-19. In addition, the Food and Drug Administration (FDA) provided clear communication to the pharmaceutical industry pertaining to the scientific data and information needed for safe and effective vaccines. Provided certain criteria are met, manufacturers may submit a request for Emergency Use Authorization (EUA) to facilitate the availability and use of their vaccine.

Characteristics of an Ideal COVID-19 Vaccine

According to 'WHO Target Product Profiles for COVID-19 vaccines', an ideal or 'preferred' COVID-19 vaccine is a vaccine that is:

- Able to protect at least 70% of people
- Safe in short term and long term
- Safe in different age groups (children pregnant, elderly)
- Ideally given in a single shot
- Provide immunity for as long as possible (confers protection for at least 1 year)
- Higher storage temperatures and higher thermostability (to facilitate storage and distribution)

Vaccines Under Investigation and Production

Until December 29, 2020, 60 candidate vaccines are undergoing clinical evaluation with 172 other candidate vaccines in the preclinical evaluation phase.
Only two COVID-19 vaccines, one produced by Pfizer/BioNTech and another by Moderna, have been authorized by FDA for use under EUA to date. Both vaccines have also been authorized by the European Medicines Agency for conditional marketing authorization. Key characteristics of the two vaccines are presented in the table below:

Vaccine	Technology	Efficacy	Common Side Effects	Age indications	Number of Doses	Storage	Approximate Price
Pfizer/ BioNTech	RNA	95% (even in adults over 65 years where efficacy was more than 94%)	Pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, and fever	16 years of age and older	2 doses series separated by 21 days	-70ºC for 6 months and 2-5ºC for up to 5 days	20$ per dose
Moderna	RNA	94%	Pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, swollen lymph nodes in the same arm as the injection, nausea and vomiting, and fever	18 years of age and older	2 doses separated by 28 days	-20ºC for 6 months and 2-8ºC for 30 days	38$ per dose

Note: There is no evidence yet to suggest that the new variant of COVID-19 affects vaccine efficacy. The reason is that vaccines are polyclonal, thereby producing antibodies that target several parts of the spike protein. As a result, the virus would likely need to accumulate multiple mutations in the spike protein to evade immunity induced by vaccines or by natural infection.

Safety Assurance Measures

Counterstrategies adopted by scientists to ensure the safety of vaccines include safety investigation at every stage of vaccine development, serious adverse events monitoring after clinical trials, development of a consensus on how to adequately assess adverse events, active surveillance at the country level, and development of vaccine safety profiles. FDA notes that there should be an adequate plan for safety data collection among individuals vaccinated under an EUA vaccine.

Global Solidarity and Coordination

In April 2020, the ACT-Accelerator partnership was initiated with an aim to support fast, coordinated, and successful global efforts to develop tools to fight COVID-19. COVAX is the vaccines pillar of the ACT-Accelerator that was found with the purpose of speeding up the search for an effective vaccine. Concomitantly, COVAX is supporting manufacturing and buying capabilities so that 2 billion vaccine doses can be fairly distributed by the end of 2021. By joining COVAX, both self-financing countries and funded countries will gain access to the available portfolio of COVID-19 vaccines.

Country Readiness and Regulation

Preparation Requirements for a COVID-19 Vaccine

Numerous considerations need to be factored in for an effective country deployment of a COVID-19 vaccine. On November 16th 2020, WHO issued a document 'Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines' directed at national authorities who are responsible for managing deployment, implementation and monitoring of COVID-19 vaccines, as well as partners who provide the required support. Key considerations for any country preparing for COVID-19 vaccine deployment and distribution include:

- Regulatory Preparedness
- Planning and Coordination
- Costing and Funding
- Identification of Target Population and Delivery Strategies
- Preparation of Supply Chain and Management of Healthcare Waste
- Human Resource Management and Training
- Vaccine Acceptance and Uptake
- Vaccine Safety Monitoring
- Immunization Monitoring Systems
- COVID-19 Surveillance
- Evaluation of COVID-19 Vaccine Introduction

Public Perception of COVID-19 Vaccine

Public perception regarding COVID-19 vaccines have spanned over the whole spectrum from utmost enthusiasm and support to extreme criticism and rejection, particularly on social media posts. However, when assessed formally in a research study, positive results regarding public vaccine acceptance were predominantly revealed. Factors such as vaccine or patient characteristics, trust in research, medical and official endorsement, and political affiliation were associated with public vaccine acceptance. On the other hand, creating an enabling environment, harnessing social influences, and increasing motivation have been shown to enhance vaccine uptake.

Ethical Considerations

With a sense of urgency to develop a COVID-19 vaccine, trade-offs in scientific and social value have surfaced. Several issues such as those pertaining to the use of healthy volunteers in trials, the equitable distribution of the vaccine at the inter and intra country level, as well as the principle of autonomy in the context of a COVID-19 vaccine have been persistently a matter of debate.

Deploying a COVID-19 Vaccine in Lebanon

In Lebanon, the pandemic struck the country at a time of political, economic, and social disruption.

- The country was hit hard by the August 4 explosion which killed at least 200 people, left several hospitals with substantial damage, and accelerated the immigration of doctors and nurses, all of which resulted in over burdening an already worn-out health system
- The pandemic hits on a background political laxity, corruption, revolution, and eroded public trust.
- The pandemic arrives at the brink of an impending economic breakdown, banking sector collapse, diminished buying capacity, and threats of withholding subsidies on commodities and medicines.
- The availability of basic resources such as uninterrupted electricity, which is a must for the optimal storage of vaccines, is threatened as a result of possible withholding of subsidies on fuel.

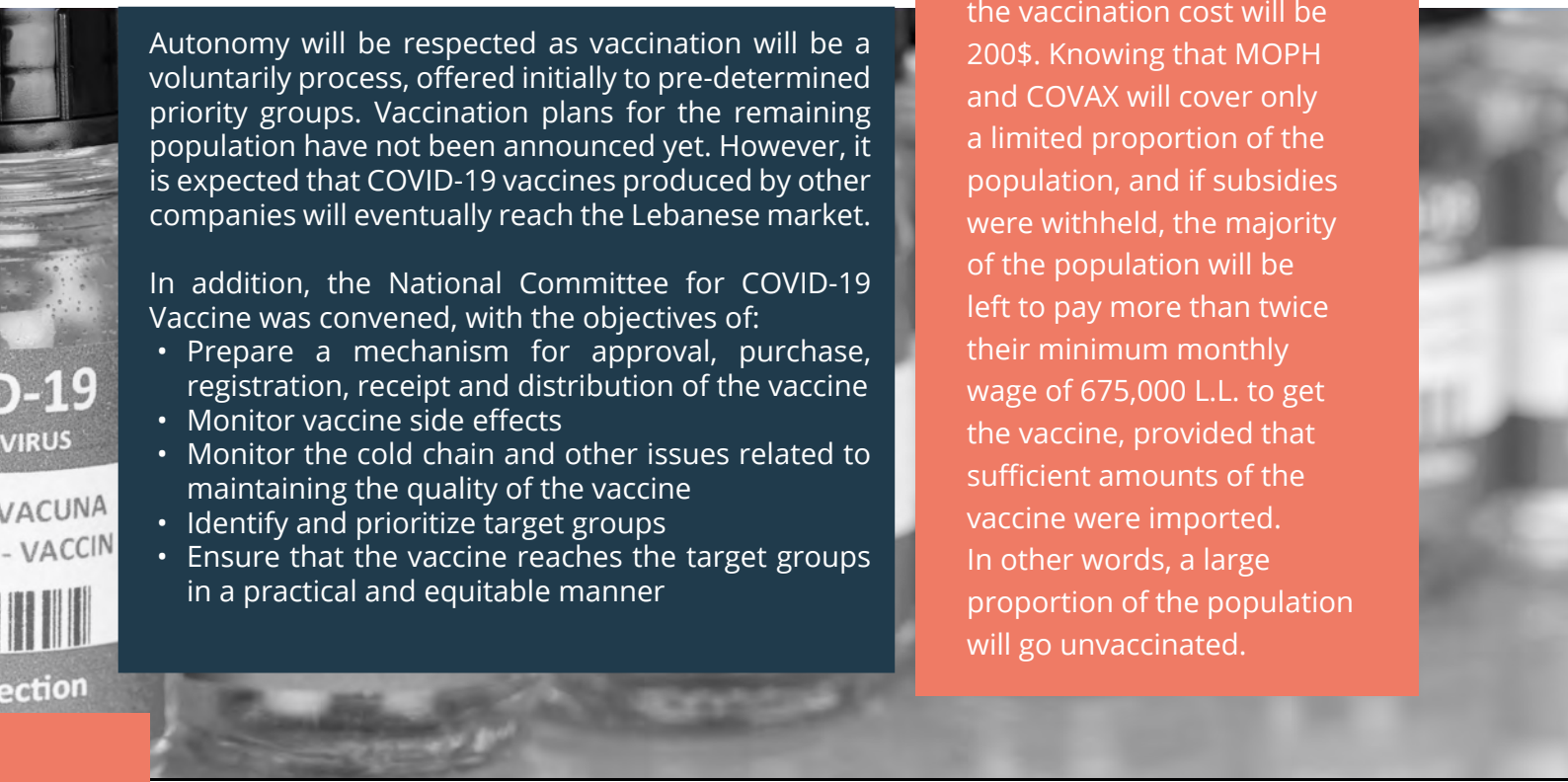
However, efforts were made to secure the country's share of the vaccine. On November 23rd 2020, the Ministry of Public Health announced that Pfizer/BioNTech vaccine will arrive in Lebanon by mid February 2021, after conducting early negotiations with the company. According to the MOPH, 15% of the population will receive the vaccine for free (covered by the MOPH), while 20% will be hopefully covered by COVAX.

Autonomy will be respected as vaccination will be a voluntarily process, offered initially to pre-determined priority groups. Vaccination plans for the remaining population have not been announced yet. However, it is expected that COVID-19 vaccines produced by other companies will eventually reach the Lebanese market.

In addition, the National Committee for COVID-19 Vaccine was convened, with the objectives of:

- Prepare a mechanism for approval, purchase, registration, receipt and distribution of the vaccine
- Monitor vaccine side effects
- Monitor the cold chain and other issues related to maintaining the quality of the vaccine
- Identify and prioritize target groups
- Ensure that the vaccine reaches the target groups in a practical and equitable manner

The awaited Pfizer/BioNTech vaccine is estimated to cost around 20$ per dose, which sums up to 40$ for the full course (Observer, 2020). For an average household of 5 persons, the vaccination cost will be 200$. Knowing that MOPH and COVAX will cover only a limited proportion of the population, and if subsidies were withheld, the majority of the population will be left to pay more than twice their minimum monthly wage of 675,000 L.L. to get the vaccine, provided that sufficient amounts of the vaccine were imported. In other words, a large proportion of the population will go unvaccinated.



In view of the turbulent state of the country, successful deployment and vaccination necessitates:

- Political will and prioritization of public health
- Transparency and communication
- Securing essential pre-requisites for all stages of deployment
- Wise use of finite resources
- Development of retention plans for health professionals
- Control of black market and side deals
- Inclusion of marginalized populations such as refugees and immigrant workers
- Minimizing out-of-pocket payments
- Commitment to the principles of autonomy and equity

الرسائل الرئيسية

مع تطور جائحة كوفيد-١٩، تستمر تداعيات الجائحة الشديدة في التأثيرعلى الصحة والاقتصاد. لقد تحدى الوباء الأنظمة الصحية و إرهقها ودفعها لتخطى قدرتها الإستيعابية، كما تطلبت الاستجابة للوباء قرارات صعبة وغير مسبوقة. من ناحية أخرى، لقد حققت التدخلات الدوائية وغير الدوائية نجاحًا محدودًا في الحد من انتشار الفيروس وأثبتت مناعة القطيع الطبيعية أنها مليئة بالمخاطر. على ضوء هذه المعطيات، بدا وأن اللقاح هو الحل الوحيد للحد من الوباء وإحدى الوسائل الواعدة لاستعادة بعض مظاهر الحياة الطبيعية.
يهدف هذا المستند إلى وصف الرحلة إلى لقاح كوفيد-١٩ من عملية الإنتاج إلى التوزيع على مستوى البلدان، مروراً بالتقبل العام للقاح والجدليات الأخلاقية حول هذا الموضوع. يوفر هذا المستند أيضًا لمحة عامة عن الإعتبارات المتعلقة بتوزيع لقاح كوفيد-١٩ في لبنان.

الحاجة الملّحة للقاح
أدّت مجموعة من العوامل الى اعتبار لقاح كوفيد-١٩ الفرصة الوحيدة للسيطرة على الوباء، وضرورة للحد من الآثار السلبية للعدوى على الصحة والنظم الصحية والاقتصاد.

ارتفاع عبء المرض
لا يزال تطور جائحة كوفيد-١٩ يؤثر على الصحة والإقتصاد بشكل واضح. فاعتباراً من ٤ كانون الثاني ٢٠٢١، تم تسجيل حوالي ٨٤ مليون حالة مؤكدة من كوفيد-١٩، من بينهم أكثر من ١,٨ مليون حالة وفاة حول العالم، بحسب أرقام منظمة الصحة العالمية. وفي لبنان، بلغ العدد التراكمي للإصابات بكوفيد-١٩ حتى ٤ كانون الثاني ٢٠٢١، ١٩٢,١٣٦ حالة منذ ظهور الوباء في ٢١ شباط ٢٠٢٠، مع تسجيل ١٤٩٩ حالة وفاة بسبب الفيروس.

محدودية نجاح التدخلات الدوائية
حتى الآن، لا يوجد علاج متاح لـ كوفيد-١٩. تم اعتماد علاجات عدّة منها ريمديسفير، والكورتيزون، واستخدام بلازما من شخص تعافى من كوفيد-١٩ (البلازما النقاهة)، ومضادات الملاريا، وكوابح IL-٦ وعلاجات بيولوجية أخرى، نتج عنها نتائج و استجابات سريرية مختلفة.

تحديات تنفيذ تدخلات غير دوائية
شكلّت التدخلات غير الدوائية، بما في ذلك فرض القيود على السفر والعزل والحجر الصحي والتباعد الجسدي والاجتماعي واستخدام الكمامات وغسل اليدين، الحجر الأساس للاستجابة لـ كوفيد-١٩ والحل الوحيد لتسطيح المنحنى الوبائي. على الرغم من النجاح المُثبت لعدد من التدخلات غير الدوائية، إلا أن التنفيذ يواجه تحديات بسبب المعوقات المتعلقة بمدى إمكانية وقبول التطبيق والالتزام به في العديد من الظروف.

ارتفاع معدل العدوى والإنتشار للفيروس
يُقلق فيروس كورونا المستجد العالم بسبب قدرته العالية على العدوى والإنتشار، بمعدل تكاثري يبلغ حوالي ٣. و يبلغ الوقت الذي يتضاعف فيه الوباء حوالي ٣-٧ أيام. أضف إلى أن من المتوقع أن تكون السلاسة الجديدة من كوفيد-١٩ الذي تم اكتشافها مؤخرًا في لندن في تشرين الثاني ٢٠٢٠، أكثر سرعة في الانتقال بحوالي ٧٠٪ من سلالات كوفيد-١٩ المنتشرة سابقًا.

صعوبة تحقيق وارتفاع كلفة مناعة القطيع
تشير التقديرات إلى أن مناعة القطيع ضد كوفيد-١٩ ستتحقق عندما يستحصل حوالي ٦٧ ٪ من السكان على مناعة ضد الفيروس، إما بشكل طبيعي من خلال العدوى أو بمساعدة اللقاح. عندئذ، سيبدأ معدل الإصابة بالعدوى في الانخفاض.
الاعتماد على العدوى الطبيعية لتحقيق مناعة القطيع يرتبط بـتحديات منها: ١) عدم المعرفة الدقيقة و الكافية حوالي مدة المناعة المكتسبة ؛ ٢) إجهاد وإرهاق النظام الصحي بسبب زيادة عدد الحالات التي تتطلب العلاج في المستشفيات والعناية المركزة ؛ والأهم ٣) التكلفة العالية من حيث الخسائر البشرية. نتيجة لذلك، يقدم اللقاح الفعّال الطريق الأسلم لتحقيق مناعة القطيع.

الطريق الى لقاح كوفيد-١٩

تقدم مُعجل في تجارب اللقاحات

لطالما ما تكون عملية تطوير اللقاح طويلة ومعقدة، غالبًا ما تستمر من ١٠ إلى ١٥ عامًا. أثناء الجائحة، قد تكون وتيرة التطوير غير اعتيادية أو سريعة. و في هذا الصدد، لقد اجتمعت الهيئات الحكومية والنظراء الدوليون والأوساط الأكاديمية والمنظمات غير الحكومية وشركات الأدوية، لتطوير وتنسيق استراتيجية لتحديد الأولويات والإسراع بتطوير العلاجات واللقاحات الواعدة لكوفيد-١٩. بالإضافة إلى ذلك، ساهمت إدارة الغذاء والدواء (FDA) بتقديم البيانات والمعلومات العلمية اللازمة لصناعة الأدوية وتطوير لقاح آمن وفعّال. و قد أجازت FDA للمصنعين تقديم طلب للحصول على تصريح استخدام في حالات الطوارئ (EUA) لتسهيل توافر واستخدام لقاحاتهم، بشرط استيفاء معايير معينة.

الخصائص المثالية للقاح كوفيد-١٩

وفقًا لـ "معايير منظمة الصحة العالمية المتعلقة بالمنتجات المستهدفة للقاحات كوفيد-١٩"، فإن اللقاح المثالي لكوفيد-١٩ أو "المفضّل" هو:

- آمن لمختلف الفئات العمرية (الأطفال، النساء الحوامل، المسنّين)
- آمن على المدى القريب والبعيد
- قادر على حماية ما لا يقل عن ٧٠٪ من الناس
- يُحفظ في درجات حرارة أعلى ولا يتأثر بدرجات حرارت عالية (لتسهيل التخزين والتوزيع)
- يؤمن مناعة لأطول فترة ممكنة (يمنح الحماية لمدة سنة واحدة على الأقل)
- يُعطى في جرعة واحدة

لقاحات قيد التطوير والإنتاج

حتى ٢٩ كانون الأول ٢٠٢٠، يخضع ٦٠ لقاحًا مرشحًا للتقييم السريري، بالإضافة الى ١٧٢ لقاحًا مرشحًا آخر في مرحلة التقييم قبل السريري.

حتى الآن، تم ترخيص لقاحين فقط من لقاح كوفيد-١٩، أحدهما من إنتاج شركة Pfizer / BioNTech والآخر من شركة Moderna، من قِبل إدارة الغذاء والدواء الأمريكية للاستخدام، بموجب "التصريح للاستخدام في حالات الطوارئ" EUA. كما و تم ترخيص كلا اللقاحين أيضًا من قبل وكالة الأدوية الأوروبية للحصول على ترخيص التسويق المشروط. تُعرض الخصائص الرئيسية للقاحين في الجدول أدناه:

اللقاح	التكنولوجية (التقنية)	الفعالية	الآثار الجانبية العامة (الشائعة)	المؤشرات العمرية	عدد الجرعات	التخزين	السعر التقريبي
Pfizer/ BioNTech	الحمض النووي الريبي	٩٥٪ (حتى لدى عند الذين من هم فوق الـ ٦٥ عاماً، حيث تخطت الفعالية الـ ٩٤٪)	ألم في موقع الحقن، تعب، صداع، ألم عضلي، قشعريرة، آلام في المفاصل، وحمى (حرارة)	١٦سنة وما فوق	سلسلة من جرعتين، يفصل بين الجرعة الأولى والثانية ٢١ يوماً	يُحفظ في حرارة ٧٠ درجة مئوية تحت الصفر حتى ٦ أشهر وفي حرارة تتراوح بين الـ ٢-٥ درجة مئوية حتى ٥ أيام	٢٠$ للجرعة الواحدة
Moderna	الحمض النووي الريبي	٩٤٪	ألم في موقع الحقن، تعب، صداع، ألم عضلي، قشعريرة ، آلام في المفاصل، تورم الغدد الليمفاوية في نفس جانب الحقن، غثيان وقيء، وحمى (حرارة)	١٨ سنة وما فوق	سلسلة من جرعتين، يفصل بين الجرعة الأولى والثانية ٢٨ يوماً	يُحفظ في حرارة ٢٠ درجة مئوية تحت الصفر حتى ٦ أشهر وفي حرارة تتراوح بين الـ ٢-٨ درجة مئوية حتى ٣٠ يوماً	٣٨$ للجرعة الواحدة

ملاحظة: حتى الآن، لا يوجد دليل يشير إلى أن السلالة الجديدة من كوفيد-١٩ لها تأثير على فعالية اللقاح. والسبب هو أن اللقاحات متعددة النسائل، وبالتالي تنتج أجسامًا مضادة تستهدف أجزاءً عديدة من البروتينات الشوكية. نتيجة لذلك، من المحتمل أن يحتاج الفيروس إلى مراكمة طفرات متعددة في البروتينات الشوكية لتفادي المناعة التي تحدثها اللقاحات أو العدوى الطبيعية.

إجراءات ضمان السلامة

شملت الاستراتيجيات التي اعتمدها الباحثون والعلماء لضمان سلامة اللقاحات استقصاءات في كل مرحلة من مراحل تطوير اللقاح، ورصد للمضاعفات السلبية في المراحل اللتي تلي التجارب السريرية، وتشكيل توافق في الآراء حول كيفية تقييم المضاعفات بشكل مناسب، والمراقبة الدائمة على مستوى الدول، وتطوير مواصفات اللقاح الآمن. كما و لحُظت إدارة الغذاء والدواء وجوب تطوير خطة مناسبة لجمع بيانات السلامة بين الأفراد الذين تم تطعيمهم بموجب "التصريح للاستخدام في حالات الطوارئ" EUA.

التضامن والتنسيق على الصعيد العالمي

في نيسان ٢٠٢٠، نشأت شراكة ACT-Accelerator بهدف دعم و تسريع الجهود العالمية والتنسيق لتطوير أدوات ناجحة لمكافحة كوفيد-١٩. "COVAX" هو ركيزة اللقاح ACT-Accelerator الذي تم إستحداثه بهدف تسريع البحث عن لقاح فعال. بالتزامن مع ذلك، يدعم COVAX قدرات التصنيع والشراء للتمكن من توزيع ملياري جرعة لقاح بشكل متوازي بحلول نهاية عام ٢٠٢١. من خلال الانضمام إلى COVAX، ستتمكن كل من البلدان ذات التمويل الذاتي والبلدان الممولة من الوصول إلى لقاحات كوفيد-١٩ المتاحة.

جاهزية الدول والتنظيم

متطلبات الإستعداد للقاح كوفيد-١٩
يجب النظر الى العديد من الاعتبارات بهدف التوزيع الفعّال للقاح كوفيد-١٩ في الدول. في ١٦ تشرين الثاني ٢٠٢٠، أصدرت منظمة الصحة العالمية وثيقة "إرشادات حول تطوير خطة وطنية لنشر اللقاحات والتطعيم ضد فيروس كورونا المستجد"، موجهة إلى السلطات الوطنية المسؤولة عن إدارة توزيع وتنفيذ ومراقبة لقاحات كوفيد-١٩، وكذلك الشركاء المعنيين في تقديم الدعم المطلوب. تشمل الاعتبارات الرئيسية لأي بلد يستعد لتوزيع لقاح كوفيد-١٩ ما يلي:

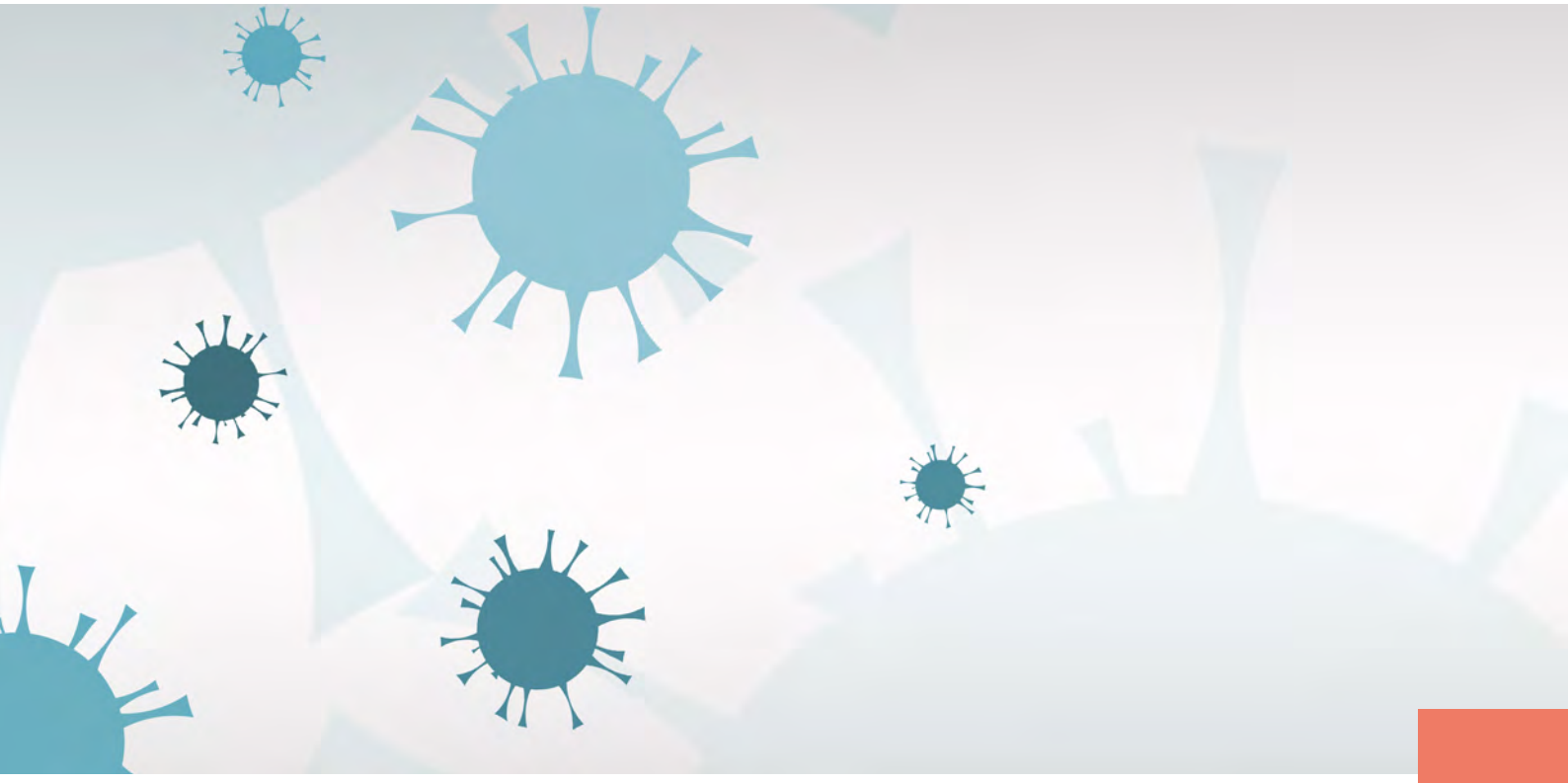
- تحديد الفئة المستهدفة واستراتيجيات توزيع اللقاح
- الكلفة والتمويل
- التخطيط والتنسيق
- مراقبة سلامة اللقاح
- تقبل اللقاح
- إدارة الموارد البشرية والتدريب
- تحضير سلسلة الإمدادات وإدارة نفايات الرعاية الصحية
- تقييم عملية استخدام اللقاح
- مراقبة جائحة كوفيد-١٩
- أنظمة مراقبة التطعيم
- الإستعداد التنظيمي

التصور العام حول لقاح كوفيد-١٩

تفاوتت الآراء والتصورات بشأن لقاحات كوفيد-١٩ بين أقصى درجات الحماس والدعم، إلى النقد والرفض الشديد، لا سيما على وسائل التواصل الاجتماعي. ومع ذلك، عند التقييم الرسمي لهذه التصورات في دراسات بحثية، تم الكشف بشكل عام عن نتائج إيجابية متعلقة بتقبل اللقاح. وارتبطت بهذا التقبل عوامل عدّة، منها خصائص اللقاح أو المريض، والثقة في البحوث العلمية، والتأييد الطبي والرسمي، والانتماءات السياسية. من ناحية أخرى، فقد ثبت أن توفير البيئة المؤاتية، والإستعانة بالتأثيرات الاجتماعية، وزيادة الحوافز يعزز من مدى تقبّل اللقاح.

الاعتبارات الاخلاقية

مع الضرورة الملحة لتطوير لقاح كوفيد-١٩، ظهرت بعد الشروخات والجدليات الأخلاقية في بعض النواحي العلمية والاجتماعية المتعلقة باللقاح. كانت العديد من القضايا مثل تلك المتعلقة باستخدام متطوعين أصحاء في التجارب، والتوزيع العادل للقاح على المستوى الدولي وداخل البلد، بالإضافة إلى مبدأ الاستقلالية و حرية القرار محور نقاش دائم.



توزيع لقاح كوفيد-١٩ في لبنان

في لبنان، تزامن انتشار الوباء مع مجموعة من الاضطرابات السياسية والاقتصادية والاجتماعية.

- يتزامن انتشار الوباء مع انفجار ٤ آب و تداعياته المستمرة، الذي أودى بحياة ٢٠٠ شخص على الأقل، وخلّف العديد الأضرار الجسمية بالمستشفيات، كما سرّع هجرة الأطباء والممرضات، ما أدى إلى إثقال كاهل النظام الصحي المرهق.
- يتزامن انتشار الوباء مع حقبة من التراخي السياسي والفساد والثورة وانعدام ثقة المواطنين بالقرارات الرسمية.
- يتزامن انتشار الوباء مع وصول البلد إلى حافة الانهيار الاقتصادي، وانهيار القطاع المصرفي، وتراجع القدرة الشرائية، وارتفاع نبرة التهديدات بوقف الدعم عن السلع والأدوية.
- يتزامن انتشار الوباء مع نقص في المقومات الأساسية، فعلى سبيل المثال، إن التخزين الأمثل للقاح يعتمد بشكل أساسي على خدمة كهرباء متواصلة، ما هو اليوم مهدد، نظراً للشحّ في عملية دعم الوقود.

تقدّر تكلفة لقاح Pfizer / BioNTech المنتظر بحوالي ٢٠ دولارًا للجرعة، وبالتالي تصل إلى ٤٠ دولارًا للجرعتين . من خلال عملية حسابية بسيطة، بالنسبة لأسرة من ٥ أفراد، فإن متوسط كلفة التلقيح هو ٢٠٠ دولار. علماً أن وزارة الصحة العامة و COVAX سيتكفلان بتغطية تكاليف اللقاح لنسبة محددة من المواطنين، وفي حال حجب الدعم عن اللقاح، فسيدفع غالبية المواطنين أكثر من ضعف الحد الأدنى الشهري للأجور البالغ ٦٧٥٠٠٠ ليرة لبنانية للحصول على اللقاح، و هذا في حال تم إستيراد كميات كافية في الدرجة الأولى. بمعنى آخر، نسبة كبيرة من المواطنين لن تستطيع الحصول الى اللقاح.

ومع ذلك، بُذلت جهود لتأمين حصّة لبنان من اللقاح. في ٢٣ تشرين الثاني ٢٠٢٠، أعلنت وزارة الصحة العامة أن لقاح Pfizer / BioNTech سيصل إلى لبنان بحلول منتصف شباط ٢٠٢١، بعد إجراء مفاوضات مبكرة مع الشركة. وفقًا لوزارة الصحة العامة، سيحصل ١٥٪ من السكان على اللقاح مجانًا (على نفقة وزارة الصحة العامة) ، بينما نأمل أن تتم تغطية ٢٠٪ من خلال COVAX.

سوف يُحترم مبدأ الإستقلالية و حرية القرار بحيث ستكون عملية التلقيح طوعية، تمنح في البداية لمجموعات ذات أولوية محددة مسبقًا. لم يتم الإعلان عن خطط التلقيح المستقبلية لمختلف الفئات حتى الآن. ومع ذلك، من المتوقع أن تصل لقاحات كوفيد-١٩ التي تنتجها شركات أخرى إلى السوق اللبنانية.

بلإضافة إلى ذلك، أُنشأت اللجنة الوطنية للقاح كوفيد-١٩، بهدف:

- إعداد آلية للموافقة على اللقاح وشرائه وتسجيله واستلامه وتوزيعه
- مراقبة الآثار الجانبية للقاح
- مراقبة سلسلة التبريد والقضايا الأخرى المتعلقة بالمحافظة على جودة اللقاح
- تحديد المجموعات المستهدفة وترتيبها حسب الأولوية
- التأكد من وصول اللقاح إلى الفئات المستهدفة بطريقة عملية ومنصفة

في ضوء الحالة المضطربة التي يمر بها لبنان، فإن التوزيع والتلقيح الناجحين يتطلبا:

- ترشيد إستخدام الموارد المحدودة
- تأمين المتطلبات الأساسية لجميع مراحل توزيع اللقاح
- الشفافية والتواصل
- إرادة سياسية واعتبار الصحة العامة أولوية
- التقليل من النفقات الشخصية على عاتق الأفراد
- إدراج الفئات المهمشة مثل اللاجئين والعمال المهاجرين
- السيطرة على السوق السوداء والصفقات الجانبية
- تطوير خطط للمحافظة على العاملين الصحيين
- الإلتزام بمبادئ الإستقلالية والإنصاف الصحي

Preamble

As the COVID-19 pandemic evolves, its substantial toll on health and the economy continues to unfold. The COVID-19 pandemic has challenged and overstretched health systems beyond capacities and the response to the pandemic has required difficult and unprecedented decisions. As desperately as countries were seeking to end COVID-19 pandemic, pharmacological and non-pharmacological interventions were unsuccessful in curtailing the spread of the virus, while natural herd immunity proved to be far-fetched and precarious. With all of this in hand, a vaccine appeared to be the only solution to control the pandemic and the most promising means for restoring a semblance of normalcy to our lives.

This document intends to describe the journey to a COVID-19 vaccine from the expedited production process to distribution at the country level, passing through public acceptance and ethical disputes. This document also provides an overview of considerations for COVID-19 vaccine deployment in Lebanon.

The Imperative Need for a Vaccine

Several factors have rendered a COVID-19 vaccine an inevitable option and the only opportunity for counties seeking to stop the extensive spread of the virus.

HIGH DISEASE BURDEN

As of January 4th, 2021, there have been 83,910,386confirmed cases of COVID-19, including 1,839,660 deaths worldwide, reported to the World Health Organization (WHO) (WHO, 2020a). At the economic front, the cost of this pandemic is estimated to be at least 1 trillion US dollars for the year 2020, with global economic growth slowing down to 2% (United Nations, 2020). Poverty is expected to rise from 30% in 2019 to 45% or more by the end of 2020, while extreme (food) poverty would more than double to reach 22% (World Bank, 2020).
In Lebanon, on January 4th 2021, the cumulative number of COVID-19 cases was 192,136 cases since the advent of the epidemic in the country on February 21st 2020 with 1499 deaths recorded due to the virus (MOPH, 2020a).

LIMITED SUCCESS OF PHARMACOLOGICAL INTERVENTIONS

Up until now, no cure has been identified for COVID-19. Only one medication, known as Remdesivir, despite its limited clinical effectiveness (Wang et al., 2020; Beigel et al., 2020), has been FDA-approved for the treatment of hospitalized patients with COVID-19 regardless of disease severity (FDA, 2020a). The WHO did not endorse the use of remdesivir for COVID-19 patients due to lack of sufficient evidence on its efficacy (WHO Solidarity Trial Consortium, 2020). Only steroids (dexamethasone) are a universally acknowledged therapy of COVID-19 patients with hypoxemia (Recovery Collaborative Group, 2020). Other interventions including convalescent plasma, anti-malarials, IL-6 inhibitors and other biological treatments and small molecules have been used in practice with varying clinical responses (UpToDate, 2020).

CHALLENGED IMPLEMENTATION OF NON-PHARMACOLOGICAL INTERVENTIONS

Thus far, non-pharmacological interventions have been the mainstay of the response to COVID-19 and are being used across the world to flatten the epidemiologic curve.

Several successful non-pharmacological interventions have been identified in the literature. Among such effective interventions are travel restrictions (Burns er al, 2020), isolation and quarantine, physical distancing, use of face masks, and hand hygiene (Odusanya, Odugbemi, Odugbemi, & Ajisegiri, 2020). Exploring real time incidence data in Lebanon before the August 4 explosion, one study revealed that nationwide lockdown was effective in reducing cases and had been successful in containing the virus (Kharroubi & Saleh, 2020). However, proper implementation of such interventions is challenged by impediments related to feasibility, acceptability, and compliance in many settings. In this regard, one study assessing the socio-economic effects of air travel ban on aviation projected that in the first quarter of 2020, the impact of aviation losses could negatively reduce World Gross Domestic Product by 0.02% to 0.12%. By the end of 2020, the loss could be as high as 1.41–1.67% and job losses may reach the up to 30 million units (Lacus et al, 2020). With such massive economic losses, flight restrictions may not be a feasible long-term option. Aside from travel restriction, one study from the UK reported that 75.1% of participants were non-adherent to self-isolation when they or someone in their household had symptoms of COVID-19 (Smith et al, 2020). Another study from the US demonstrated that lower income communities exhibited less social distancing (Weill, Stigler, Deschenes, & Springborn, 2020). Such implementation barriers understandably limit the realization of the pursued impact of strategies intended to halt the spread of COVID-19.

HIGH VIRUS INFECTIVITY

COVID-19 is a global concern because of its high infectivity and transmission capacity. Several systematic reviews have addressed epidemiologic characteristics of the virus. Current evidence suggests that it takes about 3-7 days for the epidemic to double in size (Park et al, 2020). Two other meta-analyses estimated the basic reproduction number (R0) of the virus to be 2.87 (Billah, Miah, & Khan, 2020) and 3.38 (Alimohamadi, Taghdir, & Sepandi, 2020). More recent estimates placed the R0 higher at 5.7 (Sanche et al., 2020). Even asymptomatic cases are capable of transmitting the infection. According to one systematic review, 18.8% of close contacts exposed to asymptomatic index patients were COVID-19 positive (Yanes-Lane et al, 2020).

Since November 2020, a new variant of COVID-19, referred to as SARS-CoV-2 VOC 202012/01, has been identified in England, accounting for 60% of recent infections in London. This variant contains a series of mutations and is predicted to potentially be more rapidly transmissible than other circulating strains of COVID-19 (CDC, 2020a). As a result, an estimated increase in R0 by 0.4 with an increase in transmissibility by up to 70% is expected (ECDC, 2020). Fortunately, so far, there is no evidence that this variant causes more severe illness or increased risk of death (CDC, 2020a).

The transmissibility of a virus is measured by the basic reproduction number (R0), which measures the average number of new cases generated per infectious case.

"Herd immunity is a key concept for epidemic control. It states that only a proportion of a population needs to be immune (through overcoming natural infection or through vaccination) to an infectious agent for it to stop generating large outbreaks. A key question in the current COVID-19 pandemic is how and when herd immunity can be achieved and at what cost". (Fontanet & Cauchemez, 2020)

DIFFICULT TO ATTAIN AND COSTLY HERD IMMUNITY

Herd immunity is achieved when one infected person in a population generates less than one secondary case on average (Fontanet & Cauchemez, 2020). Assuming an R0 estimate of 3 for COVID-19, the herd immunity threshold is approximately 67%. This means that the incidence of infection will start to decline once 67% of the population acquire immunity against COVID-19 (Randolph & Barreiro, 2020). (For more elaboration on the transmission and herd immunity, please refer to Appendix 1).

Two possible ways exist to build widespread immunity against COVID-19 (Randolph & Barreiro, 2020):

1. Natural immunity of the population attained through infection with the virus
2. Mass vaccination, which requires the development of an effective and safe vaccine

A number of inherent problems are confronted when relying on natural immunity for achieving herd immunity:

- It is still not very clear how long naturally acquired immunity against COVID-19 lasts, particularly among those who had mild forms of disease, and whether it might take several rounds of re-infection before robust immunity is attained (Fontanet & Cauchemez, 2020). Previous studies in confirmed SARS patients have demonstrated that neutralizing antibody responses against SARS-CoV persisted up to 2 years, although all individuals displayed low titers after about 15 months (Mo et al., 2006). Hence, protection against reinfection with coronavirus species tends to diminish given sufficient time. If this proves to be also true for COVID-19, persistent herd immunity may never be attained in the absence of vaccination.
- Particularly in the context of attaining herd immunity, a regard for finite healthcare resources cannot be overstated, as natural herd immunity inherently relies on allowing a large fraction of the population to become infected. Unchecked, the spread of COVID-19 will rapidly overwhelm healthcare systems. A depletion in healthcare resources will lead not only to elevated COVID-19 mortality but also to increased all-cause mortality. This effect will be especially devastating for countries in which hospitals have limited surge capacity, where minimal public health infrastructure exists, and among vulnerable communities (Randolph & Barreiro, 2020).
- Most importantly, the cost - in terms of human lives - of achieving herd immunity through natural infection is grave, especially in the absence of improved patient management and without optimal shielding of individuals at risk of severe complications. If we look at the global population, a case fatality rate of COVID-19 between 0.25-3.0% (Wilson et al., 2020) can add up to a huge number of fatalities if we allow the virus to run wild and infect people. Assuming an optimistic herd immunity threshold of 50% for countries such as France and the USA, this would translate into 100,000–450,000 and 500,000–2,100,000 deaths, respectively. Men, older individuals and those with comorbidities are disproportionally affected, with infection fatality ratios of 3.3% for those older than 60 years and increased mortality in individuals with diabetes, cardiac diseases, chronic respiratory diseases, or obesity (Salje et al., 2020; Flaxman et al., 2020).

An effective vaccine presents the safest way to reach herd immunity. It can slow down or halt the spread of infection, without uprising mortality or beating the health system's response capacity. Moreover, given that there are increasing numbers of reports of long-term complications even after mild COVID-19 infection, vaccines are likely to provide a safer alternative even for individuals who are not classified as at-risk (Fontanet & Cauchemez, 2020). As a result, developing and delivering a vaccine may be the most likely way to end the pandemic.

The Path to a COVID-19 Vaccine

Progressing at Pandemic Pace through Trials

According to the Food and Drug Administration (FDA), the general stages of the development cycle of a vaccine are (FDA, 2020b): (For further information related to the stages and phases of vaccine development, please refer to Appendix 2).

Typically, vaccine development is a long, complex process, often lasting 10-15 years (IFPMA, 2019). As shown in the figure below (Fig. 1), the development of many of the well-known vaccines has spanned over a decade or longer.

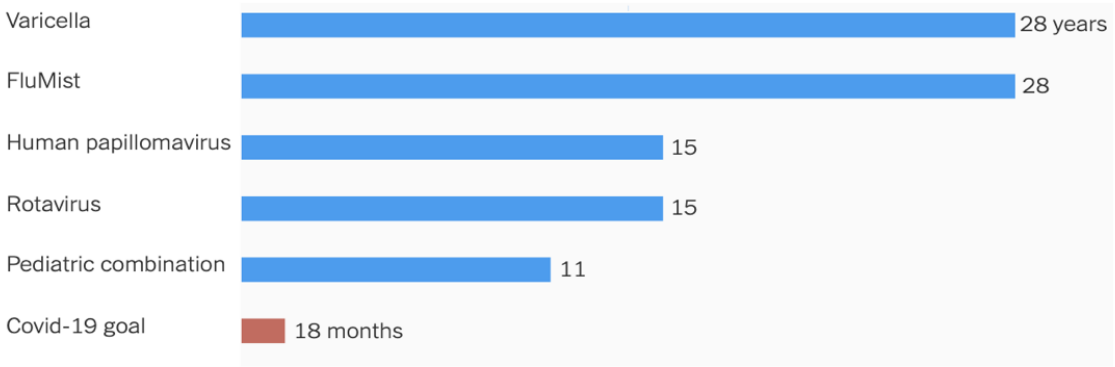


Figure 1: The vaccine development process has typically taken a decade or longer. Adopted from (Plotkin, Orenstein, & Offit, 2018)

In public health emergencies, such as a pandemic, the development process may be atypical or expedited. Governmental agencies, international counterparts, academia, nonprofit organizations and pharmaceutical companies developed a coordinated strategy for prioritizing and speeding the development of the most promising treatments and vaccines for COVID-19 (FDA, 2020b). In addition, FDA provided clear communication to the pharmaceutical industry pertaining to the scientific data and information needed for safe and effective vaccines and worked to provide advice on their proposed development plans and assessment of the data that is generated. Provided certain criteria are met, manufacturers may submit a request for Emergency Use Authorization (EUA) to FDA to facilitate the availability and use of their vaccine (FDA, 2020b). Key considerations for submission for EUA are summarized below (FDA, 2020c).

Investigational new drug
A substance that has been tested in the laboratory and has been approved by the FDA for testing in people.

Biologics License Application
Request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce

CRITERIA AND CONSIDERATIONS FOR THE ISSUANCE OF AN EUA FOR A COVID-19 VACCINE

- The agent can cause a serious or life-threatening disease or condition.
- Based on the totality of scientific evidence available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2.
- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

KEY LOGISTIC RECOMMENDATIONS FOR THE REQUEST FOR AN EUA FOR A COVID-19 VACCINE

- A detailed description of the chemistry, manufacturing, and controls data should be submitted to a relevant investigational new drug application or cross-referenced master file at least one month prior to submission of an EUA request.
- FDA strongly encourages the vaccine sponsor to provide FDA with notice within 24 hours after any interim analysis has been completed, on the basis of which submission of an EUA request is planned.

Following submission of an EUA request and issuance of an EUA, a sponsor would continue to collect placebo-controlled data in ongoing trials and would work towards submission of a Biologics License Application as soon as possible. FDA's recommendations regarding safety and effectiveness data aim to ensure that the clinical development of a COVID-19 vaccine has progressed far enough that issuance of an EUA for the vaccine would not interfere with the ability of an ongoing Phase 3 trial to demonstrate effectiveness of the vaccine to support licensure and to continue safety assessments (FDA, 2020c).

Characteristics of an Ideal COVID-19 Vaccine

In April 2020, the WHO published 'WHO Target Product Profiles for COVID-19 vaccines' which describes the preferred and minimally acceptable profiles for human vaccines for long term protection of persons at high ongoing risk of COVID-19 such as healthcare workers and for reactive use in outbreak settings with rapid onset of immunity (WHO, 2020b). In summary, according to the document, an ideal or 'preferred' COVID-19 vaccine is one that is:

- Able to protect at least 70% of people
- Safe in short term and long term
- Safe in different age groups (children pregnant, elderly)
- Ideally given in a single shot
- Provide immunity for as long as possible (confers protection for at least 1 year)
- Higher storage temperatures and higher thermostability (to facilitate storage and distribution)

Vaccines Under Investigation and Production

There are four categories of COVID-19 vaccines in used clinical trials (Gavi, 2020a): whole virus, protein subunits, nucleic acid, and viral vectors (For more details related to categories of COVID-19 vaccine, please refer to Appendix 3). Until December 29th 2020, 60 candidate vaccines are undergoing clinical evaluation with 172 other candidate vaccines in the preclinical evaluation phase (WHO, 2020c).

Only two COVID-19 vaccines, one produced by Pfizer/BioNTech (FDA, 2020d) and another by Moderna (FDA, 2020e), have been authorized to date by the FDA for use under EUA. Both vaccines have also been authorized by the European Medicines Agency (EMA) for conditional marketing authorization (CMA) (EMA, 2020a; EMA, 2020b).

Conditional Marketing Authorization

In the European Union, CMAs allow for the authorisation of medicines that fulfil an unmet medical need on the basis of less complete data than normally required. This happens if the benefit of a medicine or vaccine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available. CMAs are being used in the context of the pandemic to promptly respond to the public health threat. Once a CMA has been granted, companies must provide further data from ongoing or new studies within pre-defined deadlines to confirm that the benefits continue to outweigh the risks.

Key characteristics of the two vaccines are presented in the table below (WHO, 2020c; Gavi, 2020b; CDC, 2020b; Healthline, 2020; FDA, 2020d; FDA, 2020e)

Vaccine	Technology	Efficacy	Common Side Effects	Age indications	Number of Doses	Storage	Approximate Price
Pfizer/ BioNTech	RNA	95% (even in adults over 65 years where efficacy was more than 94%)	Pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, and fever	16 years of age and older	2 doses series separated by 21 days	-70ºC for 6 months and 2-5ºC for up to 5 days	20$ per dose
Moderna	RNA	94%	Pain at the injection site, tiredness, headache, muscle pain, chills, joint pain, swollen lymph nodes in the same arm as the injection, nausea and vomiting, and fever	18 years of age and older	2 doses separated by 28 days	-20ºC for 6 months and 2-8ºC for 30 days	38$ per dose

Other vaccines under clinical evaluation are in various phases of development. (A summary of the characteristics of vaccines undergoing Phase 3 trials is presented in Appendix 4).

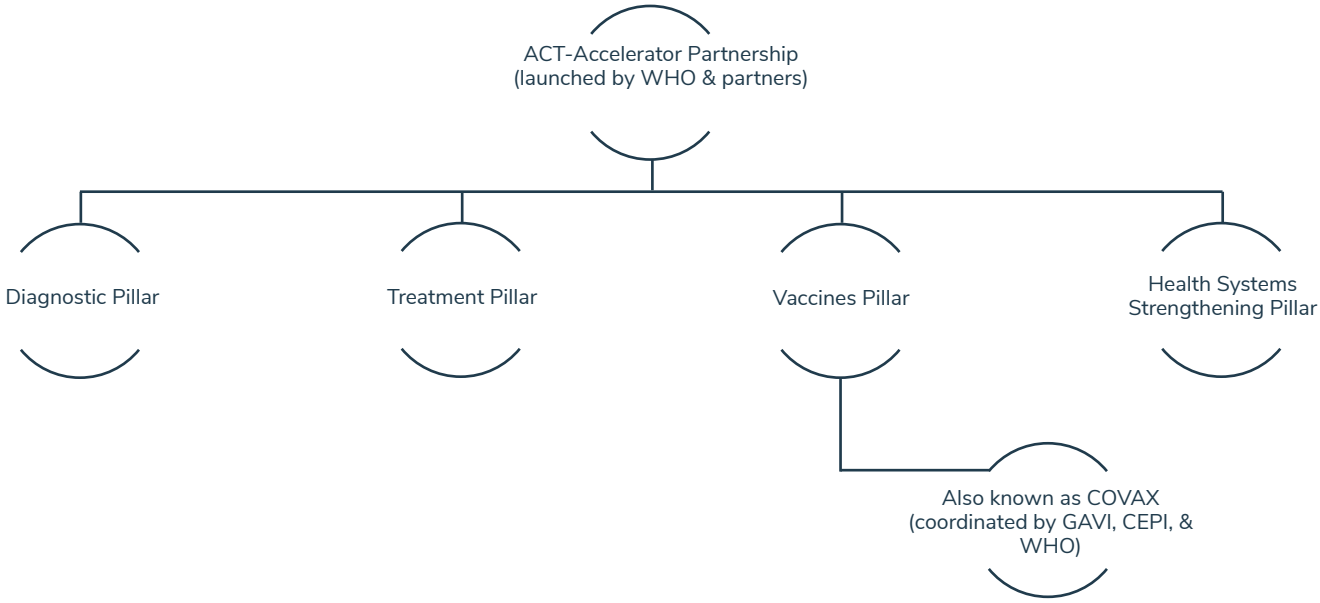
It is worth mentioning that luckily, there is no evidence yet to suggest that the new variant of COVID-19 affects vaccine efficacy. The simple reason is that vaccines are “polyclonal”, thereby producing antibodies that target several parts of the spike protein. As a result, the virus would likely need to accumulate multiple mutations in the spike protein to evade immunity induced by vaccines or by natural infection (CDC, 2020a).

Safety Assurance Measures

Given the expedited process of COVID-19 vaccines development, there remains concerns and ambiguity regarding long term effects and side effects. Counterstrategies adopted by scientists to ensure safety of vaccines include safety investigation at every stage of vaccine development, serious adverse events monitoring after clinical trials, development of a consensus on how to adequately assess disease enhancement (the so-called "vaccine-mediated enhanced disease") and other potential adverse events, active surveillance by countries to determine the background rates of adverse events, and development of vaccine safety profiles (Gavi, 2020c). In addition, FDA notes that there should be an adequate plan for safety data collection among individuals vaccinated under an EUA vaccine (FDA, 2020c).

Global Solidarity and Coordination

International efforts were mobilized to expedite the production of a COVID-19 vaccine and to develop a system for equitable global distribution of the vaccine. In April 2020, The ACT-Accelerator partnership, launched by WHO and partners, was initiated with an aim to support fast, coordinated, and successful global efforts to develop tools to fight COVID-19. The ACT-Accelerator is organized into four pillars of work: diagnostics, treatment, vaccines and health system strengthening (WHO, 2020d). COVAX is the vaccines pillar of the ACT-Accelerator, convened and coordinated by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI), and the WHO. The purpose of COVAX is to speed up the search for an effective vaccine. Concomitantly, it is supporting manufacturing and purchasing capabilities so that 2 billion vaccine doses can be fairly distributed by the end of 2021 (Gavi, 2020d).



By joining COVAX, both self-financing countries and funded countries will gain access to the portfolio of available COVID-19 vaccines. Self-financing countries can request vaccine doses sufficient to vaccinate between 10-50% of their populations, depending upon how much they buy into it. By pooling resources through the facility, participating countries and economies are essentially helping to increase the world's chances of bringing about COVID-19 vaccines as quickly as possible, and in the quantities needed. Subject to funding availability, funded countries will receive enough doses to vaccinate up to 20% of their population in the longer term. Since demand is initially likely to exceed supply, allocation will be spread across countries based on the number of doses that are available and increased as availability increases (Gavi, 2020d).


VACCINE
SARS-CoV-2
10ml

Country Readiness and Regulation

Preparation Requirements for a COVID-19 Vaccine

Numerous considerations need to be factored in for an effective country deployment of a COVID-19 vaccine. On November 16th 2020, WHO issued a document 'Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines' directed at national authorities who are responsible for managing deployment, implementation and monitoring of COVID-19 vaccines, as well as partners who provide the required support. The document covers major areas key to enabling the successful deployment, implementation and monitoring of COVID-19 vaccines. Key considerations for any country preparing for COVID-19 vaccine deployment and distribution are summarized below (WHO, 2020e):

Key Area	Considerations
Regulatory Preparedness	• Regulatory requirements including importation and customs clearance procedures • Expected challenges or exemptions that may be required regarding importation and use • National regulatory pathways being put in place to expedite vaccine availability
Planning and Coordination	• COVID-19 coordination mechanism and integrated efforts at country level • Consideration on whether the country has adapted an existing national governance mechanism or established novel channels for coordination and collaboration with advisory bodies
Costing and Funding	• Vaccine costing and funding plan • Additional costs for vaccine deployment and distribution
Identification of Target Population and Delivery Strategies	• Mechanism for order of priority • Vaccination strategies for each target group (campaigns, schools, mobile clinics,...) • System adjustments required to build/strengthen the appropriate vaccination platform, including non-conventional vaccine delivery approaches to reach identified target groups • Infection Prevention and Control measures, including adequate PPE to minimize exposure risk during immunization sessions • Opportunities for integrating COVID-19 vaccination with other health interventions
Preparation of Supply Cain and Management of Healthcare Waste	• Assessment of potential ports of entry, points of storage, transportation capacity and cold chain capacity (categorized at +2°C to +8°C, -20°C, and -60°C to -80°C storage temperatures) • Assessment of issues, requirements and challenges related to transportation of vaccines and supplies • Estimating cold chain and dry store capacity requirements, issues, challenges and solutions • Description of distribution processes including identified gaps, challenges and solutions to complete vaccine deployment prior to vaccination start date • Summary of the volumes, doses, and ancillary items to be distributed by areas/ zones • Assessment of current waste management capacity and practices and the changes or upgrades needed to accommodate additional volume of wastage due to the new vaccine, and plans for upgrading the waste management system

Key Area	Considerations
Human Resource Management and Training	• National overview of human resources by category • Determination of the need for additional human resources, including staff for community mobilization, cold chain and supply chain management, and other support functions • Training strategy • Supportive supervision system
Vaccine Acceptance and Uptake	• Development of a targeted, multicomponent and costed plan to achieve high acceptance and uptake • Design of interventions across a range of key areas: national advocacy and stakeholder engagement, communications and media engagement for public information, risk communications and community engagement, engagement and capacity building of frontline health workers to support their role as vaccine recipients and as vaccinators, and misinformation management
Vaccine Safety Monitoring	• Strategy for post-deployment surveillance • Role of national safety committee (with the participation of scientific societies, regulatory authorities and immunization programs) • Line of reporting and roles and responsibilities of staff
Immunization Monitoring Systems	• Data needs and monitoring objectives including indicators to be used • Determination of the system to be used to record, report, analyse and use vaccination data and dashboard to be used to monitor COVID-19 vaccination
COVID-19 Surveillance	• Assessment of the need for modification or replacement of COVID-19 surveillance system to respond to the country's evolving needs • Determination of the objectives and type of surveillance
Evaluation of COVID-19 Vaccine Introduction	• Evaluation of vaccine effectiveness and the technical support for such evaluation • Plans for post-introduction evaluations, including aspects of vaccine program to be evaluated (importation, regulatory, supply/cold chain, wastage, coverage among total population and key risk groups, safety monitoring, and others) • Lessons learned, in addition to a consultative exercise at national and subnational levels, involving different stakeholders

Public Perception of COVID-19 Vaccine

Public perception regarding COVID-19 vaccines have spanned over the whole spectrum from utmost enthusiasm and support to extreme criticism and rejection, particularly on social media platforms. Several conspiracy theories have recently come to light regarding an ulterior motive behind COVID-vaccines. Some anti-vaccination campaigners have claimed that a woman who took part in a UK vaccine trial died (Ball, 2020). Other narratives claim that Bill Gates had himself created the virus, patented it, and is currently supporting vaccine manufacture to control people (Ball & Maxmen, 2020), through the implantation of microchips (Ball, 2020). In Pakistan, it has been perpetuated by some that COVID-19 -including its treatments and vaccines- is a grand illusion and a conspiracy against Muslim countries (Khan et al., 2020).

Social media has a role in disseminating misleading information. One study assessing debates and discussions surrounding vaccines that emerged from the global pool of around three billion Facebook users revealed that although smaller in overall size, anti-vaccination clusters manage to become highly entangled with undecided clusters in the main online network, whereas pro-vaccination clusters were more peripheral (Johnson et al., 2020). In Twitter, one study demonstrated that falsehood diffused significantly farther, faster, deeper, and more broadly than the truth in all categories of information (Vosoughi, Roy & Aral, 2018). Expectedly, beliefs in COVID-19-related conspiracy theories were inversely related to the (a) perceived threat of the pandemic, (b) adopting preventive actions (including wearing a face mask), (c) perceived safety of vaccination, and (d) intention to be vaccinated against COVID-19 (Romer & Jamieson, 2020). In a step forward in the fight against vaccine misinformation, even months before the onset of COVID-19 pandemic, Facebook announced on September 4, 2019 that user searches for vaccine-related content will be directed to either the US Centers for Disease Control and Prevention or the World Health Organization websites for accurate information regarding vaccines (WHO, 2020f).

When assessed formally in a research study, positive results regarding public vaccine acceptance were predominantly revealed. In a study in Italy, 86.1% Italian university students reported that they would choose to have a vaccination for the COVID-19 virus while 13.9% students reported that they would not or are hesitant to get the vaccine (Barello, Nania, Dellafiore, Graffigna, & Caruso, 2020). In an online public survey in France, 26% of respondents stated that they would not use a vaccine against COVID-19 if it becomes available. The social profile of reluctant responders is worrying as this attitude was more prevalent among low-income groups (37%), who are generally more exposed to infectious diseases, among young women (36%), who typically play a crucial role regarding childhood vaccination, and among people aged older than 75 years (22%), who are inherently at an increased risk for severe illness from COVID-19 (Coconel Group, 2020). As for caregivers, 65% of caregivers reported that they intend to vaccinate their child against COVID-19 once a vaccine is available. The most common reason reported by caregivers intending to vaccinate was to protect their child (62%), and the most common reason reported by caregivers refusing vaccination was the vaccine's novelty (52%) (Goldman et al., 2020).

Several factors have been associated with vaccine acceptance and uptake:

Vaccine characteristics

- An increase in vaccine efficacy, an increase in protection duration, and a decrease in major adverse events was also associated with a higher vaccine uptake.
- An FDA emergency use authorization was associated with a lower probability of receiving a vaccine, similarly for a vaccine that originated from a non-US country (Kreps et al., 2020).

Patient Related Factors

- One analysis in six high-income countries found that among caregivers, increased intended uptake was associated with children that were older, children with no chronic illness, children up-to-date on their vaccination schedule, recent history of vaccination against influenza, and caregivers concerned their child had COVID-19 at the time of survey completion (Goldman et al., 2020).

Healthcare Provider Perceived Risk

- Employment within the healthcare sector in a high-income country did not significantly influence respondents' acceptance or rejection of a potential COVID-19 vaccine.
- Healthcare staff involved in the care of COVID-19 positive patients, and individuals considering themselves at risk of disease, were more likely to self-report acceptance of COVID-19 vaccination.
- In contrast, parents, nurses, and medical workers not caring for COVID-19 positive patients expressed higher levels of vaccine hesitancy (Dror et al., 2020).

Trust in Research and Vaccines

- In Italy, willingness to COVID-19 vaccine correlated with trust in research and in vaccines, which decreased between phase 1 and phase 2 of the Italian pandemic (Palamenghi, Barello, Boccia, & Graffigna, 2020).

Medical and Official Endorsement

- In the US, participants were more willing to get a COVID-19 vaccine if their healthcare provider would recommend it (Reiter, Pennell, & Katz, 2020).
- Endorsements from the US Centers for Disease Control and Prevention and the World Health Organization were associated with higher probabilities of choosing to take a vaccine (Kreps et al., 2020).

Political Affiliation and Interference

- In France, participants' acceptance of a vaccine against COVID-19 strongly depended on their vote at the first round of the 2017 presidential election: those who had voted for a far left or far right candidate were much more likely to state that they would refuse the vaccine, as well as those who abstained from voting (Coconel Group, 2020).
- Vaccine endorsement by President Trump was associated with a lower probability of choosing to take a vaccine (Kreps et al., 2020).
- Another expressed concern related to political interference was that political appointees may insist on an Emergency Use Authorization for a vaccine over the recommendation of FDA career scientists. Such interference would both present a direct risk to the US public and cause incalculable damage to public trust in the federal government's ability to make critical scientific decisions (Bauchner, Malani, & Sharfstein, 2020).

In 2019, the World Health Organization named vaccine hesitancy as one of the top 10 threats to global health. The call was made amid numerous measles outbreaks, when global uptake rates for the measles, mumps, and rubella vaccine slipped to 85%, down from the required target of 95% (WHO, 2019). In response to the emerging COVID-19 hesitancy, several interventions were designed to enhance acceptance and increase uptake. In particular, behavioural research has shown that vaccine acceptance and uptake can be increased by adopting the three strategies below (WHO, 2020i).

Creating an enabling environment -making vaccination practical, easy, and affordable, in all relevant respects.	Environmental factors include location, cost, time, the experience of being vaccinated, information, default arrangements, and health regulations or mandates. Reducing barriers and making it easy to get vaccinated will increase vaccine uptake, especially for people who are not deliberately avoiding vaccination (Schmid et al., 2017). Examples of enabling environments: • Setting as a default vaccinating all students will likely result in a higher vaccination rate than if the default is to provide vaccination only to those who opt in (Giubilini et al., 2019) • Making vaccines easily accessible in safe, familiar and convenient locations, such as drop-in clinics (Schoch-Spana et al., 2020) • Ensuring that proper safety measures are visibly in place (Saso, Skirrow, & Kampmann, 2020) • Ensuring that health care and community workers are well trained and well supported (WHO, 2020g)
Harnessing social influences - especially from people who are particularly trusted by and identified with members of relevant communities.	• Making social norms in favor of vaccination: Communication efforts to promote the perception that the majority of people are getting vaccinated are likely to increase vaccination acceptance (Bruine de Bruin, Parker, Galesic, & Vardavas, 2019). • Highlighting new and emerging norms in favour of vaccination: Allowing people to learn that others are increasingly engaging in certain behaviours will encourage them to follow similar behaviors (Sparkman & Walton, 2017) • Leveraging the role of health professionals: Early priority groups for COVID-19 vaccines include health professionals, who are often the most trusted source of advice on vaccination (Dubé et al., 2013). Studies have shown that health professionals are more likely to recommend vaccination if they themselves have been vaccinated. As such, targeting efforts to facilitate the vaccination of health professionals can in turn lead to greater acceptance and uptake by the general population. Such efforts can include improving health professionals' knowledge about the vaccine as well as increasing their co-workers' support for the vaccine (Paterson et al., 2016). • Supporting health professionals to promote vaccination: Health professionals should be equipped with tools to effectively encourage people to get vaccinated against COVID-19 (Leask et al., 2012). • Amplifying endorsements from trusted community members: Endorsers that share similar values and characteristics with the relevant group (such as religious or ethnic identity) are more likely to be influential (CASS, 2020). Endorsement of a COVID-19 vaccine by prominent scientists has also been found to increase trust in the vaccine (Bokemper, Huber, Gerber, James, & Omer, 2020).

Increasing motivation - through open and transparent dialogue and communication about uncertainty and risks	• Building timely trust in vaccines: Strategies which aim to change people's thoughts and feelings towards vaccination have not always been successful in increasing uptake (Brewer, Chapman, Rothman, Leask, & Kempe, 2017). It is therefore important to focus on building trust in COVID-19 vaccines before people form an opinion against them. • Widely rolling out a vaccine followed by announcements of adverse risks can lead to long-lasting damage in confidence in the vaccine (Mills, Rahal, & Brazel, 2020). Communicating consistently, transparently, empathetically and proactively about uncertainty, risks, and vaccine availability will contribute to building trust. • Leveraging anticipated regret in communications: Anticipated regret has been shown to be a strong predictor of vaccination, and there is potential promise in evoking it to encourage vaccination (Brown et al., 2010). This can be done through highlighting the consequences of inaction. • Emphasizing the social benefits of vaccination: Communicating the social benefits of vaccination has been found to increase vaccination intention, particularly when the risk associated with vaccination is low and getting vaccinated involves little effort (Betsch, Böhm, & Korn, 2013). In the context of COVID-19, where there can be prolonged duration of illness, putting emphasis on the economic benefits, such as being able to stay in the workforce and provide for one's family, might encourage vaccine uptake.

Implementation Considerations

Communication strategies about vaccines should consider the following (COVID-19 Global Evaluation Coalition, 2020):

- Identify people's concerns and misconceptions about the disease and the vaccine
- Provide information that people regard as trustworthy
- Ensure that it is easy to find information about how the vaccine was developed, its contents, effects and safety, and the background for the decision to recommend it
- Provide information that is transparent; consistent; timely; understandable; and accessible, including among hard-to-reach groups
- Provide practical information about where to get the vaccine and the vaccine procedure

Ethical Considerations

With a sense of urgency to develop a COVID-19 vaccine, trade-offs in scientific and social value have surfaced. Several issues such as those pertaining to the use of healthy volunteers in trials, the equitable distribution of the vaccine at the inter and intra country level, as well as the principle of autonomy in the context of a COVID-19 vaccine have been persistently a matter of debate. A glimpse of the controversies and ethical concerns that have emerged in the past few months is presented in the section below.

CONTROVERSIES SURROUNDING COVID-19 VACCINE RESEARCH TRIALS

Human challenge trials	Young, healthy people will be intentionally exposed to the virus responsible for COVID-19 (Callaway, 2020; Cohen, 2020), with over 38,000 people demonstrating willingness to participate in COVID-19 human challenge studies with 1Day Sooner, a non-profit organization. In this regard, the UK government has invested £33.6 million to support such trials (McPartlin et al., 2020). Human challenge trials may prove beneficial for second and third generation vaccines and can help to answer essential questions about COVID-19 immunity, such as correlates of protection and pathogenesis (McPartlin et al., 2020). Moreover, such trials have been compared to firefighting and living kidney donation, activities that are permissible and justified despite their risks (Dawson, Earl, & Livezey, 2020). On the other hand, human challenge trials have the potential to be exploitative as there are disparities in power, information, and control between researchers and volunteers (Dawson, Earl, & Livezey, 2020). The risks to participants in challenge studies are too uncertain and too great to be permitted (McPartlin et al., 2020). They are unlikely to accelerate the development of the first vaccines to hit the market (McPartlin et al., 2020) and may not even result in the development of a useable vaccine (Richards, 2020). There is also a concern that people will participate for the money without appreciating the risks (Callaway, 2020). In addition, there is a risk of community spread of the virus from participants. Participants in human challenge trials might have rightful claim to prioritization for critical care resources such as ventilators or other treatments that are in short supply. Such prioritization, which is based on the principle of reciprocity, might come at the cost of non-participants, with consequent negative health effects (Schaefer et al., 2020). Moreover, some social groups, including Black, Asian, and minority ethnic groups, are at higher risk of the virus because of structural injustice. Selecting people form these groups for participation in challenge studies would compound unfairness and wrongly increase the burdens they face (McPartlin et al., 2020). Additionally, conducting these experiments may damage the reputation of research and researchers and may lead to long-lasting diminished public trust, in other words 'the start of a slippery slope in research' (Richards, 2020).

Using human fetuses in research	Senior Catholic leaders in the U.S. and Canada, along with other antiabortion groups raised ethical objections to COVID-19 vaccine candidates that are manufactured using cells derived from human fetuses electively aborted decades ago. Such fetal cells are used as factories to make adenoviruses that carry genes for COVID-19 (Wadman, 2020).
Participation of disadvantaged populations	Care must be taken when testing COVID-19 vaccine in disadvantaged populations such as prisoners (Strassle et al., 2020; Wang et al., 2020) and certain ethnic groups. In Africa, for example the benefits of testing a coronavirus vaccine where there are no masks or treatments available is questioned (Hellmann et al., 2020). However, the exclusion of African populations from COVID-19 vaccine trials rests on the assumption that an efficacious vaccine developed and tested elsewhere is effective in African populations which unfortunately may turn out not to be the case (Singh, 2020).
Selecting the comparative arm when testing a new vaccine	Scientists and researchers must find the most ethical way to proceed when comparing a purportedly promising vaccine against a purportedly less promising one. The same challenge arises when one effective vaccine has been successfully developed against an epidemic disease and researchers seek to test the efficacy of another vaccine for the same pathogen in clinical trials involving human subjects. On one hand, it is a firm principle of medical ethics that an effective treatment or vaccine should not be withheld from patients. On the other hand, it may be justified to conduct a trial for a candidate vaccine if it is expected to have certain advantages compared with the existing product (Eyal & Lipsitch, 2020).

CONTROVERSIES SURROUNDING COVID-19 VACCINE IN REAL LIFE PRACTICE

Prescribing vaccines before data is publicly available	On one hand, insisting on normal practice may delay potentially life-saving interventions. On the other hand, the trust placed in licensed medicines is a strong reason for insisting on full data transparency and reporting, even in the face of a pandemic (Johnson et al., 2020).
Immunity Passports	Chile, Germany, and the UK, among others, have indicated they will implement certifications that a person has contracted and recovered from COVID-19 or has received a COVID-19 vaccine. Certifications of immunity, also known as "immunity passports", raise important questions about fairness, stigma, and counterproductive incentives. Despite intended for public health benefit, immunity passports could cause more harm than good by creating a false sense of immunity and facilitating spread. More seriously, perceived gains of immunity passports might encourage uninfected people to relax protective measures and actively seek infection (Persad & Emanuel, 2020). Moreover, positive serology requirements of immunity passports could encourage forgery, illegal markets, or fraud by unethical physicians or testing facilities. If equal access to an effective vaccine cannot be provided, the economic and social disadvantages of being unvaccinated will create an incentive for people to try and obtain a vaccine or an immunity status by unlawful means. Black market, fake vaccines, sale of false vaccination certificates, and crime are all expected to rise then (Cheong, Allotey, & Reidpath, 2020).
Autonomy	Unfair access to vaccines will also create inequalities in rights and freedom. Those who are unable to obtain the vaccine may find their privacy threatened with temporary monitoring measures becoming permanent fixtures in their lives, exposing details of their movements and activities. The unvaccinated may also find themselves restricted from travel, public areas, and health care facilities. Their children may be restricted from nurseries and employment opportunities may be limited for them (Cheong, Allotey, & Reidpath, 2020; Persad & Emanuel, 2020).

Equity	Organizations globally have affirmed the commitment to fair global access. Barriers for low-income countries include the inability to afford vaccines as well as inadequate resources to vaccinate (Liu, Salwi, & Drolet, 2020). In this regard, recent history is not encouraging, as powerful antiviral drugs revolutionized HIV treatment in the West in 1996, saving many lives, but it took 7 years for the drugs to become widely available in Africa, the hardest hit continent by the disease (Kupferschmidt, 2020). To secure equity across countries, COVAX is working on accelerating the development and manufacturing of COVID-19 vaccines and ensuring that there is fair and equitable access to these vaccines for all countries. This is done through supporting low-income countries and organizing the process of vaccine distribution among funded and self-financing countries (Gavi, 2020d). Within countries, The WHO has also published a guidance document to inform the prioritization of COVID-19 use during each epidemiological setting (community transmission, sporadic cases/cluster of cases, and no cases). This roadmap document takes into account the heightened risk of infection and complications imposed by COVID-19 virus on specific populations such as healthcare workers, elderly, those with comorbidities, and those with specific sociodemographic characteristics (WHO, 2020h).
Politicization of COVID-19 Vaccines	Despite being a global public good, it is clear that the vaccine allocation across countries would not be an easy process because supply is likely to remain much below the demand, especially during the initial stages. Concerns of 'vaccine nationalism', where deals are being struck between powerful countries and manufacturers to garner the initial and major shares possible of doses being produced, have been heard (Gupta & Baru, 2020). On another note, in April 2020, a whistle-blower lawsuit was filed alleging inappropriate pressure from the White House to promote an unproven treatment (hydroxychloroquine) for COVID-19. Under pressure from President Donald Trump, the FDA had issued an emergency-use authorization for the medication in March, only to backtrack weeks later. In addition, In August 2020, the FDA commissioner, Stephen Hahn, stood with the president on the eve of the Republican National Convention to announce the authorization of convalescent plasma as treatment for COVID-19. The president made misleading statements about the evidence supporting this treatment and asserted without evidence that FDA staff were holding up approvals for political reasons. Such incidents, which were intended to produce political gains, have undoubtedly affected the integrity of FDA. Similar political interferences are feared during the development process of COVID-19 vaccines (Sharfstein, 2020).

Deploying a COVID-19 Vaccine in Lebanon

The case in Lebanon is like no other country. The pandemic struck at a time of political, economic, and social disruption. The country was hit hard by the August 4 explosion which killed at least 200 people, injured more than 6000, and left 300,000 homeless. Following the explosion, three hospitals were non-functional and another two suffered substantial damage. In addition, 17 containers with essential medical supplies and a shipment of personal protective equipment were destroyed at the port (Devi, 2020). Emigration of doctors and nurses accelerated post the explosion (The National News, 2020a), further adding strain to an already threatened health system. The pandemic also arrives at the brink of an impending economic breakdown, banking sector collapse, diminished buying capacity, and threats of withholding subsidies on commodities and medicines. The availability of basic resources such as uninterrupted electricity, which is a must for the optimal storage of the vaccine, is threatened as a result of possible withholding of subsidies on fuel. Moreover, the pandemic hits on a background political laxity, corruption, revolution, and eroded public trust.

The awaited Pfizer/BioNTech vaccine is estimated to cost around 20$ per dose, which sums up to 40$ for the full course (Observer, 2020). For an average household of 5 persons, the vaccination cost will be 200$. Knowing that MOPH and COVAX will cover only a limited proportion of the population, and if subsidies were withheld, the majority of the population will be left to pay more than twice the minimum monthly wage of 675,000 L.L. to get the vaccine, provided that sufficient amounts of the vaccine were imported. In other words, a large proportion of the population will go unvaccinated.

However, notwithstanding the ongoing health, political, and economic crises in Lebanon, efforts were made to secure the country's share of the vaccine. On November 23rd 2020, the Ministry of Public Health announced that Pfizer/BioNTech vaccine will arrive in Lebanon by mid February 2021, after conducting early negotiations with the company. According to the MOPH, 15% of the population will receive the vaccine for free (covered by the MOPH), while 20% will be hopefully covered by COVAX (MOPH, 2020c). Autonomy will be respected as vaccination will be a voluntarily process, offered initially to pre-determined priority groups (Lebanon Debate, 2020). Vaccination plans for the remaining population have not been announced yet. However, it is expected that COVID-19 vaccines produced by other companies will eventually reach the Lebanese market (Lebanon Debate, 2020).

Alongside the MOPH efforts to secure Pfizer/BioNTech vaccine, the National Committee for COVID-19 Vaccine was convened. The goal of the committee is to (MOPH, 2020d):

- Prepare a mechanism for approval, purchase, registration, receipt and distribution of the vaccine
- Monitor side effects
- Monitor the cold chain and other issues related to maintaining the quality of the vaccine
- Identify and prioritize target groups
- Ensure that the vaccine reaches the target groups in a practical and equitable manner

On another note, there exists 12 refrigerators in Lebanon where the vaccine can be stored between minus 80°C and minus 60°C. The WHO has promised to provide six more (The National News, 2020b).

Similar to other countries, Lebanon needs to take into account the general considerations outlined in WHO document "Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines". However, in view of the turbulent state of the country, successful deployment and vaccination necessitates:

- Political will and prioritization of public health over all other considerations
- Rebuild of public trust through transparency and communication
- Securing essential pre-requisites for all stages of deployment
- Wise use of the finite resources
- Development of retention plans for health professionals
- Control of black market and side deals
- Inclusion of marginalized populations such as refugees and immigrant workers
- Minimizing out-of-pocket payments
- Commitment to the principles of autonomy and equity

References

- Alimohamadi, Y., Taghdir, M., & Sepandi, M. (2020). Estimate of the Basic Reproduction Number for COVID-19: A Systematic Review and Meta-analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi, 53(3), 151–157. https://doi.org/10.3961/jpmph.20.076
- Ball, P. (2020). Anti-vaccine movement could undermine efforts to end coronavirus pandemic, researchers warn. Nature, 581(7808), 251.
- Ball, P., & Maxmen, A. (2020). The epic battle against coronavirus misinformation and conspiracy theories. Nature, 581(7809), 371-374.
- Barello, S., Nania, T., Dellafiore, F., Graffigna, G., & Caruso, R. (2020). 'Vaccine hesitancy' among university students in Italy during the COVID-19 pandemic. European Journal of Epidemiology, 35(8), 781-783.
- Bauchner, H., Malani, P. N., & Sharfstein, J. (2020). Reassuring the Public and Clinical Community About the Scientific Review and Approval of a COVID-19 Vaccine. JAMA, 324(13), 1296-1297.
- Betsch, C., Böhm, R., & Korn, L. (2013). Inviting free-riders or appealing to prosocial behavior? Game-theoretical reflections on communicating herd immunity in vaccine advocacy. Health Psychology, 32(9), 978.
- Billah, M. A., Miah, M. M., & Khan, M. N. (2020). Reproductive number of coronavirus: A systematic review and meta-analysis based on global level evidence. PloS one, 15(11), e0242128.
- Bokemper, S. E., Huber, G. A., Gerber, A. S., James, E. K., & Omer, S. B. (2020). Timing of COVID-19 Vaccine Approval and Endorsement by Public Figures.
- Brewer, N. T., Chapman, G. B., Rothman, A. J., Leask, J., & Kempe, A. (2017). Increasing vaccination: putting psychological science into action. Psychological Science in the Public Interest, 18(3), 149-207.
- Brown, K. F., Kroll, J. S., Hudson, M. J., Ramsay, M., Green, J., Long, S. J., ... & Sevdalis, N. (2010). Factors underlying parental decisions about combination childhood vaccinations including MMR: a systematic review. Vaccine, 28(26), 4235-4248.
- Bruine de Bruin, W., Parker, A. M., Galesic, M., & Vardavas, R. (2019). Reports of social circles' and own vaccination behavior: A national longitudinal survey. Health Psychology, 38(11), 975.
- Burns, J., Movsisyan, A., Stratil, J. M., Coenen, M., Emmert-Fees, K. M., Geffert, K., ... & Philipsborn, P. (2020). Travel-related control measures to contain the COVID-19 pandemic: a rapid review. Cochrane Database of Systematic Reviews, (9).
- Callaway, E. (2020). Dozens to be deliberately infected with coronavirus in UK 'human challenge' trials. Nature, 586(7831), 651-652.
- Cellule d'Analyse en Sciences Sociales (2020). Humanitarian programme recommendations for COVID-19 based on social sciences evidence from the DRC Ebola outbreak response. Social science support for COVID-19: lessons learned brief 3. Available at: https:// www.unicef.org/drcongo/media/4131/ file/CASS-Brief3-recommendations.pdf
- Centers for Disease Control and Prevention (2020a). Implications of the Emerging SARS-CoV-2 Variant VOC 202012/01. Available at https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-emerging-variant.html
- Centers for Disease Control and Prevention (2020b). Product Info by US Vaccine. Available at https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html
- Cheong, M. W. L., Allotey, P., & Reidpath, D. D. (2020). Unequal Access to Vaccines Will Exacerbate Other Inequalities. Asia-Pacific Journal of Public Health, 32(6-7), 379-380.
- Coconel Group, C. (2020). A future vaccination campaign against COVID-19 at risk of vaccine hesitancy and politicisation. The Lancet Infectious Diseases, 20(7), 769-770.
- Cohen, J. (2020). Infect volunteers to speed a coronavirus vaccine? Science, 368(6486), 16. Dawson, L., Earl, J., & Livezey, J. (2020). Severe Acute Respiratory Syndrome Coronavirus 2 Human Challenge Trials: Too Risky, Too Soon. Journal of Infectious Diseases, 222(3), 514-516.
- COVID-19 Global Evaluation Coalition (2020). Communicating with the public about vaccines: Implementation considerations.
- Devi S. Lebanon faces humanitarian emergency after blast. Lancet. 2020;396(10249):456. doi:10.1016/S0140-6736(20)31750-5
- Dror, A. A., Eisenbach, N., Taiber, S., Morozov, N. G., Mizrachi, M., Zigron, A., . . . Sela, E. (2020). Vaccine hesitancy: the next challenge in the fight against COVID-19. European Journal of Epidemiology, 35(8), 775-779.
- Dubé, E., Laberge, C., Guay, M., Bramadat, P., Roy, R., & Bettinger, J. A. (2013). Vaccine hesitancy: an overview. Human vaccines & immunotherapeutics, 9(8), 1763-1773.
- EMA (2020a). EMA receives application for conditional marketing authorisation of COVID-19 mRNA vaccine BNT162b2. Available at https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-covid-19-mrna-vaccine-bnt162b2
- EMA (2020b). EMA receives application for conditional marketing authorisation of Moderna COVID-19 vaccine. Available at https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-moderna-covid-19-vaccine
- European Centre for Disease Prevention and Control (2020). Rapid increase of SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom. Available at https://www.ecdc.europa.eu/sites/default/files/documents/

SARS-CoV-2-variant-multiple-spike-protein-mutations-United-Kingdom.pdf

- Eyal, N., & Lipsitch, M. (2020). Opinion: It's ethical to test promising coronavirus vaccines against less-promising ones. Proceedings of the National Academy of Sciences of the United States of America, 117(32), 18898-18901.
- Flaxman, S., Mishra, S., Gandy, A., Unwin, H. J. T., Mellan, T. A., Coupland, H., ... & Monod, M. (2020). Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. Nature, 584(7820), 257-261.
- Fontanet, A., & Cauchemez, S. (2020). COVID-19 herd immunity: where are we?. Nature Reviews Immunology, 20(10), 583-584.
- Food and Drug Administration (2020a). Available at https://www.fda.gov/media/137564/download
- Food and Drug Administration (2020b). Vaccine Development – 101. Available at https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101
- Food and Drug Administration (2020c). Emergency Use Authorization for Vaccines to Prevent COVID-19 Guidance for Industry. Available at https://www.fda.gov/media/142749/download
- Food and Drug Administration (2020d). Pfizer-BioNTech COVID-19 Vaccine. Available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine
- Food and Drug Administration (2020e). Moderna COVID-19 Vaccine. Available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/moderna-covid-19-vaccine
- Gavi (2020a). There are four types of COVID-19 vaccines: here's how they work. Available at https://www.gavi.org/vaccineswork/there-are-four-types-covid-19-vaccines-heres-how-they-work
- Gavi (2020b). The COVID-19 vaccine race. Available at https://www.gavi.org/vaccineswork/covid-19-vaccine-race
- Gavi (2020c). Five ways that scientists are ensuring the safety of COVID-19 vaccines. Available at https://www.gavi.org/vaccineswork/five-ways-scientists-are-ensuring-safety-covid-19-vaccines
- Gavi (2020d). COVAX explained. Available at https://www.gavi.org/vaccineswork/covax-explained
- Giubilini, A., Caviola, L., Maslen, H., Douglas, T., Nussberger, A. M., Faber, N., ... & Savulescu, J. (2019, December). Nudging Immunity: The Case for Vaccinating Children in School and Day Care by Default. In Hec Forum (Vol. 31, No. 4, pp. 325-344). Springer Netherlands.
- Gupta, I., & Baru, R. (2020). Economics & ethics of the COVID-19 vaccine: How prepared are we? Indian Journal of Medical Research, 152(1 & 2), 153-155.
- Goldman, R. D., Yan, T. D., Seiler, M., Parra Cotanda, C., Brown, J. C., Klein, E. J., . . . International, C.-P. A. S. G. (2020). Caregiver willingness to vaccinate their children against COVID-19: Cross sectional survey. Vaccine, 38(48), 7668-7673.
- Iacus, S. M., Natale, F., Santamaria, C., Spyratos, S., & Vespe, M. (2020). Estimating and projecting air passenger traffic during the COVID-19 coronavirus outbreak and its socio-economic impact. Safety Science, 104791.
- Healthline (2020). How Much Will It Cost to Get a COVID-19 Vaccine? Available at https://www.healthline.com/health-news/how-much-will-it-cost-to-get-a-covid-19-vaccine
- Hellmann, F., Williams-Jones, B., & Garrafa, V. (2020). COVID-19 and Moral Imperialism in Multinational Clinical Research. Archives of Medical Research, 51(6), 572-573.
- International Federation of Pharmaceutical Manufacturers & Associations (2019). THE COMPLEX JOURNEY OF A VACCINE. Available at https://www.ifpma.org/wp-content/uploads/2019/07/IFPMA-ComplexJourney-2019_FINAL.pdf
- Johnson, N. F., Velasquez, N., Restrepo, N. J., Leahy, R., Gabriel, N., El Oud, S., . . . Lupu, Y. (2020). The online competition between pro- and anti-vaccination views. Nature, 582(7811), 230-233.
- Johnson, R. M., Doshi, P., & Healy, D. (2020). Covid-19: Should doctors recommend treatments and vaccines when full data are not publicly available? BMJ, 370, m3260.
- Khan, Y. H., Mallhi, T. H., Alotaibi, N. H., Alzarea, A. I., Alanazi, A. S., Tanveer, N., & Hashmi, F. K. (2020). Threat of COVID-19 Vaccine Hesitancy in Pakistan: The Need for Measures to Neutralize Misleading Narratives. American Journal of Tropical Medicine & Hygiene, 103(2), 603-604.
- Kharroubi, S., & Saleh, F. (2020). Are Lockdown Measures Effective Against COVID-19?. Frontiers in Public Health, 8, 610.
- Kreps, S., Prasad, S., Brownstein, J. S., Hswen, Y., Garibaldi, B. T., Zhang, B., & Kriner, D. L. (2020). Factors Associated With US Adults' Likelihood of Accepting COVID-19 Vaccination. JAMA Network Open, 3(10), e2025594.
- Kupferschmidt, K. (2020). Global plan seeks to promote vaccine equity, spread risks. Science, 369(6503), 489-490.
- Leask, J., Kinnersley, P., Jackson, C., Cheater, F., Bedford, H., & Rowles, G. (2012). Communicating with parents about vaccination: a framework for health professionals. BMC pediatrics, 12(1), 154.
- Lebanon Debate (2020). كورونا... "يحقّ للمواطن اللّبناني إختيار التّلقيح من عدمه"! Available at https://www.lebanondebate.com/news/512429
- Liu, Y., Salwi, S., & Drolet, B. C. (2020). Multivalue ethical framework for fair global allocation of a COVID-19 vaccine. Journal of Medical Ethics, 46(8), 499-501.
- McPartlin, S. O., Morrison, J., Rohrig, A., & Weijer, C. (2020). Covid-19 vaccines: Should we allow human challenge studies to infect healthy volunteers with SARS-CoV-2? BMJ, 371, m4258.

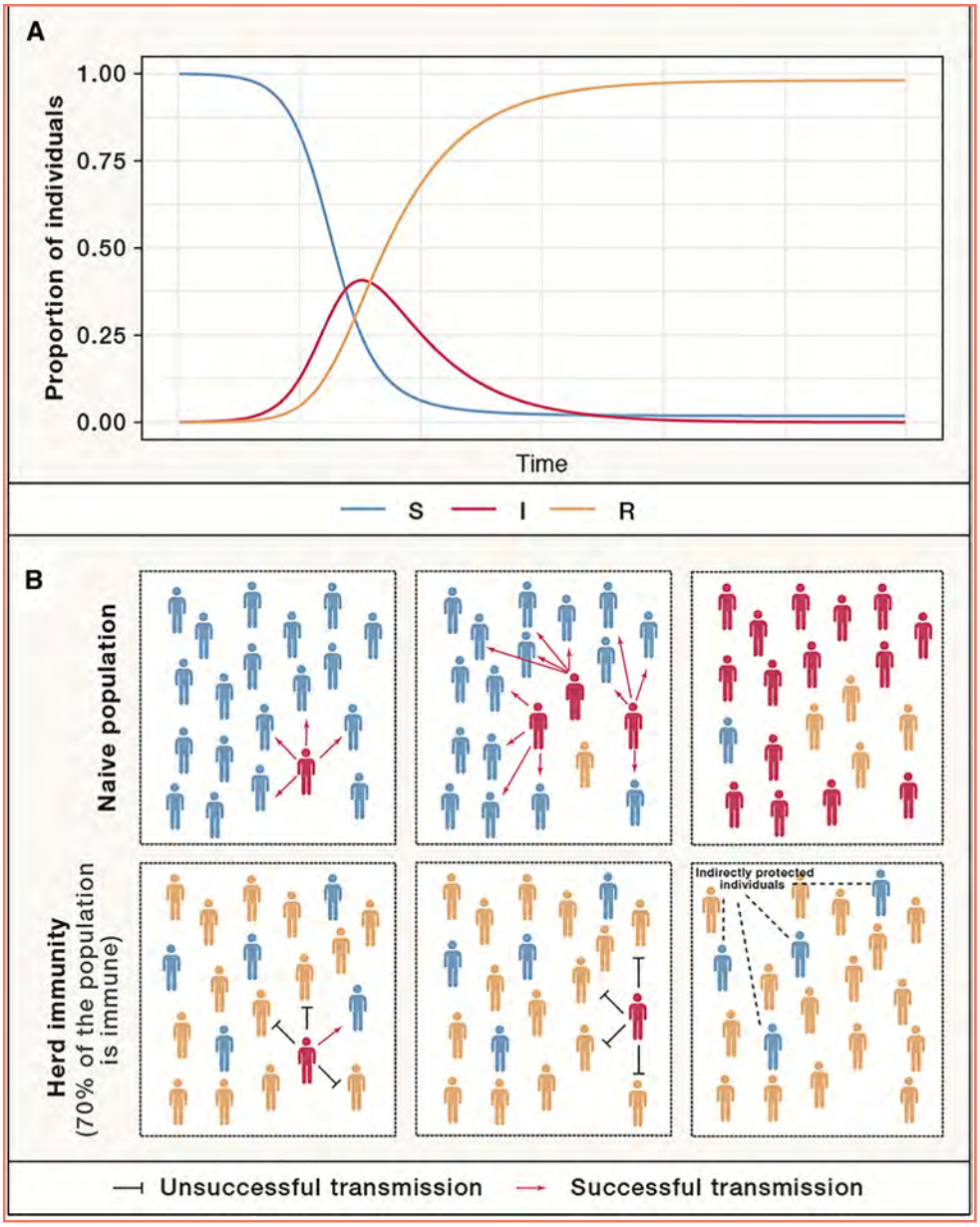
- Menikoff, J. (2020). The Regulation of COVID-19 "Challenge" Studies. American Journal of Bioethics, 20(7), 80-82.
- Mills, M., Rahal, C., & Brazel, D. M. (2020). COVID-19 vaccine deployment: Behaviour, ethics, misinformation and policy strategies.
- Ministry of Public Health (2020a). Monitoring of COVID-19 Infection in Lebanon-8/12/2020. Available at https://www.moph.gov.lb/en/Media/view/43642/novel-coronavirus-2019-
- Ministry of Public Health (2020b). Letter No.20/1/43141 of 4/12/2020 Addressed to the Governmental and Private Hospitals in Lebanon. Available at https://www.moph.gov.lb/en/Pages/17/43408/letter-no20-1-43141-issued-on-4-12-2020-to-the-pulbic-and-private-hospitals-in-lebanon#/en/Pages/17/43408/letter-no20-1-43141-issued-on-4-12-2020-to-the-pulbic-and-private-hospitals-in-lebanon
- Ministry of Public Health News (2020c). Hasan: Pfizer Vaccine will Arrive in Lebanon by mid-February. Available at https://www.moph.gov.lb/en/Pages/127/42948/hasan-pfizer-vaccine-will-arrive-in-lebanon-by-mid-february
- Ministry of Public Health (2020d). Minister Hasan Chairs the Meeting of the National Committee for COVID-19 Vaccine. Available at https://www.moph.gov.lb/en/Pages/17/43042/minister-hasan-chairs-the-meeting-of-the-national-committee-for-covid-19-vaccine
- Mo, H., Zeng, G., Ren, X., Li, H., Ke, C., Tan, Y., Cai, C., Lai, K., Chen, R., Chan- Yeung, M., and Zhong, N. (2006). Longitudinal profile of antibodies against SARS-coronavirus in SARS patients and their clinical significance. Respirology 11, 49–53.
- Monrad, J. T. (2020). Ethical considerations for epidemic vaccine trials. Journal of Medical Ethics, 46(7), 465-469.
- Observer (2020). COVID-19 Vaccine Prices Revealed From Pfizer, Moderna, and AstraZeneca. Available at https://observer.com/2020/11/covid19-vaccine-price-pfizer-moderna-astrazeneca-oxford/
- Odusanya, O. O., Odugbemi, B. A., Odugbemi, T. O., & Ajisegiri, W. S. (2020). COVID-19: A review of the effectiveness of non-pharmacological interventions. Nigerian Postgraduate Medical Journal, 27(4), 261.
- Palamenghi, L., Barello, S., Boccia, S., & Graffigna, G. (2020). Mistrust in biomedical research and vaccine hesitancy: the forefront challenge in the battle against COVID-19 in Italy. European Journal of Epidemiology, 35(8), 785-788.
- Park, M., Cook, A. R., Lim, J. T., Sun, Y., & Dickens, B. L. (2020). A systematic review of COVID-19 epidemiology based on current evidence. Journal of Clinical Medicine, 9(4), 967.
- Paterson, P., Meurice, F., Stanberry, L. R., Glismann, S., Rosenthal, S. L., & Larson, H. J. (2016). Vaccine hesitancy and healthcare providers. Vaccine, 34(52), 6700-6706.
- Persad, G., & Emanuel, E. J. (2020). The Ethics of COVID-19 Immunity-Based Licenses ("Immunity Passports"). JAMA, 323(22), 2241-2242.
- Plotkin, S. A., Orenstein, W. A., & Offit, P. A. (2018). Plotkin's vaccines (Seventh ed.). Philadelphia, PA: Elsevier.World Health Organization (2020). Draft landscape of COVID-19 candidate vaccines. Available at https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
- Randolph, H. E., & Barreiro, L. B. (2020). Herd Immunity: Understanding COVID-19. Immunity, 52(5), 737-741.
- RECOVERY Collaborative Group. (2020). Dexamethasone in hospitalized patients with Covid-19—preliminary report. New England Journal of Medicine.
- Reiter, P. L., Pennell, M. L., & Katz, M. L. (2020). Acceptability of a COVID-19 vaccine among adults in the United States: How many people would get vaccinated? Vaccine, 38(42), 6500-6507.
- Romer, D., & Jamieson, K. H. (2020). Conspiracy theories as barriers to controlling the spread of COVID-19 in the U.S. Social Science & Medicine, 263, 113356.
- Salje, H., Kiem, C. T., Lefrancq, N., Courtejoie, N., Bosetti, P., Paireau, J., ... & Le Strat, Y. (2020). Estimating the burden of SARS-CoV-2 in France. Science.
- Richards, A. D. (2020). Ethical guidelines for deliberately infecting volunteers with COVID-19. Journal of Medical Ethics, 46(8), 502-504.
- Sanche, S., Lin, Y.T., Xu, C., Romero-Severson, E., Hengartner, N., and Ke, R. (2020). High contagiousness and rapid spread of severe acute respiratory syn- drome coronavirus 2. Emerg. Infect. Dis. 26, https://doi.org/10.3201/eid2607. 200282.
- Saso, A., Skirrow, H., & Kampmann, B. (2020). Impact of COVID-19 on Immunization Services for Maternal and Infant Vaccines: Results of a Survey Conducted by Imprint—The Immunising Pregnant Women and Infants Network. Vaccines, 8(3), 556.
- Schaefer, G. O., Tam, C. C., Savulescu, J., & Voo, T. C. (2020). COVID-19 vaccine development: Time to consider SARS-CoV-2 challenge studies? Vaccine, 38(33), 5085-5088. Sharfstein, J. (2020). How the FDA should protect its integrity from politics. Nature, 585(7824), 161.
- Schoch-Spana, M., Brunson, E. K., Long, R., Ruth, A., Ravi, S. J., Trotochaud, M., ... & Hall, L. L. (2020). The public's role in COVID-19 vaccination: Human-centered recommendations to enhance pandemic vaccine awareness, access, and acceptance in the United States. Vaccine.
- Schmid, P., Rauber, D., Betsch, C., Lidolt, G., & Denker, M. L. (2017). Barriers of influenza vaccination intention and behavior–a systematic review of influenza vaccine hesitancy, 2005–2016. PloS one, 12(1), e0170550.
- Singh, J. A. (2020). The Case for Why Africa Should Host COVID-19 Candidate Vaccine Trials. Journal of Infectious Diseases,

222(3), 351-355.

- Smith, L. E., Amlot, R., Lambert, H., Oliver, I., Robin, C., Yardley, L., & Rubin, G. J. (2020). Factors associated with adherence to self-isolation and lockdown measures in the UK: A cross-sectional survey. Public Health (London), 187, 41-52. doi:10.1016/j.puhe.2020.07.024
- Sparkman, G., & Walton, G. M. (2017). Dynamic norms promote sustainable behavior, even if it is counternormative. Psychological science, 28(11), 1663-1674.
- Strassle, C., Jardas, E., Ochoa, J., Berkman, B. E., Danis, M., Rid, A., & Taylor, H. A. (2020). Covid-19 Vaccine Trials and Incarcerated People - The Ethics of Inclusion. New England Journal of Medicine, 383(20), 1897-1899.
- The National News (2020a). Lebanon hospitals under threat as doctors and nurses emigrate. Available at https://www.thenationalnews.com/world/mena/lebanon-hospitals-under-threat-as-doctors-and-nurses-emigrate-1.1077418
- The National News (2020b). Lebanon has reserved coronavirus vaccines for nearly 1 million people. Available at https://www.thenationalnews.com/world/lebanon-has-reserved-coronavirus-vaccines-for-nearly-1-million-people-1.1136603
- UpToDate (2020). Coronavirus disease 2019 (COVID-19): Management in hospitalized adults. Available at https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-management-in-hospitalized-adults?csi=097a5125-d69d-43ba-a337-89bf1fafa6fc&source=contentShare#H2576622514
- United Nations (2020). This is how much the coronavirus will cost the world's economy, according to the UN. Available at https://www.weforum.org/agenda/2020/03/coronavirus-covid-19-cost-economy-2020-un-trade-economics-pandemic/
- Vosoughi, S., Roy, D., & Aral, S. (2018). The spread of true and false news online. Science, 359(6380), 1146-1151.
- Wadman, M. (2020). Vaccines that use human fetal cells draw fire. Science, 368(6496), 1170-1171.
- Wang, E. A., Zenilman, J., & Brinkley-Rubinstein, L. (2020). Ethical Considerations for COVID-19 Vaccine Trials in Correctional Facilities. JAMA, 324(11), 1031-1032.
- Wang, Y., Zhang, D., Du, G., Du, R., Zhao, J., Jin, Y., ... & Hu, Y. (2020). Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. The Lancet.
- Weill, J. A., Stigler, M., Deschenes, O., & Springborn, M. R. (2020). Social distancing responses to COVID-19 emergency declarations strongly differentiated by income. Proceedings of the National Academy of Sciences, 117(33), 19658-19660.
- Wilson, N., Kvalsvig, A., Barnard, L. T., & Baker, M. G. (2020). Case-fatality risk estimates for COVID-19 calculated by using a lag time for fatality. Emerging infectious diseases, 26(6), 1339.
- World Bank (2020). Updated Poverty Numbers in Lebanon
- WHO (2019). Immunization coverage. Available at www.who.int/ news-room/fact-sheets/detail/immunization-coverage.
- WHO (2020a). WHO Coronavirus Disease (COVID-19) Dashboard. Available at https://covid19.who.int
- WHO (2020b). WHO Target Product Profiles for COVID-19 Vaccines. Available at https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines
- WHO (2020c). Draft landscape of COVID-19 candidate vaccines. Available at https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
- WHO (2020d). The Access to COVID-19 Tools (ACT) Accelerator. Available at https://www.who.int/initiatives/act-accelerator
- WHO (2020e). Guidance on developing a national deployment and vaccination plan for COVID-19 vaccines. Available at https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccine_deployment-2020.1
- WHO (2020f). Vaccine Misinformation: Statement by WHO Director-General on Facebook and Instagram. Available at: https://www.who.int/news-room/detail/04-09-2019-vaccine-misinformation-statement-by-who-director-general-on-facebook-and-instagram
- WHO (2020g). Strategic considerations in preparing for deployment of COVID-19 vaccine and vaccination in the WHO European Region. Available at: https:// apps.who.int/iris/hand le/10665/335940
- WHO (2020h). WHO Sage Roadmap for Prioritizing Uses of Covid-19 Vaccines in The Context of Limited Supply. Available at https://www.who.int/docs/default-source/immunization/sage/covid/sage-prioritization-roadmap-covid19-vaccines.pdf?Status=Temp&sfvrsn=bf227443_2
- WHO (2020i). Behavioural Considerations For Acceptance And Uptake Of Covid-19 Vaccines
- WHO Solidarity Trial Consortium. (2020). Repurposed antiviral drugs for COVID-19—interim WHO SOLIDARITY trial results. New England Journal of Medicine.
- Yanes-Lane, M., Winters, N., Fregonese, F., Bastos, M., Perlman-Arrow, S., Campbell, J. R., & Menzies, D. (2020). Proportion of asymptomatic infection among COVID-19 positive persons and their transmission potential: A systematic review and meta-analysis. PloS one, 15(11), e0241536.

Appendices

Appendix 1: COVID-19 Transmission and the Role of Herd Immunity



Adopted from Randolph & Barreiro, 2020

(A) SIR (susceptible, infectious, recovered) model for a completely immunizing infection with an R0 = 4. The model assumes a closed population in which no people leave and no new cases are introduced. Following the introduction of a single infected individual, the proportion of infected individuals (red line) increases rapidly until reaching its peak, which corresponds to the herd immunity threshold. After this point, newly infected individuals infect fewer than one susceptible individual, as a sufficient proportion of the population has become resistant, preventing further spread of the pathogen (orange line).

(B) Schematic depiction of the disease propagation dynamics when one infected individual is introduced into a completely susceptible population (top panel) versus a situation in which an infected individual is introduced into a population that has reached the herd immunity threshold (bottom panel). In the naive population, an outbreak quickly emerges, whereas under the scenario of herd immunity, the virus fails to spread and persist in the population.

Appendix 2: Stages of Vaccine Development (FDA, 2020b)

Research and Discovery: Scientists develop a rationale for a vaccine based on how the infectious organism causes disease. The scientists then conduct laboratory research to test their idea for a vaccine candidate.

Preclinical: Before a vaccine can be tested in people, a researcher performs additional laboratory research and testing in animals to obtain information about how the vaccine works and whether it's likely to be safe in humans.

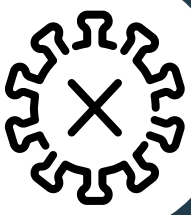
Clinical Development: When the researcher is ready to begin studies in humans, they compile the results of their laboratory and other preclinical testing, as well as information pertaining to the manufacturing technology and the quality of the vaccine and submit these to FDA in the form of an Investigational New Drug application. Under the oversight of FDA, studies conducted in people typically cover three phases that may progress sequentially or overlap.

Phase 1 - Emphasis during this phase is on safety and generally includes 20-100 volunteers who haven't been exposed to the disease being studied and who are generally otherwise healthy. These studies are used to determine whether there are adverse reactions with increasing doses and, if possible, to gain early information about how well the vaccine works to induce an immune response in people.

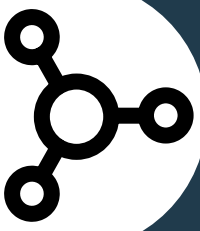
Phase 2 - In the absence of safety concerns from phase 1 studies, phase 2 studies include more people, where various dosages are tested on hundreds of people with typically varying health statuses and from different demographic groups, in randomized-controlled studies. These studies provide additional safety information, examine the relationship between the dose administered and the immune response, and provide initial information regarding the effectiveness of the vaccine. Studies typically also include a control group consisting of people who may receive an FDA-approved vaccine, a placebo or another substance.

Phase 3 - The vaccine is generally administered to thousands of people and the study generates critical information on effectiveness and additional important safety data. This phase includes additional information about immune response and compares those who receive the vaccine to those who receive a control. These studies also provide information about the vaccine's safety including the identification of less common side effects.

Appendix 3: Categories of COVID-19 Vaccines (Gavi, 2020a)

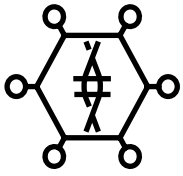


WHOLE VIRUS Use whole viruses to trigger an immune response. There are two main approaches. Live attenuated vaccines use a weakened form of the virus that can still replicate without causing illness. Inactivated vaccines use viruses whose genetic material has been destroyed so they cannot replicate, but can still trigger an immune response. Both types use well-established technology and pathways for regulatory approval, but live attenuated ones may risk causing disease in people with weak immune systems and often require careful cold storage, making their use more challenging in low-resource countries. Inactivated virus vaccines can be given to people with compromised immune systems but might also need cold storage.



PROTEIN SUBUNIT Subunit vaccines use pieces of the pathogen, often fragments of protein, to trigger an immune response. Doing so minimises the risk of side effects, but it also means the immune response may be weaker. They often require adjuvants, to help boost the immune response.

NUCLEIC ACID Use genetic material, either RNA or DNA, to provide cells with the instructions to make the antigen. In the case of COVID-19, vaccine uses the viral spike protein. Once this genetic material gets into human cells, cells' protein factories make the antigen that will trigger an immune response. RNA vaccines encode the antigen of interest in messenger RNA. Because of its transitory nature, there is zero risk of it integrating into patients' own genetic material.The advantages of such vaccines are that they are easy to make, cheap, and are able to mount a strong immune response. A downside is that so far, no DNA or RNA vaccines have been licensed for human use, which may cause more hurdles with regulatory approval. In addition, RNA vaccines need to be kept at ultra-cold temperatures, -70C or lower, which could prove challenging for countries that don't have specialised cold storage equipment, particularly low- and middle-income countries.



VIRAL VECTOR Viral vector vaccines also work by giving cells genetic instructions to produce antigens. But they differ from nucleic acid vaccines in that they use a harmless virus, different from the one the vaccine is targeting, to deliver these instructions into the cell. One type of virus that has often been used as a vector is adenovirus, which causes the common cold. As with nucleic acid vaccines, our own cellular machinery is hijacked to produce the antigen from those instructions, in order to trigger an immune response. Viral vector vaccines can mimic natural viral infection and should therefore trigger a strong immune response. However, since there is a chance that many people may have already been exposed to the viruses being used as vectors, some may be immune to it, making the vaccine less effective.

Appendix 4: COVID-19 Vaccines in Phase 3 of Development (WHO, 2020c)

COVID-19 Vaccine developer/ manufacturer (Country)	Vaccine platform	Type of candidate vaccine	Number of doses	Timing of doses	Route of Administration
Sinovac (China)	Inactivated	Inactivated	2	0,14 days	IM
Wuhan Institute of Biological Products/ Sinopharm (China)	Inactivated	Inactivated	2	0,21 days	IM
Beijing Institute of Biological Products/ Sinopharm (China)	Inactivated	Inactivated	2	0,21 days	IM
University of Oxford/ AstraZeneca (UK)	Non-Replicating Viral Vector	ChAdOx1-S	2	0,28 days	IM
CanSino Biological Inc./Beijing Institute of Biotechnology (China)	Non-Replicating Viral Vector	Adenovirus Type 5 Vector	1		IM
Gamaleya Research Institute (Russia)	Non-Replicating Viral Vector	Adeno-based (rAd26-S+rAd5-S)	2	0, 21 days	IM
Janssen Pharmaceutical Companies (US)	Non-Replicating Viral Vector	Adenovirus Type 26 vector	1 2	0 0, 56 days	IM
Novavax (US)	Protein Subunit	Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	2	0, 21 days	IM

Appendix 4: COVID-19 Vaccines in Phase 3 of Development (WHO, 2020c) (cont'd)

COVID-19 Vaccine developer/ manufacturer (Country)	Vaccine platform	Type of candidate vaccine	Number of doses	Timing of doses	Route of Administration
Moderna/NIAID (USA)	RNA	LNP-encapsulated mRNA	2	0, 28 days	IM
BioNTech/Fosun Pharma/Pfizer (Germany)	RNA	3 LNP-mRNAs	2	0, 28 days	IM
Medicago Inc. (Canada)	VLP	Plant-derived VLP adjuvanted with AS03	2	0, 21 days	IM
Anhui Zhifei Longcom Biopharmaceutical/ Institute of Microbiology, Chinese Academy of Sciences (China)	Protein Subunit	Adjuvanted recombinant protein (RBD-Dimer) expressed in CHO cells	3	0, 28, 56 days	IM
Bharat Biotech (India)	Inactivated	Whole-Virion Inactivated	2	0, 28 days	IM
Inovio Pharmaceuticals + International Vaccine Institute (US)	DNA based vaccine	INO- 4800+ electroporation	2	0, 28 days	ID
CureVac AG	RNA based vaccine	CVnCoV Vaccine	2	0 + 28	IM

DNA: deoxyribonucleic acid RNA: ribonucleic acid VLP: virus like particle IM: intra-muscular ID: intra-dermal

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