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Standards For Multivariable COVID-19 Health Passports

This paper addresses the discussion and needs of a vaccine passport. The continually emerging scientific knowledge regarding COVID-19 and its variants have brought into question the viable options for a usable and ethical vaccine passport during the pandemic and after. With data protection in mind along with global differences we recommend the need for a multivariable health passport and provide details on requirements. A multivariable passport is needed to handle different states' or countries' testing requirements, new vaccines with differing efficacies, new viral strains, and different policies required for mobilization, with a goal of providing a coordinated framework to facilitate travel and other sectors.

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Overview

- Coronavirus or “COVID19”, a global pandemic declared by WHO, is a highly contagious viral respiratory disease that is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and may be fatal.
- SARS-CoV-2 transmission occurs in infected individuals through contaminated secretions, such as saliva and respiratory secretions, or through respiratory droplets that are generated whenever an infected individual coughs, sneezes, speaks or sings by either direct, indirect, or close contact.
- Social distancing, isolation, quarantine, and vaccinations are the current effective way of reducing the number of cases adopted by various governments around the world.
- If the majority of a population is immune to an infectious disease, this provides indirect protection / herd immunity to those who are not immune to the disease.
- Health Passports, also called immunity passports or immunity certificates, offer digital proof - via a QR code, a certificate, wristband, mobile application, for instances - that a person is free of COVID-19 and allowed to travel.
- The Immunity passports not only have benefits of helping individuals to resume normal activities but also a much greater help of facilitating economic recovery.
- The ethics of COVID-19 immunity licenses can be evaluated with respect to three fundamental ethical values: the maximization of benefit; priority to the people who are most vulnerable; and treating people equally.
- Although wealthier countries have purchased enough doses to vaccinate their entire populations, it is estimated that almost 90% of the population in 67 countries will not be able to receive a COVID-19 vaccine in 2021, even though the COVID-19 cases among them are relatively high.
- With the prospect of several vaccines coming on line and with less stringent restrictions, it’s possible 2021 will bring about the beginnings of a pandemic recovery

1. Introduction

The COVID-19 pandemic has unquestionably brought about change to the entire globe, altering how we interact with each other. One strategy suggested to help this resumption is the identification and documentation of immunity: sometimes called immunity passports.[1] Some countries have had to introduce restrictive 'lockdown' policies on their citizens to control the spread of the Covid-19 pandemic. Immunity passports have been proposed as a measure to ease such policies' harms and be used in combination with other infection control strategies. The introduction of immunity passports introduces many practical and ethical challenges that need addressing for proper implementation.[2]

Immunity-based certificates have the potential to help realize essential values such as enhancing the freedom of individuals who were infected with COVID-19 while not intensifying the situation of those who have not been infected. Furthermore, enhancing advantages to individuals and society by permitting those with immunity to participate in economic activity and protecting the least advantaged by authorizing safer care for vulnerable populations.[3]

Due to COVID-19, the fragile economy, travel restrictions, and widespread concern, the concept of antibodies as a "declaration of immunity" or "passport" is sweeping the world. Numerous scientific and ethical issues confound the concept of an antibody passport.[4]

2. Disease Background

Coronavirus disease 19 (COVID-19) is a communicable viral respiratory disease that is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has not only caused a global pandemic, but public health crisis.[5] The name SARS-CoV-2 was adopted because of the virus genetic relatedness to the coronavirus that caused the 2003 SARS outbreak. Corona means crown, and represents the crown-shaped spikes on the outer surface of the virus. The crown-shaped spikes are used by SARS-CoV-2 for binding to the host angiotensin-converting enzyme 2 (ACE2) receptor in successful infection, hence the host ACE2 distribution determines the SARS-CoV-2 ability to cause infection.[6]

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1. Rebecca C Brown et al., "The Scientific and Ethical Feasibility of Immunity Passports," *The Lancet Infectious Diseases*, October 16, 2020, pp. 1, https://doi.org/10.1016/s1473-3099(20)30766-0.
2. Rebecca C Brown et al., "Passport to Freedom? Immunity Passports for COVID-19," *Journal of Medical Ethics* 46, no. 10 (2020): pp. 652, https://doi.org/10.1136/medethics-2020-106365.
3. Govind Persad and Ezekiel J. Emanuel, "The Ethics of COVID-19 Immunity-Based Licenses ('Immunity Passports')," *JAMA* 323, no. 22 (September 2020): p. 2241, https://doi.org/10.1001/jama.2020.8102.
4. Katrina A. Bramstedt, "Antibodies as Currency: COVID-19's Golden Passport," *Journal of Bioethical Inquiry* 17, no. 4 (2020): pp. 687-689, https://doi.org/10.1007/s11673-020-09996-5.
5. Muhammad Adnan Shereen et al., "COVID-19 Infection: Origin, Transmission, and Characteristics of Human Coronaviruses," *Journal of Advanced Research* 24 (2020): pp. 91-98, https://doi.org/10.1016/j.jare.2020.03.005.
6. Markus Hoffmann et al., "SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor," *Cell* 181, no. 2 (2020): pp. 271-280, https://doi.org/10.1016/j.cell.2020.02.052.

Coronaviruses are tiny (65–125 nm in diameter) and contain single-stranded RNA as the nucleic material. The SARS-CoV, H1N1 2009, H5N1 influenza A and Middle East respiratory syndrome coronavirus (MERS-CoV) is all characterized by acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), which can lead to pulmonary failure and cause death.[7]

The coronavirus disease 2019 (COVID-19) pandemic has resulted in severe people mobility problems in many countries. These come at a monumental social cost, and there are ethical and economic imperatives to use proportionate strategies that minimize the duration of Lockdowns. A key challenge is that social distancing measures can keep the transmission in control, but, without widely available vaccines, up-lifting restrictions risks surges in transmission. This will occur until a sufficient portion of the population has been infected and/or acquired immunity to the extent that outbreaks can no longer be sustained. During the pandemic, many countries took measures to decrease cross-border travel with the hopes of paralyzing the spread of COVID-19. In early April, 194 countries implemented visa restrictions and 143 shut down their borders.[8]

These proactive measures have had a significant economic downturn in almost all countries. "Immunity passports" or certificates have been advocated to ease restrictions on infected and recovered individuals, allowing some people to return to work and kick-start economic recovery.

2.1. Factors Associated With Transmission Of SARS-CoV-2

SARS-CoV-2 has a far greater infectivity potential relative to other coronaviruses, such as MERS-CoV and SARS-CoV, which makes it spread exponentially around the world.[9] Despite a lower-case fatality rate, due to the greater infectivity potentials relative to other coronaviruses, COVID-19 has so far resulted in more deaths.[10]

Worst still, it is hard to accurately predict its development[11]. Li et al. (2020)[12] using the logistic regression model, identified factors associated with COVID-19 cases, death, and case-fatality rates in the US and around the world. Among the many drivers of COVID-19 infections, economic inequality increased the risk of COVID-19 transmission. Hospital beds per capita showed a negative correlation with deaths attributable to COVID-19.

The susceptibility to COVID-19 infection also increases with age; children under 10 years of age

7. Yudong Yin and Richard G. Wunderink, "MERS, SARS and Other Coronaviruses as Causes of Pneumonia," *Respirology* 23, no. 2 (2017): pp. 130-137, https://doi.org/10.1111/resp.13196.

8. "Weekly operational update on COVID-19 - 15 April 2020," Publication, World Health Organization, last modified May 7, 2020a. https://www.who.int/publications/m/item/weekly-update-on-covid-19---15-april-2020.

9. Jieliang Chen, "Pathogenicity and Transmissibility of 2019-NCoV—A Quick Overview and Comparison with Other Emerging Viruses," *Microbes and Infection* 22, no. 2 (2020): pp. 69-71, https://doi.org/10.1016/j.micinf.2020.01.004.

10. Elisabeth Mahase, "Coronavirus: Covid-19 Has Killed More People than SARS and MERS Combined, despite Lower Case Fatality Rate," *BMJ*, 2020, p. m641, https://doi.org/10.1136/bmj.m641.

11. Weston C. Roda et al., "Why Is It Difficult to Accurately Predict the COVID-19 Epidemic?," *Infectious Disease Modelling* 5 (2020): pp. 271-281, https://doi.org/10.1016/j.idm.2020.03.001.

12. Mengyuan Li et al., "Identifying Novel Factors Associated with COVID-19 Transmission and Fatality Using the Machine Learning Approach," *Science of The Total Environment* 764 (2021): p. 142810, https://doi.org/10.1016/j.scitotenv.2020.142810.

are about half as susceptible as adults.[13] This discrepancy has been attributed to reduced ACE2 expression in children compared to adults.[14]

Other factors affecting COVID-19 transmission and fatality included social distancing, smoking, climate, urbanization level, health investment, and race. High temperature was a stronger factor in mitigating the transmission of COVID-19 compared to low temperature.[12]

Respiratory viruses are spread in three major ways. First, through contact, when a person comes into direct contact with an infected person or touches a contaminated surface. Second, through droplet transmission of large and small respiratory droplets contaminated with the virus, which occurs when in proximity to an infected person. Third, through airborne transmission of small droplets and particles that remain suspended over longer distances and time compared to droplet transmission.[15] During the early stages of the pandemic, there were concerns about the surface transmission of the virus. However, recent studies have shown that this is unlikely, as attempts to cultivate the virus from these surfaces have been unsuccessful even though there is evidence that SARS-CoV-2 can persist for up to 3 days on various surfaces.[13]

Initially, airborne transmission of SARS-CoV-2 was believed to be unlikely, however, recent research suggests that COVID-19 infection could occur at distances greater than 2 meters in confined spaces where ventilation is poor and with an extended exposure of over 30 min.[15]

There are also instances where transmission from humans to animals has been suspected. Pet animals such as dogs, cats, lions and tigers that have been exposed to infected humans have tested positive for the virus.[16] [17] [18] In addition, there is evidence that SARS-CoV-2 replicates in cats and could be transmitted between cats and ferrets.[19] However, there are no ascertained instances of transmission from domestic pets to humans.

COVID-19 has a very high infectivity rate. Possible modes of transmission for SARS-CoV-2, including contact, droplet, airborne, fomite, fecaloral, bloodborne, mother-to-child, and animal-to-human transmission (Table 1).[20]

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13. Eric A. Meyerowitz et al., "Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors," *Annals of Internal Medicine* 174, no. 1 (2021): pp. 69-79, https://doi.org/10.7326/m20-5008.

14. Supinda Bunyavanich, Anh Do, and Alfin Vicencio, "Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children and Adults," *JAMA* 323, no. 23 (2020): p. 2427, https://doi.org/10.1001/jama.2020.8707.

15. The Lancet Respiratory Medicine, "COVID-19 Transmission—up in the Air," *The Lancet Respiratory Medicine* 8, no. 12 (2020): p. 1159, https://doi.org/10.1016/s2213-2600(20)30514-2.

16. Mathilde Richard et al., "SARS-CoV-2 Is Transmitted via Contact and via the Air between Ferrets," *Nature Communications* 11, no. 1 (August 2020), https://doi.org/10.1038/s41467-020-17367-2.

17. Jianzhong Shi et al., "Susceptibility of Ferrets, Cats, Dogs, and Other Domesticated Animals to SARS–Coronavirus 2," *Science* 368, no. 6494 (August 2020): pp. 1016-1020, https://doi.org/10.1126/science.abb7015.

18. Thomas H. Sit et al., "Infection of Dogs with SARS-CoV-2," *Nature* 586, no. 7831 (2020): pp. 776-778, https://doi.org/10.1038/s41586-020-2334-5.

19. Peter J. Halfmann et al., "Transmission of SARS-CoV-2 in Domestic Cats," *New England Journal of Medicine* 383, no. 6 (June 2020): pp. 592-594, https://doi.org/10.1056/nejmc2013400.

20. Melika Lotfi, Michael R. Hamblin, and Nima Rezaei, "COVID-19: Transmission, Prevention, and Potential Therapeutic Opportunities," *Clinica Chimica Acta* 508 (2020): pp. 254-266, https://doi.org/10.1016/j.cca.2020.05.044.

SYMPTOMATIC TRANSMISSION	PRESYMPTOMATIC TRANSMISSION	ASYMPTOMATIC TRANSMISSION
A symptomatic COVID-19 person is one, who has signs and symptoms that are corresponding with the COVID-19 data from published epidemiologic and virologic studies. Symptomatic transmission refers to transmission from an individual experiencing symptoms primarily transmitted to others who are in close contact through respiratory droplets, by direct contact with infected persons, or by contact with contaminated objects and surfaces. Biological samples from COVID-19 patients show evidence that scattering of the virus is highest in the upper respiratory tract (nose and throat) during the course of the disease.	The incubation period is the time between exposure to the virus (becoming infected) and symptom onset, is on average 5-6 days, but could go up to 14 days. During this "pre-symptomatic" period, some infected individuals may become contagious. In a small number of case reports and studies, pre-symptomatic transmission was documented through contact screening efforts and further study of clusters of confirmed cases. Evidence suggests some individuals may test positive for COVID-19 one to three days before symptoms appear. As a result, people infected with COVID-19 may be able to pass on the virus before significant symptoms occur. It is important to recognize that pre-symptomatic transmission still requires the virus to spread through infectious droplets or through contact with contaminated surfaces.	A laboratory confirmed asymptomatic case is someone infected with COVID-19 who does not experience any symptoms during the course of infection. Asymptomatic (never symptomatic) transmission refers to transmission of the virus by a non-symptomatic person. Previous estimates that 80% of infections were asymptomatic were too high and have since been revised downward to range from 17% to 20% of infected individuals. About 49% of people initially defined as asymptomatic become symptomatic. The asymptomatic contribution to the CDC-documented endpoints of disease transmission by an asymptomatic individual is just as likely to transmit the infection as the symptomatic individual.

Table 1: The Route Of Transmission of SARS-CoV-2.[21 22 23 24]
Source: WHO/CDC/Yanes-Lane et al. article in PLOS One

2.2. The Importance Of Self-Monitoring, Social Distancing, Isolation And Quarantine

Governments all over the world are advising people to use physical distancing, also known as social distancing, quarantine and self-isolation to help reduce the spread of the new coronavirus. The purpose of isolation and quarantine is to control the spread of contagious illness.

The below chart explains your state in this pandemic and where you should be positioned at any point of time, according to the activity you performed (Table 2). Self-Monitoring and Social Distancing should always be followed till the WHO announces the End of Pandemic, while others like isolation and quarantine are depending on need basis.[25]

21. "Coronavirus disease 2019 (COVID-19): Situation Report – 73," Coronavirus situational updates, World Health Organization, last modified April 2, 2020b, https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73-covid-19.pdf?sfvrsn=5ae25bc7_6#:~:text=Symptomatic%20transmission,while%20they%20are%20experiencing%20symptoms.

22. "COVID-19 Pandemic Planning Scenarios," Coronavirus, Centers for Disease Control and Prevention, last modified September 10, 2020a, https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html.

23. Mercedes Yanes-Lane et al., "Proportion of Asymptomatic Infection Among COVID-19 Positive Persons and Their Transmission Potential: A Systematic Review and Meta-Analysis," *PLOS ONE* 15, no. 11 (2020), https://doi.org/10.1371/journal.pone.0241536.

24. Michael A. Johansson et al., "SARS-CoV-2 Transmission From People Without COVID-19 Symptoms," *JAMA Network Open* 4, no. 1 (July 2021): p. e2035057, https://doi.org/10.1001/jamanetworkopen.2020.35057.

25. "Public health considerations while resuming international travel," COVID-19 Travel Advice, World Health Organization, last modified July 30, 2020c, https://www.who.int/news-room/articles-detail/public-health-considerations-while-resuming-international-travel.

	SELF-MONITORING	SOCIAL DISTANCING	SELF-ISOLATION	SELF-QUARANTINE
MEANS	Self-monitoring involves closely observing for symptoms of COVID-19 in you and your dependents	Social distancing is a conscious effort to maintain a physical distance between you and others to minimize the spread of the COVID-19 disease	Self-isolation keeps someone infected with the virus, either at hospital or at home depending on severity	Self-quarantine keeps someone possibly exposed to the virus away from others mostly at home
WHO HAVE	• no symptoms • you believe there's a possibility you were exposed to the virus	• no symptoms • you believe you have not been exposed to the virus	• You do not need to be in hospital as your doctor suspects mild symptoms of Covid-19 and advises you to self-isolate at home • You only stay at home isolated from others at home so that they do not get infected and you go out only for medical care	• If you believe you have been in contact with a COVID-19 infected person, you should be restricting and separating from others, even if you have no symptoms. • Awaiting lab results for COVID-19
SAFEGUARDING YOURSELF	• monitor yourself • practice a temporary increase in physical distance from other people to slow down the infection rates without social disconnection or exclusion. • check to see if there is fever or respiratory symptoms	• monitor yourself • stay at least 6 feet from each other. • keep travel to a minimum (it is preferred to stay at home as much as possible)	• stay at home and keep track of your symptoms, even mild, 14 days • Avoid contact to prevent the spread of disease. • avoid other people at your residence	• until your public health authority advises you are no longer at risk of spreading the virus, stay at home • avoid contact with high-risk populations including the elderly, and those medically vulnerable
KEEP IN MIND	**Self-monitor if:** • you think you were possibly exposed • you are not in close contact with seniors or those who are medically vulnerable • go for a solitary walk, a hike or a jog • Allow employees to work from home • until the pandemic ends	**Social distancing if:** • you think you were never exposed • you are not in close contact with seniors or those who are medically vulnerable • go for a solitary walk, a hike or a jog • Allow employees to work from home • until the pandemic ends	**Self-isolate if:** • cannot leave the house at least 14 days after the symptoms appear • you are advised to self-isolate if you have traveled outside borders/country • you received advice from a public health authority to isolate yourself • until improvement in respiratory symptoms and other symptoms are better	**Self-quarantine if:** • cannot leave the house for at least 10 to a maximum of 14 days • you are awaiting lab results for COVID-19 • you received advice from a public health authority to quarantine yourself • up to14 days post-exposure, free from symptoms and without testing
WHO YOU CAN INTERACT / MOVE WITH	• roommate(s) • family member(s) you live with		• no social contact • remain alone in the room if you live with people or in your home if you live alone • ask friends, family members, or delivery services to drop off supplies but do not touch or speak to them	

Table 2: The importance of self-monitoring, social distancing, isolation and quarantine.[25 26 27 28 29 30]
Source: WHO/Public Health Agency of Canada/University of Guelph/CDC/UT University Health Services/Augusta Health

26. "Coronavirus disease (COVID-19): Prevention and risks," Coronavirus disease (COVID-19), Public Health Agency of Canada, last modified February 12, 2021, https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/prevention-risks.html

27. "COVID-19: Self-isolation and quarantine: What you need to know," Homewood Health, University of Guelph, last modified March 26, 2020, https://www.uoguelph.ca/wellnessatwork/news/2020/03/covid-19-self-isolation-and-quarantine-what-you-need-know.

28. "Social distancing, monitoring, quarantine or isolation? (COVID-19)," COVID-19 Exposure Action Chart, UT University Health Services, last reviewed December 15, 2020, https://healthyhorns.utexas.edu/coronavirus_exposure_action_chart.html.

29. "Social Distancing," coronavirus, Centers for Disease Control and Prevention, last modified November 17, 2020b. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/social-distancing.html.

30. "COVID-19: When to Quarantine," Centers for Disease Control and Prevention, updated February 11, 2021a. https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html.

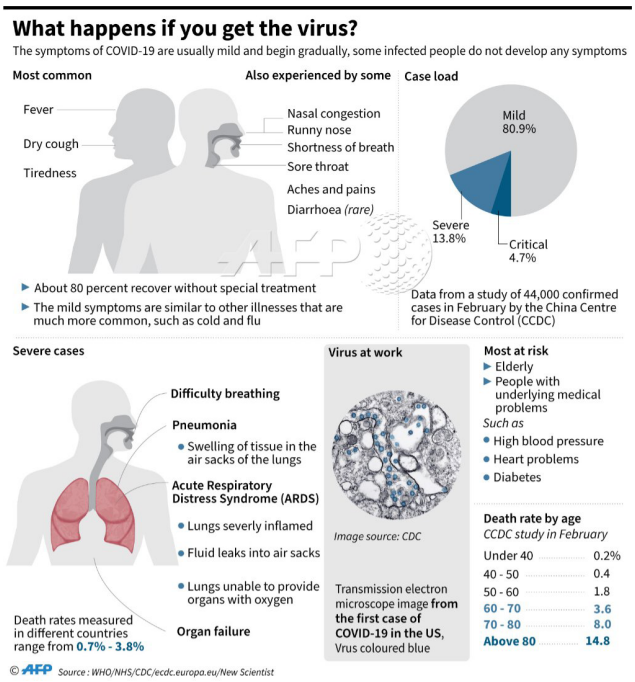


Figure 1: What happens in you get the virus[32]

2.3. COVID-19 Symptoms

General not comprehensive symptoms list as an indicator for COVID-19 is shown below (Figure 3). The symptoms are usually soft and start gradually (Figure 1 and 2). Those who become seriously ill and develop difficulty breathing due to COVID-19 are 1 out of every 6 people.[31]

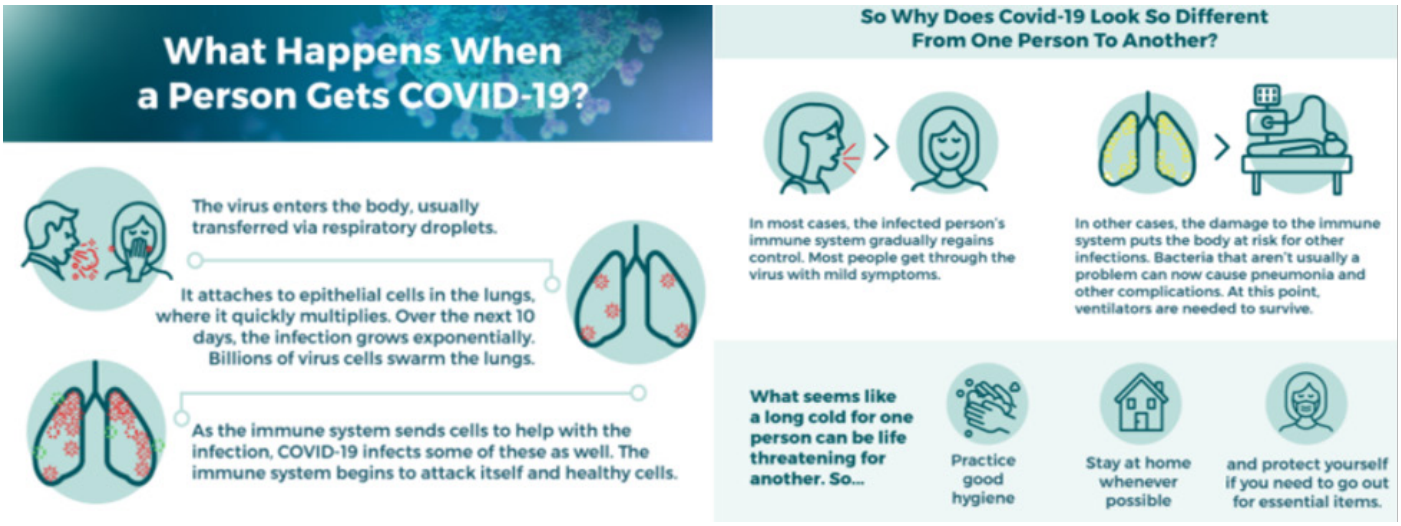


Figure 2: Impact of COVID-19 on humans.[33]

2.3.1. High-Risk Populations

Adults of all ages who have some underlying health problems are at an increased risk of serious illness due to the virus that causes COVID-19 (Figure 3). Serious illnesses associated with COVID-19 are defined as hospitalization, admission to critical care, intubation or mechanical ventilation, or death.[34]

31. Leiwen Fu et al., "Clinical Characteristics of Coronavirus Disease 2019 (COVID-19) in China: A Systematic Review and Meta-Analysis," *Journal of Infection* 80, no. 6 (2020): pp. 656-665, https://doi.org/10.1016/j.jinf.2020.03.041.

32. Agence France-Presse (@AFP), "What happens if you get the virus?," Twitter photo, March 18, 2020, https://twitter.com/AFP/status/1240184225107673088.

33. "What happens when a person gets COVID-19?," Healthy Resources, CHI St. Luke's Health, last modified April 20, 2020, https://www.stlukeshealth.org/resources/what-happens-when-person-gets-covid-19.

34. "People with Certain Medical Conditions," COVID-19, Centers for Disease Control and Prevention, last modified February 3,

ADULTS OF ANY AGE WITH THE FOLLOWING CONDITIONS **ARE AT INCREASED RISK** OF SEVERE ILLNESS FROM COVID-19	ADULTS OF ANY AGE WITH THE FOLLOWING CONDITIONS **MIGHT BE AT AN INCREASED RISK** FOR SEVERE ILLNESS FROM COVID-19	HIGH RISK VULNERABLE PEOPLE **MIGHT BE AT AN INCREASED RISK**
1. Cancer	1. Asthma (moderate-to-severe)	1. People Living in Rural Communities
2. Chronic kidney disease	2. Cerebrovascular disease (affects blood vessels and blood supply to the brain)	2. People with Disabilities
3. Chronic Obstructive Pulmonary Disease (COPD)	3. Cystic fibrosis	3. People with Developmental & Behavioral Disorders
4. Down Syndrome	4. Hypertension or high blood pressure	4. People Experiencing Homelessness
5. Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies	5. Immunocompromised state (weakened immune system) from blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune weakening medicines	5. Pregnant People and Breastfeeding
6. Immunocompromised state (weakened immune system) from solid organ transplant	6. Neurologic conditions, such as dementia	6. People with Seasonal Allergies
7. Obesity (body mass index (BMI) of 30 kg/m2 or higher but < 40 kg/m2)	7. Liver disease	7. Racial & Ethnic Minority Groups
8. Severe Obesity (BMI ≥ 40 kg/m2)	8. Overweight (BMI > 25 kg/m2, but < 30 kg/m2)	
9. Pregnancy	9. Pulmonary fibrosis (having damaged or scarred lung tissues)	
10. Sickle cell disease	10. Thalassemia (a type of blood disorder)	
11. Smoking	11. Type 1 diabetes mellitus	
12. Type 2 diabetes mellitus		

Older adults are at greatest risk, and the severity goes with the age as follows 90>80>70>60>50>40

Figure 3: Population at high risk of complication from COVID-19 [34 35 36]
Source: CDC/Harvard Health

2.4. Immunity - Immune Response And Memory To SARS-CoV-2 Infection

- According to Dan's study, around 95% of individuals sustained immune memory at ~6 months after infection. In addition, simple serological tests for SARS-CoV-2 antibodies do not contemplate the richness and lastingness of immune memory to SARS-CoV-2.[37]
- Herd immunity is the concept that if sufficient people are saved from infection, either by gaining immunity from having the infection or receiving a vaccine, then the chance of a non-immune person acquiring the disease is exceedingly low.[38]
- Until now, most of the medical researchers who have studied coronaviruses associated with the pathogen that causes COVID-19 including SARS, MERS and common cold. Medical researchers are confident that people who do recover gain some immunity to SARS-CoV-2 which has supported preliminary studies and case reports of the SARS-CoV-2 virus

2021b, https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html.

35. "Others At Risk for COVID-19." Centers for Disease Control and Prevention, last modified February 19, 2021c. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/other-at-risk-populations.html.

36. "If You Are at Higher Risk," Harvard Health, last modified February 25, 2021, https://www.health.harvard.edu/diseases-and-conditions/if-you-are-at-higher-risk#:~:text=The%20risk%20of%20serious%20illness,conditions%2C%20obesity%2C%20or%20diabetes.

37. Jennifer M. Dan et al., "Immunological Memory to SARS-CoV-2 Assessed for up to 8 Months after Infection," *Science* 371, no. 6529 (June 2021), https://doi.org/10.1126/science.abf4063.

38. "Coronavirus Disease (COVID-19): Herd Immunity, Lockdowns and COVID-19," World Health Organization, last modified December 31, 2020d, https://www.who.int/news-room/q-a-detail/herd-immunity-lockdowns-and-covid-19.

Lengths of Resistance

Average amount of time that people retain immunity to selected viral diseases

	ILLNESS	VIRUS	LENGTH OF IMMUNITY
CORONAVIRUSES	Covid-19	SARS-CoV-2	Unknown
	Common cold	HCV-229E	6 months
	Severe acute respiratory syndrome	SARS-CoV	24 months
	Middle Eastern respiratory syndrome	MERS-CoV	34 months
OTHERS	Flu	Influenza A	6 months
	Measles	Rubeola	Lifelong

Sources: Nextstrain; Epidemiology & Infection; Emerging Infectious Diseases Journal of Medical Virology

Figure 4: Comparison of Immunity in Virus Caused Illnesses[39]

(Figure 4).[39]

2.4.1. Lasting Immunity Against SARS-CoV-2 Infection

Our immune system, like our memory, remembers a few infections indeed well, however, will in general fail to remember some others. For instance, the immunization given for measles, the MMR antibody, gives deep rooted invulnerability against the infection. In any case, some influenza immunizations require a yearly shot as the antibodies last for a restricted period in the immune system.

In relation to production of antibodies in SARS-CoV-2 infections, detection of IgM antibodies occurs from the fourth day of infection, increasing with time until reaching the 20th day and reducing, while the detection of IgG occurred from the seventh day to the peak on the twenty-fifth day and maintain high levels after 4 weeks of infection.[40]

2.4.2. Immunological Memory To SARS-CoV-2

Immunological memory duration after SARS-CoV-2 infection is unclear. Immunological memory can consist of memory B cells, antibodies, helper T cells, and killer T cells.[35] SARS-CoV-2 enters lung cells via the Angiotensin-Converting Enzyme 2 (ACE2) receptor. This is followed by the production of mediators that cause the activation of immune cells.[41]

Epitope Predictions: More importantly, T-cell-based cellular immunity is essential for cleaning SARS-CoV-2 infection because it is memory based.[42]

The immune system of a healthy individual already has strong immunity against infections, but the elderly and immunodeficient/chronically ill individuals are at risk for an increased incidence and severity of certain infections. IgM and IgG are both produced in asymptomatic persons; however, the production of IgG was markedly higher in symptomatic persons compared to asymptomatic persons during the acute phase. The infection is usually mild or moderate, or even asymptomatic (which makes diagnosis difficult) in children in spite of the viral RNA quantity being very high in their nasopharynx for kids under 5 years of age.[40]

Having immunity shields you from the illness and lessens the impact of the infection on your body. Understanding who is in danger of getting and spreading the disease is vital to facilitate

39. Robert Lee Hotz, "Does Covid-19 Infection Equal Immunity?," The Wall Street Journal, April 19, 2020, https://www.wsj.com/articles/does-covid-19-infection-equal-immunity-11587314824.

40. Daniela S. Oliveira, Nayara I. Medeiros, and Juliana A.S. Gomes, "Immune Response in COVID-19: What Do We Currently Know?," *Microbial Pathogenesis* 148 (2020): p. 104484, https://doi.org/10.1016/j.micpath.2020.104484.

41. Wentao Ni et al., "Role of Angiotensin-Converting Enzyme 2 (ACE2) in COVID-19," *Critical Care* 24, no. 1 (2020): p. 422, https://doi.org/10.1186/s13054-020-03120-0.

42. Renu Jakhar and S. K. Gakhar, "An Immunoinformatics Study to Predict Epitopes in the Envelope Protein of SARS-CoV-2," *Canadian Journal of Infectious Diseases and Medical Microbiology* 2020 (2020): pp. 1-14, https://doi.org/10.1155/2020/7079356.

the lockdown guidelines. The span of invulnerability accomplished either by contamination or by inoculation will choose how viably the infection can be contained. How long the antibodies and resistance against the infection endures will likewise choose if the immunization is life long, or requires yearly shots.[43]

2.5. Current Understanding About The SARS-CoV-2 Antibody Testing

COVID-19 antibody tests can't be used to diagnose the COVID-19, but these tests help us to find out if you've ever had it. There is a widespread discussion at the local, state and national level on the use of COVID-19 antibody tests to be done at the whole population level for returning back to work and restart the economy.

2.5.1. Predictability

- The presence of positive antibodies could indicate at least short-term immunity to infection with SARS-CoV-2.
- Neutralizing antibodies may safeguard against reinfection and reduce disease severity.
- There are several reliable serological tests available that harmonize with neutralizing antibody titers.
- In non-human primate models, post-infection immunity lasts at least 4 weeks.[44]
- Antibody testing should be performed at least two weeks after the onset of symptoms.
- The sensitivity and specificity of antibody tests change over time. In the context of clinical history, the outcomes should be interpreted with it.
- Antibody testing might prove to be very promising in diagnosing COVID-19 in patients with prolonged symptoms, late presentation or negative results from reverse transcription PCR tests.
- Individuals with SARS-CoV-2 antibodies, currently the evidence for protective immunity is unsufficient.[45]

2.5.2. Uncertainties

43."WHO SAGE Values Framework for the Allocation and Prioritization of COVID-19 Vaccination," Coronavirus, World Health Organization, last modified September 14, 2020e, https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_prioritization-2020.1-eng.pdf.

44."Interim Guidelines for COVID-19 Antibody Testing," COVID-19, Centers for Disease Control and Prevention, last modified August 1, 2020c. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html.

45.Jessica Watson, Alex Richter, and Jonathan Deeks, "Testing for SARS-CoV-2 Antibodies," *The BMJ*, August 2020, p. m3325, https://doi.org/10.1136/bmj.m3325.

- Most studies on antibody tests are from infected patients in hospital, whereas we do not know how the tests work in patients with mild illness or with people who are asymptomatic, who never visit the hospital.
- Does the presence of antibodies confers lasting immunity to protect against future COVID-19 infection.[45]

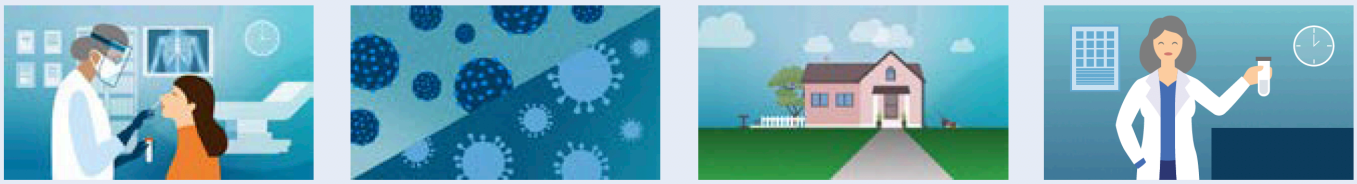
2.6. COVID-19 Testing

You've probably heard a lot about coronavirus disease 2019 (COVID-19) testing recently (Figure 5). If you think you have COVID-19 and need a test, contact your healthcare provider, local pharmacy, or local health department immediately. The accessibility of critical medical products, including tests for SARS-CoV-2, the virus that causes COVID-19, to fight the COVID-19 pandemic has been worked upon by the FDA round the clock.[46]

	MOLECULAR TEST	ANTIGEN TEST	ANTIBODY TEST
Also known as...	Diagnostic test, viral test, molecular test, nucleic acid amplification test (NAAT), RT-PCR test, LAMP test	Rapid diagnostic test (Some molecular tests are also rapid tests.)	Serological test, serology, blood test, serology test
How the sample is taken...	Nasal or throat swab (most tests) Saliva (a few tests)	Nasal or throat swab	Finger stick or blood draw
How long it takes to get results...	Same day (some locations) or up to a week	One hour or less	Same day (many locations) or 1-3 days
Is another test needed...	This test is typically highly accurate and usually does not need to be repeated.	Positive results are usually highly accurate but negative results may need to be confirmed with a molecular test.	Sometimes a second antibody test is needed for accurate results.
What it shows...	Diagnoses active coronavirus infection	Diagnoses active coronavirus infection	Shows if you've been infected by coronavirus in the past
What it can't do...	Show if you ever had COVID-19 or were infected with the coronavirus in the past	Definitively rule out active coronavirus infection. Antigen tests are more likely to miss an active coronavirus infection compared to molecular tests. Your health care provider may order a molecular test if your antigen test shows a negative result but you have symptoms of COVID-19.	Diagnose active coronavirus infection at the time of the test or show that you do not have COVID-19

Figure 5: Different Types of Coronavirus Tests.[46]

46."Coronavirus Disease 2019 Testing Basics," Consumer updates, U.S. Food and Drug Administration (FDA), last modified June 11, 2020, https://www.fda.gov/consumers/consumer-updates/coronavirus-disease-2019-testing-basics.



- **Rapid, point-of-care** diagnostic tests use a mucus sample from the nose or throat but can be analyzed at the doctor's office or clinic where the sample is collected and results may be available in minutes. These may be molecular or antigen tests.
- **Combination tests** can test for the flu and the coronavirus at the same time. Some can test for many different types of respiratory viruses, including the one that causes COVID-19.
- **At-home collection** tests, available only by prescription from a doctor, allow the patient to collect the sample at home and send it directly to the lab for analysis. Some at-home collection tests have a health care provider oversee the sample collection by video with the patient.
- **Saliva tests** allow a patient to spit into a tube rather than get their nose or throat swabbed. Saliva tests may be more comfortable for some people and may be safer for health care workers who can be farther away during the sample collection.

Figure 6: Diagnostic tests are now available with alternative methods and benefits.[46]

Importance of Accurate Testing: The spreading of infection can be controlled by accurate testing of people who might need treatment, or who need to isolate themselves. A false negative result, can delay treatment and further risk of infection to others. A false positive result, can lead to un-needed further testing, treatment, and isolation of the person and their close contacts.

Antibody test results from the people known to have COVID19 and not having COVID19 were compared to identify false negative and false positive results. Participants involved in study were classified as known and nor known to have COVID19 based on the benchmark called as 'reference standard'.[46]

2.7. Potential Endpoints Of An Efficacious COVID-19 Vaccine

An effective and efficacious vaccine against SARS-CoV-2 might prevent infection, could bring down the likeliness of infection of an individual, severity of disease in an individual and cease further transmission of the virus (Figure 7).[47]

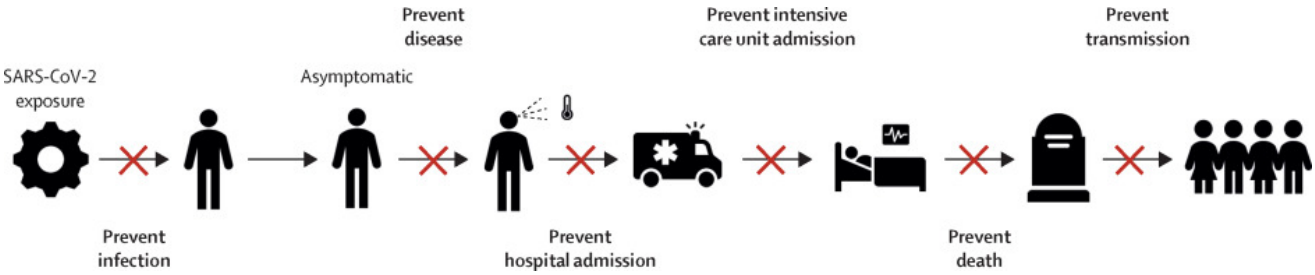


Figure 7: Potential endpoints of an efficacious COVID-19 vaccine [47]

47.Susanne H Hodgson et al., "What Defines an Efficacious COVID-19 Vaccine? A Review of the Challenges Assessing the Clinical Efficacy of Vaccines against SARS-CoV-2," *The Lancet Infectious Diseases* 21, no. 2 (2021), https://doi.org/10.1016/s1473-3099(20)30773-8.

The worldwide effort to produce a safe and effective COVID-19 vaccine is yielding affirmative results. A small number of vaccines now have been authorized around the globe, many more remain in development and in different phases. All vaccines submitted in this report are either approved for full use or early/limited use as of 28th February 2021 (Table 3).

VACCINE NAME	VACCINE TYPE	EFFICACY	DOSE	MODE OF ADMINISTRATION AND AGE	STORAGE	PRIMARY DEVELOPERS	COUNTRY OF ORIGIN	AUTHORIZATION/ APPROVAL	AUTHORIZATION/APPROVAL
Brand name: Comirnaty Other name: BNT162b2, tozinameran	Component vaccine - RNA-based - messenger RNA (mRNA)	95%	2 doses, 3 weeks apart	Intramuscularly - people aged 16 years and older	Freezer storage only at –13°F to 5°F (–25°C to –15°C) for 2 weeks. 6 months at -90 °C to -60 °C.	Pfizer, BioNTech; Fosun Pharma	Several Countries	Authorized by U.S. FDA On December 11, 2020	Approved for use in Bahrain, Brazi, Zealand, Saudi Arabia, Switzerland Emergency use in Argentina, Australia, Canada, Chile, Colombia, Costa Rica, Ecuador, European Union, Hong Kong, Iceland, Iraq, Israel, Japan, Jordan, Kuwait, Lebanon, Malaysia, Mexico, Mongolia, Norway, Oman, Panama, Peru, Philippines, Qatar, Serbia, Singapore, Tunisia, United Arab Emirates, United Kingdom, United States. Emergency use validation from the World Health Organization.
Brand name: mRNA-1273 Other names: mRNA-1273, CX-024414, COVID-19 Vaccine Moderna, COVID-19 mRNA Vaccine Moderna	Component vaccine – RNA-based - messenger RNA (mRNA)	94.50%	2 doses, 4 weeks apart	Intramuscularly - people aged 18 years and older	30 days with refrigeration, 6 months at –4°F (–20°C)	NIH and Moderna, BARDA, NIAID	United States	Authorized by U.S. FDA On December 18, 2020	Approved for use in Switzerland Emergency use in Canada, European Union, Iceland, Israel, Mongolia, Norway, Qatar, Singapore, United Kingdom, United States
Brand name: Sputnik V Other names: Gam-Covid-Vac	Component vaccine - Non-Replicating Viral Vector -Recombinant adenovirus (rAd26 and rAd5)	91.6%	2 doses, 3 weeks apart	Intramuscularly - people aged 18 years and older	Freezer storage. Developing an alternative formulation that can be refrigerated	Gamaleya Research Institute, Acellena Contract Drug Research, and Development	Russia	Approved by Russian health care regulator	Early use in Russia Emergency use in Algeria, Argentina, Armenia, Bahrain, Belarus, Bolivia, Bosnian Serb Republic, Egypt, Honduras, Gabon, Ghana, Guatemala, Guinea, Guyana, Hungary, Iran, Kazakhstan, Kyrgyzstan, Lebanon, Mexico, Mongolia, Montenegro, Myanmar, Nicaragua, Pakistan, Palestinian Authority, Paraguay, San Marino, St. Vincent and the Grenadines, Serbia, Tunisia, Turkmenistan, United Arab Emirates, Uzbekistan, Venezuela"
Brand name: AZD1222 (AstraZeneca) Other name: ChAdOx1 nCoV-19; Covishield in India	Component vaccine - Non-Replicating Viral Vector - Adenovirus vaccine	63.09%	2 doses, 4 weeks apart	Intramuscularly - people aged 18 years and older	Temperatures up to 30 °C. Stable in the refrigerator for at least 6 months	The University of Oxford, AstraZeneca, BARDA, OWS	UK	Awaiting emergency or regular approval from the FDA.	Emergency use in: Algeria, Argentina, Australia, Bangladesh, Bhutan, Brazil, Chile, Dominican Republic, Egypt, El Salvador, European Union, Iceland, India, Iraq, Kuwait, Maldives, Mexico, Mongolia, Morocco, Nepal, Nigeria, Norway, Pakistan, Philippines, Saudi Arabia, Seychelles, Sri Lanka, South Africa, South Korea, Thailand, United Kingdom, Vietnam. Emergency use validation from the World Health Organization
Brand name: Convidecia Other name: Ad5-nCoV	Component vaccine - Non-Replicating Viral Vector -Recombinant (adenovirus type 5 vector)	65.28%	Single dose	Intramuscularly - people aged 18 years and older	Refrigerated stored at the temperature of 2-8°C	CanSino Biologics	China	Approved by the Health Bureau of the Logistics Support Department of the Central Military Commission	Emergency use in: Mexico, Pakistan Limited use in: China
Brand name: JNJ-78436735 Other names: Ad26.COV2.S	Component vaccine - Non-Replicating Viral Vector	72% in the United States, 64% in South Africa, 61% in Latin America	Single dose	Intramuscularly – people aged 18 and older	Up to two years frozen at –4° F (–20° C), and up to three months refrigerated at 36–46° F (2–8° C)	Janssen Pharmaceutica, a Belgium-based division of Johnson & Johnson	The Netherlands, US	Submitted an Emergency Use Authorization (EUA) request to FDA.	Emergency use in Saint Vincent and the Grenadines, Bahrain, and United States
Brand name: EpiVacCorona	Component vaccine -Protein Subunit - Peptide	Unknown	2 doses, 3 weeks apart	Intramuscularly - people aged 16 years and older	Stable in the refrigerator for up to two years	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology Russia	Russia	Russian Health Ministry granted regulatory approval	Early use in Russia
Brand name: BBIBP-CorV	Whole vaccine – Inactivated	79.34%	2 doses, 3 weeks apart	Intramuscularly- people aged 18 to 59 or 60 and older	Normal refrigeration temperatures	Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	Approval provided by Chinese Government	Approved for use in Bahrain, China, United Arab Emirates Emergency use in Argentina, Cambodia, Egypt, Guyana, Hungary, Iraq, Jordan, Nepal, Pakistan, Peru Limited use in Serbia, Seychelles

continued on page 16

VACCINE NAME	VACCINE TYPE	EFFICACY	DOSE	MODE OF ADMINISTRATION AND AGE	STORAGE	PRIMARY DEVELOPERS	COUNTRY OF ORIGIN	AUTHORIZATION/ APPROVAL	AUTHORIZATION/APPROVAL
Brand name: CoronaVac Other names: PiCoVacc	Whole vaccine – Inactivated vaccine (formalin with alum adjuvant)	50.38%	2 doses, 2 weeks apart	Intramuscularly - people aged 18 years and older	If refrigerated at 2 to 8 degrees Celsius stable for up to three years else 42 days when stored at 25 degrees.	Sinovac	China	Approval provided by Chinese Government	Approved for use in China Emergency use in Azerbaijan, Brazil, Chile, Colombia, Hong Kong, Indonesia, Laos, Mexico, Philippines, Thailand, Turkey, Uruguay
No name announced	Whole vaccine – Inactivated vaccine	86% efficacy as per UAE	2 doses (21-28 days as per UAE recommendation)	Intramuscularly - people aged 18 years and older	2 to 8 degrees Celsius	Wuhan Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	Approval provided by Chinese Government	Limited use in China, United Arab Emirates
Brand name: Covaxin Other name: BBV152A, BBV152B and BBV152C	Whole vaccine – Inactivated vaccine	Unknown - The interim efficacy estimate will be generated by the end of Feb, 2021	2 doses, 4 weeks apart	Intramuscularly - people aged 18 years and older	At least a week at room temperature	Bharat Biotech, ICMR	India	Emergency Use Authorization (EUA) provided by the Indian Government	Emergency use in India
Brand name: CoviVac	Inactivated vaccine	Efficacy has not yet begun	2 doses, 14 days apart	Intranasal - a single-dose -drops into each nostril - people aged 18 to 60 years old	Normal fridge temperatures, of 2 to 8 degrees Celsius (35.6 to 46.4 Fahrenheit)	Chumakov Federal Scientific Center for Research and Development of Immune and Biological Products	Russia	Russia granted regulatory approval	Early use in Russia

Table 3: Approved or Authorized Vaccines as of Feb 27th, 2021[48 49 50 51 52 53 54 55]
Source: McGill COVID-19 Vaccine Tracker Team/The New York Times (NYT)/European Medicines Agency (EMA)/Regulatory Affairs Professionals Society (RAPS)/CDC/National Geographic/WHO/Reuters

2.8. Rationale For Vaccinating Minor Children And Adolescents

In young children and in adolescents, morbidity and mortality associated with SARS-CoV-2 infection are significantly lower, and children may be less susceptible to infection. Children are mostly very mild with COVID-19 disease symptoms and their treatment is just by providing supportive care, but very few exceptional cases have led to mortality. As the severity of the COVID-19 disease symptom increases, even children with most adults have met with fatality.[56]

48. "COVID-19 Vaccine Tracker," COVID19 Vaccine, McGill COVID19 Vaccine Tracker Team, accessed February 28, 2021, https://covid19.trackvaccines.org/vaccines/.

49. Carl Zimmer et al., "Coronavirus Vaccine Tracker," *The New York Times*, February 27, 2021, https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

50. "COVID-19 Vaccines," Human regulatory, European Medicines Agency (EMA), accessed February 26, 2021, https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines.

51. "COVID-19 Vaccine Tracker," Regulatory Focus, Regulatory Affairs Professionals Society (RAPS), last modified February 27th, 2021, https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker.

52. "Different COVID-19 Vaccines," Coronavirus, Centers for Disease Control and Prevention, last modified January 15, 2021d, https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html.

53. "Latest: Developments of coronavirus vaccine," Coronavirus Coverage, National Geographic, published February 27, 2021, https://www.nationalgeographic.com/science/article/coronavirus-vaccine-tracker-how-they-work-latest-developments-cvd.

54 "Interim Recommendations for Use of the AZD1222 (ChAdOx1-S (Recombinant)) Vaccine against COVID-19 Developed by Oxford University and AstraZeneca," Interim guidance,World Health Organization, posted February 10, 2021a, https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1.

55. "UAE Says Sinopharm Vaccine Has 86% Efficacy against COVID-19," Healthcare and Pharmaceuticals, Reuters, last updated December 9, 2020, https://www.reuters.com/article/health-coronavirus-emirates-idUSKBN28J0G4.

56. Ayesha Mirza, "Coronavirus Disease 2019 (COVID-19) in Children: Practice Essentials, Background, Pathophysiology," Medscape, last modified March 1, 2021, https://emedicine.medscape.com/article/2500132-overview.

Increasingly, the test results suggest that infected children and adolescents can infect other children and adults. To protect society as a whole, including older adults, and to decrease household transmission of SARS-CoV-2, it may make sense to vaccinate children and adolescents, as well as adults.[57]

Critical populations like teachers and staff in K-12 schools and in out-of-home childcare settings needed to maintain core societal functions and should receive prioritized access to SARS-CoV-2 vaccines when supplies are limited according to the CDC, National Academies of Sciences Engineering and Medicine (NASEM), and Johns Hopkins Center for Health Security. Minor children are not considered as a high priority group by none of their allocation frameworks. One could argue that part of protecting teachers and staff working in K-12 schools would be to also prioritize vaccination of students.[57]

Although children may not be in a high-risk category, we do not yet understand the virus enough to determine the virus's long-term effects. Potentially, children with pre-existing conditions could be at a higher risk than their peers.

3. Health Passports

With the proposal of introducing immunity passports into a global society, it is important to differentiate the meaning between the terms "health passport" and "immunity passport", which have been used interchangeably.

A health passport is a booklet containing some or all of the reported details regarding a patient's medical information or visits in public healthcare. The patient retains this book for safekeeping. The private sector does not utilize this system.[58] It is a global communication tool important for someone with a chronic condition or disability, has support needs, or could benefit from using a Health Passport. It is taken along with the patient when attending hospitals or other wellness or disability services. The patient includes information that may cause them anxiety, or they want to communicate with the health professional. It prevents the patient from having to reiterate information or communicate when they are unable.[59]

In April of 2020, WHO published some governments had proposed that the detection of antibodies to the virus SARS-CoV-2 could serve as the foundation for an "immunity passport" or a "risk-free certificate" that would permit someone to travel or return to work, assuming that they were protected against re-infection, from a previous viral infection or vaccination. However, there is no

57. Gregory D. Zimet, Ross D. Silverman, and J. Dennis Fortenberry, "Coronavirus Disease 2019 and Vaccination of Children and Adolescents: Prospects and Challenges," *The Journal of Pediatrics*, 2020, https://doi.org/10.1016/j.jpeds.2020.11.002.

58. Clarris Shiri et al., "The Role of Insight into and Beliefs about Medicines of Hypertensive Patients," *Cardiovascular journal of Africa* 18, no. 6. (2007): pp. 353-357, https://www.ncbi.nlm.nih.gov/pubmed/18092108.

59. "What Is a Health Passport?," Disability responsiveness, Capital & Coast District Health Board, accessed March 4, 2021, https://www.ccdhb.org.nz/your-health/disability-responsiveness/what-is-a-health-passport/.

proof that people are immune when they recover from COVID-19 and are provided protection from a second infection.[60]

History Of Passports

The earliest reference to a document which operated as a passport, stretches back to 1500 BC in Egypt, where people were required to have permission documents before leaving port. The word itself, passport, is considered to have its roots in the French word passer (to pass) and port, as this document allowed the holder to travel from ports in ships.

However, the concept of identification based on physical characteristics while on travel, was first observed in ancient China, where features such as name and age were included in the document.[61] As Lloyd describes in his book, documents with a passport quality have been utilized for various purposes in many cultures, but almost all of them serve some basic concepts. The first of them is to administer permission to travel. History shows that passports have been used by civilizations as a way to regulate the movement of their own citizens, and to efficiently control who can infiltrate. Various countries, such as China and Canada, have also implemented the use of passports to supervise the movement of people within their country, in case individuals wanted to move from their local territory.

Secondly, these kinds of documents have also served as a form of protection for the traveller. Specifically, during times of war, many regions used certain documents called safe conducts, in order to enable the traveller to safely pass-through enemy lands if it was necessary.

Finally, throughout history passports have served as a means of freedom. Freedom of movement is considered a fundamental right of human life in various civilizations, and while passports have acted as way to certify this freedom, at the same time societies have utilized their properties in order to regulate it, with an aim to safeguard the proper functioning and security of their states.[62]

The notion of a passport similar to what we possess today, acting as a proof of citizenship, was first implemented at the time when Henry V was the king of England. During this time, at around 1420, the emperors of England put the passport concept into action, in an effort to give their citizens the chance to prove their identity, while traveling in a foreign land.

Many years later, during the mid-20th century and while the world has been at war, governments decided to increase their security policies. Passport controls became strict within the country's borders and this tactic persevered even after the end of the war.[63]

Similar standards to today's passports were set in 1980 by International Civil Aviation Organization. The ICAO suggested standardization directions to governments around the world, in order to

60. "Immunity Passports" in the Context of COVID-19," World Health Organization, Scientific brief, last modified April 24, 2021, https://www.who.int/publications/i/item/immunity-passports-in-the-context-of-covid-19.

61. Thomas Ehrlich, "Passports," *In Stanford Law Review*, ed. Douglas E. Kliever (Stanford, CA: Stanford University Press, 1966-1967), 129.

62. Martin Lloyd, *The Passport: The History Of Man's Most Travelled Document* (England: Sutton Publishing, 2003).

63. Jane Caplan and John Torpey, *Documenting individual identity: The development of state practices in the modern world* (Princeton: Princeton University Press, 2001).

facilitate the traveling procedure for everyone.

Throughout history, the passport has evolved from handwritten papers to advanced biometrics, but the aim behind them still remains the same: to ensure the safety of the global community.[64]

3.1. Generic Details On Immunity Passports

- Immunity Passports can include a wristband, certificate, mobile application, or any other form of record. They are a way of documenting a person's presumed immunity to COVID-19 due to past infection or from receiving a vaccination. It would need to be verified by testing at the time of infection or afterward for antibodies.
- Holding an Immunity Passport could allow people the freedom to return to work or reward them with the experience of socializing with others, advantages taken away during lockdowns.
- Currently, it is unknown how long immunity lasts for COVID-19. Passports should be designed with an expiration date, or people need to retest to verify the status of their immunity to COVID-19.
- Immunity Passports could be combined with other measures, such as global testing and contact tracing.[2]
- An Immunity Passport's idea has progressed, whereby serologic tests for SARS-CoV-2 protein detection signifies resistance to a second infection. In regards to international travel, it would gratify anxious travelers and travel bans within countries. Under International Health Regulations, documentation regarding vaccination or prophylaxis for yellow fever already exists.[65]

Gartner research confirms that Health Passports and new social distancing technologies would be emerging technologies with health passports coming in less than two years with high impact in their Hype Cycle (Figure 8).[66]

64. John Torpey, *The invention of the passport: Surveillance, citizenship and the state* (Cambridge University Press, 2018)

65. Chee H Liew and Gerard T Flaherty, "Immunity Passports to Travel during the COVID-19 Pandemic: Controversies and Public Health Risks," *Journal of Public Health*, May 2020, p. Fdaa125, https://doi.org/10.1093/pubmed/fdaa125.

66. "The Gartner Hype Cycle for Emerging Technologies, 2020 highlights 30 technology profiles that will significantly change society and business over the next five to ten years," Smarter With Gartner, Gartner Research, last modified August 18, 2020, https://www.gartner.com/smarterwithgartner/5-trends-drive-the-gartner-hype-cycle-for-emerging-technologies-2020/.

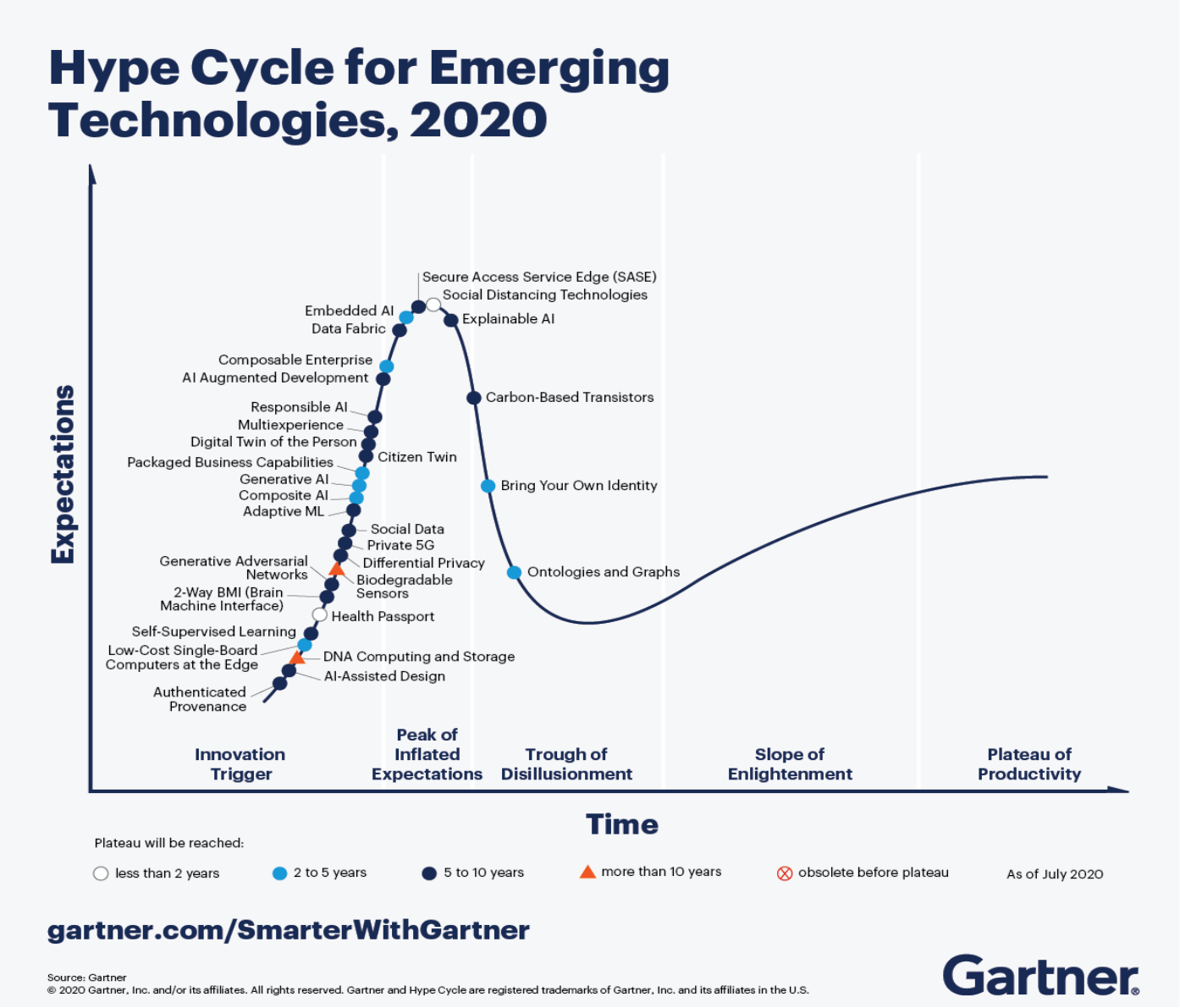


Figure 8: Hype Cycle for Emerging Technologies [66]

There are some criteria to be satisfied for any immunity certificate to be valid in the case of COVID-19.[65] Based on the inference from Liew & Flaherty template we have created the following table with various criterion points including ethical consideration.

CRITERION POINTS TO PONDER	CONTEMPLATION FOR COVID-19 HEALTH PASSPORT
Disease prevalence	Population studies are still ongoing with low seroprevalence to date
Antibody response to infectious disease	Uncertainty about the level of antibody production for mild or asymptomatic cases
The presence of protective immunity against disease	It has not been determined whether the production of antibodies amounts to immunity against the second infection
Duration of immune response	It is unclear whether neutralizing antibodies persist for more than 40 days after the onset of symptoms
Attainability of antibody test	The affordability of commercial antibody test by all may not be possible
Level of test performance	Extremely sensitive and particular tests are available at the same time tests of lesser quality exist
Test error	No test is perfect. In swab tests, a positive test is always positive while a negative test is sometimes false.
Incentive and counterfeits	Results should be processed and confirmed by licensed laboratories to be authenticated and avoid counterfeit
Viability of retesting	Many people may have to undergo a retest to establish their present immunity levels
Impregnable authentication processes	Documents must resist attempts to infringe
Privacy concerns	The privacy rights of individuals should not be jeopardized if electronic applications are used
Stigma	Trusted agencies should only be allowed to control the database to minimize the data abuse
Public health initiatives	Risk of not complying with a face mask or social distancing adherence
Ethical justification	Transparency and Inclusiveness must be paramount with Consistency and Accountability
Ethical concern	Different layers in society must be addressed while safeguarding their livelihood
Global Data Protection	Safeguard against theft or loss and have a disaster recovery plan
Prioritization and costs for vaccine	Vaccination must be provided free of cost to the socially and economically challenged

Table 4: Health passport validation criteria for COVID-19.[65 67 68 69 70 71]
Source: WHO/Bulletin of the World Health Organization/MIT Medical/Publications in Oxford Academic/Publication in ACP Journals by McGill University Health Centre

67. "Ethics and COVID-19: Resource Allocation and Priority-Setting," Global health ethics, World Health Organization, accessed March 04, 2021, https://www.who.int/ethics/publications/ethics-and-covid-19-resource-allocation-and-priority-setting/en/.

68. Teck Chuan Voo et al., "Immunity Certification for COVID-19: Ethical Considerations," *Bulletin of the World Health Organization* 99, no. 2 (January 2020a): pp. 155-161, https://doi.org/10.2471/blt.20.280701.

69. "How accurate are the laboratory tests used to diagnose COVID-19?," Covid-19 Updates, MIT Medical, last modified April 29, 2020, https://medical.mit.edu/covid-19-updates/2020/06/how-accurate-diagnostic-tests-covid-19.

70. Angus Dawson et al., "Key Ethical Concepts and Their Application to COVID-19 Research," *Public Health Ethics,* July 13, no. 2 (2020): pp. 127-132, https://doi.org/10.1093/phe/phaa017.

71. Matthew P. Cheng et al., "Serodiagnostics for Severe Acute Respiratory Syndrome–Related Coronavirus 2," *Annals of Internal Medicine* 173, no. 6 (2020): pp. 450-460, https://doi.org/10.7326/m20-2854.

Bioethics and research in social sciences can be intact in order to improve research, policy and practice on current and future infectious diseases. Moral suffering is a helpful area for further research in bioethics and social sciences because it can shed light on the underlying content and sources of the most pressing ethical concerns among health professionals.[72]

The type of doubt and forced options in which health professionals attempt to act according to familiar best practices could be generated by COVID-19. Prior public health and humanitarian emergencies have created moral distress, presenting us significant witness for predicting these hurdles should they arise in the future. Moral distress is an idea that emerged from nursing ethics and has propagated to all health professions, including cases in which a health professional believes that he or she knows the morally correct thing to do but cannot do so.[72]

It is possible that a blockchain system would enable anyone with an Immunity passport to share a fingerprint in the formation of a hash with anyone to prove they're negative for COVID-19 infection or their immunity. Personal information enwrapped in the immunity passport is not revealed because the hash impression on blockchain allows access to the PDF of affirmative results from a trusted lab only.[73]

Seifert concludes that companies and governments examine how to properly roll-out secure digital Health passports. Their launch will not be feasible until the antibody test confirms that end-users remain immune.[73]

3.2. Design Of Immunity Certificates

Immunity passports may be created to be secure and give portability of immunity status. Moreover, the foundation sustaining digital passports can trace every vaccine vial and its distribution to each individual. Likewise, the passports would need to be standardized globally and transportable within and across borders while linked to passport data for a cross-border application. Governments can require secure verification devices while requiring users to disclose minimal personal information. Consequently, some have fought for biometric registries to operate as COVID-19 "immunity passports" that prove immunity (by past infection or vaccination) and enable someone to move about freely.

Another concern that needs addressing is the interoperability of such digital passports across industries, governments, and health care systems. Some airlines intend to introduce COVID-19 health pass apps to verify passengers' COVID-19 results. While these digital passports could facilitate reopening society, they heighten anxieties regarding privacy and equality. Vulnerable residents with limited access to vaccination services and smart devices could effectively be

72. Karen M. Meagher et al., "COVID-19 Ethics and Research," *Mayo Clinic Proceedings* 95, no. 6 (2020): pp. 1119-1123, https://doi.org/10.1016/j.mayocp.2020.04.019.

73. "Covid-19 Immunity Passports: How to Protect Health Data," COVID-19, Medical Technology, last modified August 4, 2020, https://medical-technology.nridigital.com/medical_technology_aug20/covid-19_immunity_passports_health_data.

restricted access to places of employment, businesses, and schools.

In regards to privacy concerns, it is essential to think about nationwide vaccine rollouts. For example, strong security controls should be established beforehand to prevent stolen personal data. Conformity should be guaranteed by exploring regulations and rules set by the Centers for Medicare & Medicaid Services and aligning federal and state regulations to circumvent how personal data should be managed.

Medical identity theft is one likely barrier that could impact a COVID-19 vaccine identification or registry. People may attempt to use stolen or fake identities to obtain their vaccination earlier than they would typically under guidelines. Phishing campaigns targeted upon those expected to receive their vaccination earlier may be a possibility. Another inherent danger is fraudulent records indicating an individual has received their COVID-19 vaccination when they have not.[74]

3.3. Potential Benefits Of Health Passport For COVID-19

"An immunity passport is a presentable proof of immunity to Covid-19," said Husayn Kassai, co-founder and CEO of Onfido, a London-based technology company specialising in facial biometric certification.[75]

According to Voo et. al article for the purpose of prioritization of vaccine allocation, the essential workers can be identified from the information on the serological status of workers in various sectors. Insecure patient groups affected by no-visitor policies can be allowed visits by family members with affirmed serological status.[77]

Immunity passports could be used along with the currently used vaccination certificates for international travel that aid in reducing the risk of international epidemic spreading. This would certainly require following internationally accepted standards and compliance set by the International Health Regulations (2005) Third Edition.[76] In addition, IHR relaxes the state to implement additional control measures without being more invasive or too intrusive to people for optimal health protection by innovating proper workarounds.[77]

The Health passport could also admit sports and entertainment venues to reopen safely, as well as the global conference and exhibition industry. The healthy travelers could be spared from quarantine.[78]

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74. "Rolling Out the Covid Vaccine Is a Huge IT Challenge," Technology, Harvard Business Review, last modified December 21, 2020, https://hbr.org/2020/12/rolling-out-the-covid-vaccine-is-a-huge-it-challenge.

75. Justin Meneguzzi, "Travel - Will You Need an 'Immunity Passport' to Travel?," *British Broadcasting Corporation (BBC)*, August 31, 2020, http://www.bbc.com/travel/story/20200831-coronavirus-will-you-need-an-immunity-passport-to-travel.

76. "International Health Regulations (2005) Third Edition," Publication, World Health Organization, last modified January 01,2 2016, https://www.who.int/publications/i/item/9789241580496.

77. Teck Chuan Voo, Hannah Clapham, and Clarence C Tam, "Ethical Implementation of Immunity Passports During the COVID-19 Pandemic," *The Journal of Infectious Diseases* 222, no. 5 (2020): pp. 715-718, https://doi.org/10.1093/infdis/jiaa352.

78. "Could This COVID-19 'Health Passport' Be the Future of Travel and Events?" Emerging Technologies, The World Economic Forum, last modified July 30, 2020. https://www.weforum.org/agenda/2020/07/covid-19-passport-app-health-travel-covidpass-quarantine-event/.

3.4 The Need For a Multivariable Health Passport

COVID-19 pandemic has caused massive disruption of travel along with other aspects of life. The travel industry is a major part of the global economy. With 1.5 billion international tourist arrivals in 2019, the travel industry is the world's third-largest export category and international tourism generated US$1.7 trillion exports in 2018 or nearly US$5 billion daily. International tourism contributes immensely to global exports, accounting for 7% of global exports and 29% of the world's services exports.[79]

The ongoing COVID-19 pandemic requires detailed consideration of many factors especially in decisions about long-distance travel, although many of the same issues apply to domestic travel and return to the workplace and other daily activities.

The following factors should be considered:

1. Traveller's personal risk stratification, which considers
    a. The individual traveller's risk factors for severe COVID-19 disease (age and underlying diseases)
    b. Threshold for risk.[80]
    c. Assessment of immunity.[81]
2. Elements of travel (trip details - ship/cruise, airplane, bus, train travel or private vehicle trip)
3. Policies imposed by health insurance, employer and government regulations at both origin and destination countries

The rationale for the implementation of the Health Pass with multiple variables is complex and based on the integration of different factors mentioned above, to achieve a specific goal, preventing the export and import of the virus. Current understanding of COVID-19 pathology, ways of transmission, diagnostic methods allow us better control the spread of the virus, but the constant appearance of new strains of SARS-Cov-2 virus, development of new vaccines with different percentage of efficacy, unanswered questions regarding immunity after COVID-19 led us to the idea of a multivariable health passport. Additionally, each state or country has its own requirements, so a multivariable health passport can adjust and keep track of all those factors and the person will be fit with the requirements of the particular area.

79. "International Tourism Continues to Outpace the Global Economy," *International Tourism Highlights, World Tourism Organization*, last modified July 2019, https://www.e-unwto.org/doi/pdf/10.18111/9789284421152.

80. Marc R. Larochelle, "'Is It Safe for Me to Go to Work?' Risk Stratification for Workers during the Covid-19 Pandemic," *New England Journal of Medicine* 383, no. 5 (2020), https://doi.org/10.1056/nejmp2013413.

81. Lin H Chen, David O Freedman, and Leo G Visser, "COVID-19 Immunity Passport to Ease Travel Restrictions?" *Journal of Travel Medicine* 27, no. 5 (2020), https://doi.org/10.1093/jtm/taaa085.

An effective health passport would include the following variables:

1. **Vaccination Tracking**

Enables users to enter information whether they are vaccinated or not. As of February 2021 there are over 180 official vaccine projects, about 70 of them have reached human experimentation and few of these are currently administered to some sectors of the general population.[82]

Using different technologies, these COVID-19 candidate vaccines are targeting the whole SARS-CoV-2, molecules or fragments of molecules expressed on this virus surface and exploited to elicit a protective immune response. However, almost every vaccine project has its peculiarities that make it unique and which could have significant consequences regarding the efficacy or duration of the induced protection or the safety of the vaccine.

It will likely be a long time before industrial policies and national political issues could allow a solid comparative assessment of the efficacy of the various vaccines. Quantitative comparisons of the efficacy of different vaccines in inducing immune responses are delayed by the lack of international standards. For instance, there is no international standard at the moment for titrating IgG anti-Spike serum antibodies, let alone for neutralization assays or T cell responses. This current technological limitation makes it difficult to compare immune responses elicited by vaccines in different trials.[83]

Moreover, as vaccines developed on distinct technological platforms, they could induce different forms of immunity, each of them appropriate in different environmental and human contexts and the evolution of the pandemic could make some vaccines more appropriate in different geographic contexts or for different clusters (e.g., infants, elderly) of the human population.[84]

Although the vaccine trials show that, after having both doses of a COVID-19 vaccine, most people will be protected against the virus, but there is a long list of unanswered questions which are associated with the pressure brought on by the pandemic and the speed at which these vaccines are being developed.

Unknown Variables

Whether vaccines also prevent someone from spreading the virus
The studies needed to determine whether vaccines stop virus spread are among the most difficult to do and there are several aspects to be taken into account:

- Many countries have implemented lockdowns of varying degrees. So it is hard to know what is contributing to the stop of viral spread, vaccines or lockdowns or behaviour

82. "Draft Landscape and Tracker of COVID-19 Candidate Vaccines," Publication, *World Health Organization*, last modified March 5, 2021, https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines.

83. Guido Forni and Alberto Mantovani, "COVID-19 Vaccines: Where We Stand and Challenges Ahead," *Cell Death and Differentiation* 28 (2021): pp. 626-639, https://doi.org/https://doi.org/10.1038/s41418-020-00720-9.

84. Aldo Tagliabue and Guido Forni, "COVID-19: Who Will Produce the Vaccine?," *Accademia Nazionale dei Lincei*, last modified July 13, 2020, https://www.lincei.it/it/article/covid-19-who-will-produce-vaccine.

changes.

- Countries with an emergency vaccine rollout due to the severity of the situation, have a highly vaccinated population. In this case, monitoring of viral spread was difficult due to the large number of cases.
- It is known that most of the vaccine rollout programs have focused on those most vulnerable and at risk, but most of those people are in places with lots of hygiene and protective activities in place. And it is hard to estimate the vaccine contribution in preventing spread of the virus.

Although most clinical trials of COVID-19 vaccines showed that vaccines prevented the disease, some trial results show that shots might prevent infection.

During the trial of Moderna's vaccine, researchers swabbed all participants to see if they had any viral RNA. They saw a two-thirds drop in the number of asymptomatic infections among people who received the first shot of the two-dose vaccine, compared with those who received a placebo. But they tested people only twice, about a month apart, so might have missed infections.

The UK trial of the vaccine produced by the University of Oxford and AstraZeneca swabbed participants every week, and estimated a 49.3% reduction in asymptomatic infections among a subset of vaccinated participants compared with the unvaccinated group.

Pfizer, says that it will start swabbing participants every two weeks in vaccine trials taking place in the United States and Argentina, to see whether the shot can prevent infection.[85]

And even if the vaccine doesn't prevent transmission of Sars-CoV-2 in most cases, there is already evidence that a non-vaccinated person who catches the virus from a vaccinated person will develop a less severe disease.

Marks et al. show that the viral load of index cases was a leading driver of SARS-CoV-2 transmission. The risk of symptomatic COVID-19 was strongly associated with the viral load of contacts at baseline and shortened the incubation time of COVID-19 in a dose-dependent manner.[86]

Levine-Tiefenbrun et al. observed that the viral load is reduced 4-fold for infections occurring 12-28 days after the first dose of the Pfizer vaccine. These reduced viral loads hint to lower infectiousness, further contributing to vaccine impact on virus spread.[87]

How long it takes to build immunity – Functional neutralising antibodies specific to SARS-CoV-2 are considered important for viral neutralisation and clearance. That is why antibody titres might be good biomarkers for the protective efficacy of antibodies. The kinetic of the antibody response

85. Smriti Mallapaty, "Can COVID Vaccines Stop Transmission? Scientists Race to Find Answers," *Nature News* (Nature Publishing Group, last modified February 19, 2021), https://doi.org/10.1038/d41586-021-00450-z.

86. Michael Marks et al., "Transmission of COVID-19 in 282 Clusters in Catalonia, Spain: a Cohort Study," *The Lancet Infectious Diseases*, 2021, https://doi.org/10.1016/s1473-3099(20)30985-3.

87. Matan Levine-Tiefenbrun et al., "Decreased SARS-CoV-2 Viral Load Following Vaccination," Preprint at *medRxiv* 2021.02.06.21251283, posted February 08, 2021, https://doi.org/10.1101/2021.02.06.21251283.

is characterized by seroconversion 7–14 days following symptom onset and antibody concentrations persisting for weeks to months after infection and viral clearance (IgM - antibodies reached high titres at 10–12 days that subsequently declined 18 days after the onset of symptoms, IgG - titres increased during the first 3 weeks and began to decrease by 8 weeks).[88]

Recent reports on Moderna and Pfizer-BionTech vaccines have shown that, 8 weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-SARS-CoV-2 spike protein, receptor binding domain binding titers. Additionally, the plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells were equivalent to individuals who recovered from natural infection.[89]

AstraZeneca vaccine study showed the induction of humoral responses, characterised by anti-spike glycoprotein IgG and neutralising antibodies, and T-cell responses in most recipients after the first dose of vaccine and an additional increase in humoral immune outcomes after the second dose of vaccine. Humoral immune outcomes in vaccine recipients were similar to those observed in plasma from patients who had recovered from COVID-19.[88]

Duration of Immunity from Vaccine – Reinfection, after documented infection, has been shown in patients with SARS-CoV-2. It is unclear, whether such reinfection represents non-durable protective immunity, different strains of the same virus or both.[90]

Understanding the mechanisms for short-duration immunity after a live viral infection is important because these processes might have considerable implications for the protection and durability of immunity induced by vaccines.[88]

Early in the COVID-19 pandemic initial focus was on defining virus neutralising antibodies from B cells after infection and early reports indicated that neutralising antibodies declined substantially over less than six months, raising questions about how long protective immunity might last following infection. It is known that T cells are important in protecting against many viral infections (cellular immunity). Both memory T cell and B cell responses specific to SARS-CoV-2 have now been found up to six months after infection.[91]

Similar T and B cell responses might be expected following vaccination, and may account for the good efficacy suggested by interim results from the three vaccine candidates, such as Pfizer-Bi oNTech, Moderna and Oxford-AstraZeneca.[92]

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88. Gregory A Poland, Inna G Ovsyannikova, and Richard B Kennedy, "SARS-CoV-2 Immunity: Review and Applications to Phase 3 Vaccine Candidates," *Lancet* (London, England) (Elsevier Ltd., November 14, 2020), https://doi.org/ 10.1016/S0140-6736(20)32137-1

89. Zijun Wang et al., "MRNA Vaccine-Elicited Antibodies to SARS-CoV-2 and Circulating Variants," bioRxiv : the preprint server for biology (U.S. National Library of Medicine), accessed March 18, 2021, https://doi.org/10.1101/2021.01.15.426911.

90. Kelvin Kai-Wang To et al., "COVID-19 Re-Infection by a Phylogenetically Distinct SARS-Coronavirus-2 Strain Confirmed by Whole Genome Sequencing," Clinical infectious diseases : an official publication of the Infectious Diseases Society of America (Oxford University Press, August 25, 2020), https://doi.org/10.1093/cid/ciaa1275.

91. Herb F Sewell et al., "Covid-19 Vaccines: Delivering Protective Immunity," *The BMJ* (British Medical Journal Publishing Group, December 17, 2020), https://doi.org/10.1136/bmj.m4838.

92. Elisabeth Mahase, "Covid-19: What Do We Know about the Late Stage Vaccine Candidates?," *The BMJ* (British Medical Journal Publishing Group, November 24, 2020), https://doi.org/10.1136/bmj.m4576.

In course of time, more high-quality studies that examine the duration of protection by neutralizing antibodies and T cells, following vaccination are needed.

Vaccination Efficacy against Variants – (SARS-CoV-2 is an RNA virus and generally they have a high mutation rate)?

Preliminary clinical trial results of Oxford/AstraZeneca vaccine showed 74% efficacy in the UK,[93] but only 22% in South Africa [94] whereas Novavax Covid vaccine, showed 89% efficacy in the UK but only 49% efficacy in South Africa, where the 501Y.V2 variant predominates.[95]

On January 25.2021 Moderna Inc. announced results from in vitro neutralization studies of sera from individuals vaccinated with Moderna COVID-19 Vaccine showing activity against emerging strains of SARS-CoV-2. Vaccination with the Moderna COVID-19 Vaccine produced neutralizing titers against all key emerging variants tested, including B.1.1.7 and B.1.351, first identified in the UK and Republic of South Africa, respectively. The study showed no significant impact on neutralizing titers against the B.1.1.7 variant relative to prior variants. A six-fold reduction in neutralizing titers was observed with the B.1.351 variant relative to prior variants. Despite this reduction, neutralizing titer levels with B.1.351 remain above levels that are expected to be protective. So, the two-dose regimen of the Moderna COVID-19 Vaccine at the 100 µg dose is expected to be protective against emerging strains detected to date.[96]

On February 17. 2021 Pfizer Inc. and BioNTech SE announced results from an *in vitro* study that provides additional data on the capability of sera from individuals immunized with the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) to neutralize SARS-CoV-2 with the South African variant spike protein. The current *in vitro* study investigated the full set of South African variant (also known as B.1.351 lineage) spike mutations. Although the results indicated a reduction in neutralization of virus with all the South African variant spike glycoprotein mutations, all the sera neutralized all the viruses tested. Pfizer and BioNTech are currently evaluating neutralization of SARS-CoV-2 with the Brazilian strain spike mutations, as well as mutations from other emerging SARS-CoV-2 variants, and they continue to conduct studies to monitor the vaccine's real-world effectiveness.[97]

93. Merryn Voysey et al., "Safety and Efficacy of the ChAdOx1 NCoV-19 Vaccine (AZD1222) against SARS-CoV-2: an Interim Analysis of Four Randomised Controlled Trials in Brazil, South Africa, and the UK," *The Lancet* 397, no. 10269 (2021): pp. 99-111, https://doi.org/10.1016/s0140-6736(20)32661-1.

94. "South Africa Suspends Use of AstraZeneca's COVID-19 Vaccine after It Fails to Clearly Stop Virus Variant," Science news, American Association for the Advancement of Science, last modified February 8, 2021, https://www.sciencemag.org/news/2021/02/south-africa-suspends-use-astrazenecas-covid-19-vaccine-after-it-fails-clearly-stop.

95. "Novavax Vaccine Delivers 89% Efficacy against COVID-19 in U.K.—but Is Less Potent in South Africa," Science news, American Association for the Advancement of Science, last modified January 28, 2021, https://www.sciencemag.org/news/2021/01/novavax-vaccine-delivers-89-efficacy-against-covid-19-uk-less-potent-south-africa.

96. "Moderna COVID-19 Vaccine Retains Neutralizing Activity Against Emerging Variants First Identified in the U.K. and the Republic of South Africa," Press Releases (Moderna, released January 25, 2021), https://investors.modernatx.com/news-releases/news-release-details/moderna-covid-19-vaccine-retains-neutralizing-activity-against.

97. "In Vitro Study Published in The New England Journal of Medicine Demonstrates Sera from Individuals Immunized with the Pfizer-BioNTech COVID-19 Vaccine Neutralize SARS-CoV-2 with South African Variant Spike Mutations," GlobeNewswire (Biontech, last modified February 17, 2021), https://www.globenewswire.com/news-release/2021/02/17/2177559/0/en/In-Vitro-Study-Published-in-The-New-England-Journal-of-Medicine-Demonstrates-Sera-from-Individuals-Immunized-with-the-Pfizer-BioNTech-COVID-19-Vaccine-Neutralize-SARS-CoV-2-with-So.html.

As we know Phase III trials are mainly focused on a healthy population and it is not clear yet if vaccines that are effective on this population work equally well in elderly and other at-risk individuals.

Vaccination of Children

Another concern is related to children – even if children are not a high risk group, detailed contact tracing data show children can play a role in virus transmission from child care settings, schools to household contacts.[98]

Additionally, there is a suggestion that children with underlying conditions are at greater risk of infection or more severe disease.[99]

Appearance of more transmissible SARS-CoV-2 variants, higher vaccine coverage will be required to achieve herd immunity, and vaccinating children might also be necessary to reach this coverage.[100]

By the time of publication of this paper, the available vaccines are only approved for 16 and older (e.g., AstraZeneca, Moderna age indications – 18 years of age and older,[101] Pfizer-BioNTech – 16 years of age and older.[102]

Although, Pfizer and Moderna have enrolled children 12 and older in clinical trials of their vaccines and hope to have results by the summer and three other companies: Johnson & Johnson, Novavax, and AstraZeneca, also plan to test their vaccines in children but are further behind.[103]

But before that those age groups are going to continue to be at risk of both disease and infection and being able to transmit to other people.

Pregnant women

Because pregnant persons were excluded from the initial phase 3 clinical trials of COVID-19 vaccines, limited data are available on their efficacy and safety during pregnancy. Some companies that developed COVID-19 vaccines may plan to include pregnant persons in clinical trials in the future, but all current studies not only excluded pregnant participants but requested confirmation of a contraception plan for weeks to months after injection.[104]

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98. Adriana S. Lopez et al., "Transmission Dynamics of COVID-19 Outbreaks Associated with Child Care Facilities — Salt Lake City, Utah, April–July 2020," *MMWR. Morbidity and Mortality Weekly Report* 69, no. 37 (2020): pp. 1319-1323, https://doi.org/10.15585/mmwr.mm6937e3.

99. Nisha S Mehta et al., "SARS-CoV-2 (COVID-19): What Do We Know About Children? A Systematic Review," *Clinical Infectious Diseases*, November 24, 2020, pp. 2469-2479, https://doi.org/https://dx.doi.org/10.1093%2Fcid%2Fciaa556.

100. Eric Levenson and Maggie Fox, "Herd Immunity Could Come When We Vaccinate Children Too, Fauci Says," *Cable News Network (CNN)*, March 19, 2021, https://www.cnn.com/2021/03/18/health/us-coronavirus-thursday/index.html.

101. "Moderna COVID-19 Vaccine Information," Vaccines & Immunizations, Centers for Disease Control and Prevention, last modified February 22, 2021, https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/index.html.

102. "Pfizer-BioNTech COVID-19 Vaccine Information," Vaccines & Immunizations, Centers for Disease Control and Prevention, last modified February 22, 2021, https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html.

103. Apoorva Mandavilli, "Covid Vaccines for Kids Are Coming, but Not for Many Months," *The New York Times*, February 12, 2021, https://www.nytimes.com/2021/02/12/health/covid-vaccines-children.html.

104. Sonja A. Rasmussen et al., "Coronavirus Disease 2019 (COVID-19) Vaccines and Pregnancy," *Obstetrics & Gynecology* 137, no. 3 (March 2021): pp. 408-414, https://doi.org/10.1097/aog.0000000000004290.

Techincal Problems

Technical Problems connected with the production of billions of vaccine doses and ethical issues connected with the availability of these vaccines also in the poorest countries, are challenges facing the complexities of a health passport.[83]

Vaccine Mistrust

Next issue is Vaccine mistrust which could cause a rejection of vaccination by the person that has access to the vaccine. The chief concern is that the vaccine approval process would move too quickly without taking the time to properly establish safety and effectiveness. These vaccines will have had a short documentation history and might elicit hypothetical side effects after a long time that could not have been previously appreciated.[83]

As we can see there are many unanswered questions and concerns about vaccines and by the time of publication of this paper we have a situation where there is still very broad transmission in many countries and that is why many countries require that all arriving passengers provide verifiable proof of a negative COVID-19 test taken within a prescribed number of days prior to arriving in the respective country, regardless of vaccination.

There are three main ways to establish infection with SARS-CoV-2; 1) Nucleic acid tests to detect the presence of RNA (e.g. RT-PCR) 2) Antigen testing for the presence of a viral antigen, usually a surface protein and 3)Antibody tests to detect prior infection. These tests do not replace but compliment each other, as air travellers are a mostly non-symptomatic subpopulation, with variable but decreased probability of COVID-19 compared to the general population (estimated prevalence of COVID-19 in travellers is approximately 1%).[105]

The use of any diagnostic test for screening purposes, in a low prevalence population can lead to a number of false negative and false positive results and one of the reasons for implementation of the Multivariable Heath Pass is to minimize this risk.

2. PCR Test

For diagnostic testing the gold standard currently is naso-/oropharyngeal swabbing with subsequent RT-qPCR analysis.This method is rapid, sensitive and specific, but in the real-world the risk of false negative and false positive results should not be forgotten.

Additionally, positive RT-PCR test does not necessarily mean that the tested person is infectious since recovering cases can remain RT-PCR positive for weeks.

Researchers at John Hopkins University declared that the false negative ratio of RT-PCR test in patients infected with COVID-19 is approximately 1 in 5.[106]

False Negative Results

105. Jessica Watson, Penny F Whiting, and John E Brush, "Interpreting a Covid-19 Test Result," *The BMJ*, December 2020, p. m1808, https://doi.org/10.1136/bmj.m1808.

106. Lauren M. Kucirka et al., "Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure," *Annals of Internal Medicine* 173, no. 4 (2020): pp. 262-267, https://doi.org/10.7326/m20-1495.

There are several probable factors that affect the sensitivity of RT-PCR test, such as:

Sampling Error

Errors that can occur during sample collecting, transporting, and handling of RNA. The sensitivity varies greatly based on who performs the test and how it is being performed. Sometimes sample collection is inadequate or health workers do not insert nose swabs deep enough. After sample collection swabs should be placed in transport medium immediately after collection. In addition, the time between sample collection and test performance should not be too long. The sample should be stored at 2-8°C for maximum of 72 hours. If transporting is not possible during 72 hours, they should be stored at -70°C to prevent viral RNA degradation.[107]

Viral Load

Viral Load is the quantity or titre of virus in a volume of fluid at a given time. It is important to know when an infected individual has an optimum viral load. Like many other airborne viral diseass, penetration into the upper airways is the first step of the infection. Higher viral loads, soon after symptom onset, were detected in the nose than in the throat.[108] Wolfel et al. reported that maximum COVID-19 replication in the throat is five days after symptom onset.[109]

The evidence to date suggests that the viral load in respiratory tract samples peaks around symptom onset and decreases within one to three weeks. Although the duration of detection and the size of the viral load differs between patients, viral RNA generally becomes undetectable (from upper respiratory tract specimens) about two weeks after symptom onset (median 14.5 days).

The viral load between asymptomatic and severe cases is similar thus suggesting the potential of infection transmission by both groups.[107]

Duration of Virus Exposure

It is important to consider how the predictive value of the test varies with time from exposure to SARS-CoV-2 and symptom onset to avoid being falsely reassured by negative results from tests done early in the course of infection. Kucirka et al. reported this issue, showing that the probability of a false negative RT-PCR test on day 1 after infection is 100% and it decreased respectively to 67% on day 4, 20 % on day 8, and increased again to 66% on day 21 after infection. In other words, the risk of false negative will be highest for RT-PCR when the test was used too early. [105]

False Positive Results

These are factors that can be responsible for false positive results: Technical problems including contamination during sampling (eg, a swab accidentally touches a contaminated glove or surface), contamination by PCR amplicons, contamination of reagents, sample cross-contami-

107. Fatemeh Bahreini et al., "Reducing False Negative PCR Test for COVID-19," *International Journal of Maternal and Child Health and AIDS* 9, no. 3 (August 2020): pp. 408-410, https://doi.org/10.21106/ijma.421.

108. Lirong Zou et al., "SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients," *New England Journal of Medicine* 382, no. 12 (2020): pp. 1177-1179, https://doi.org/10.1056/nejmc2001737.

109. Roman Wölfel et al., "Virological Assessment of Hospitalized Patients with COVID-2019," *Nature* 581, no. 7809 (January 2020): pp. 465-469, https://doi.org/10.1038/s41586-020-2196-x.

nation, and cross-reactions with other viruses or genetic material could also be responsible for false-positive results.[110]

A number of countries have implemented requirements for a recent negative COVID-19 RT-PCR test result in order to allow entry into their territory. According to modelling studies, performing a single RT-PCR test immediately upon arrival would prevent only 40% to 50% of local transmission from imported cases. Furthermore, modelling studies have shown that pre-flight testing is less effective in preventing the importation of the virus than a similar test performed upon arrival. The longer the time between the sample collection from a person without symptoms for a pre-flight test and the scheduled time of departure, the less effective the test will be. If a pre-departure negative test is requested, the sample should ideally be collected within 48 hours before departure.[111] Pre-departure testing reflects the situation of the tested individuals on the day the test is performed and cannot guarantee that they will not become positive in the immediate future. However, predeparture testing may reduce the chances of transmission during travel, especially from areas with very high transmission levels.

Additionally, with COVID-19 new strains appearing, there are concerns how these mutations could affect diagnostic tests performance. Earlier researchers reported that PCR tests still can detect them, but recently researchers in southern Finland have discovered a new, "unique" variant of the coronavirus. The variant, dubbed Fin-796H, displayed some mutations previously discovered in the British and South African variants of the virus but in a combination it called "unique" and it may not show up in PCR tests that search for particular genetic sequences in the virus' RNA.[112]

3. Antigen Test

Antigen tests are another option, as they are cost-efective and provide immediate results (15 - 30 minutes). The sensitivities and specificities of Anitigen Tests vary in the range from 29% to 93.9% for test sensitivity and from 80.2% to 100% for test specificity, depending on the time of sampling.

Antigen tests perform best in cases with high viral load, in pre-symptomatic and early symptomatic cases up to five days from symptom onset, so Antigen Tests may miss individuals with low viral loads, for example during the pre-symptomatic phase and/or towards the end of the active infection. The use of rapid antigen tests can be more effective for testing individuals irrespective of symptoms in settings where the proportion of test positivity is expected to be equal to or higher than 10%.[113]

110. Elena Surkova, Vladyslav Nikolayevskyy, and Francis Drobniewski, "False-Positive COVID-19 Results: Hidden Problems and Costs," *The Lancet Respiratory Medicine* 8, no. 12 (2020): pp. 1167-1168, https://doi.org/10.1016/s2213-2600(20)30453-7.

111. Samuel Clifford et al., "Strategies to Reduce the Risk of SARS-CoV-2 Re-Introduction from International Travellers," Preprint at medRxiv 2020.07.24.20161281, posted July 25, 2020, https://doi.org/10.1101/2020.07.24.20161281.

112. "New Coronavirus Variant Discovered in Finland," Uutiset news, Yle Uutiset, last modified February 18, 2021, https://yle.fi/uutiset/osasto/news/new_coronavirus_variant_discovered_in_finland/11796958.

113. "Options for the Use of Rapid Antigen Tests for COVID-19 in the EU/EEA and the UK," publications & data, European Centre for Disease Prevention and Control, last modified November 19, 2020, https://www.ecdc.europa.eu/en/publications-data/options-use-rapid-antigen-tests-covid-19-eueea-and-uk.

In a low-prevalence population, such as travellers, the use of Antigen Tests may be useful for diagnosing suspected cases (e.g. travellers who suddenly develop COVID-19 compatible symptoms) and positive results need confirmation by RT-PCR.

4. Antibody Test

Differences in COVID-19 testing and tracing across countries, as well as changes in testing within each country over time, make it difficult to estimate the true (population) infection rate based on the confirmed number of cases obtained through current practices to diagnose COVID-19.

Reliable antibody testing against SARS-CoV-2 has the potential to uncover the population-wide spread of COVID-19, which is critical for making informed healthcare and economic decisions.

In general, a positive antibody test is presumed to mean a person has been infected with SARS-CoV-2, at some point in the past and antibody test results should not be used to diagnose someone with an active infection.[114] Reliable antibody testing against SARS-CoV-2 has the potential to uncover the population-wide spread of COVID-19, which is critical for making informed healthcare and economic decisions.[115]

As with vaccines and diagnostic test, we have unanswered questions and concerns about Antibody tests, such as:

- Antibody tests are important for monitoring development of herd immunity as well. But for SARS-CoV-2, the exact threshold to achieve herd immunity is unclear[116] and estimates are complicated by differences between countries, with most estimations between 50% and 80%.[117]
- Antibody tests for SARS-CoV-2 frequently test for IgM and IgG antibody isotypes to cover early (IgM) as well progressing (IgG) immune responses. Antibody tests for SARS-CoV-2 typically detect antibodies against single antigens, such as the spike glycoprotein or the nucleocapsid protein and current antibody tests do not allow discrimination between SARS-CoV2 strains having accumulated different mutations, and only genome sequencing can resolve phylogenetic relationships.[118]
- It is known that in addition to SARS-CoV-2, six more CoVs are known to infect humans and are potential candidates to elicit cross-reactive antibodies that could interfere with serological tests. Antibodies of individuals with COVID-19 cross-react against the full-

114. "Using Antibody Tests for COVID-19," COVID-19, Centers for Disease Control and Prevention, last modified November 3, 2020, https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests.html.

115. Rafael R. de Assis et al., "Analysis of SARS-CoV-2 Antibodies in COVID-19 Convalescent Blood Using a Coronavirus Antigen Microarray," *Nature Communications* 12, no. 6 (2020), https://doi.org/10.1101/2020.04.15.043364.

116. Rita Rubin, "Difficult to Determine Herd Immunity Threshold for COVID-19," *JAMA* 324, no. 8 (2020): p. 732, https://doi.org/10.1001/jama.2020.14778.

117. K. A. Callow et al., "The Time Course of the Immune Response to Experimental Coronavirus Infection of Man," *Epidemiology and Infection* 105, no. 2 (1990): pp. 435-446, https://doi.org/10.1017/s0950268800048019.

118. Thomas Vogl, Sigal Leviatan, and Eran Segal, "SARS-CoV-2 Antibody Testing for Estimating COVID-19 Prevalence in the Population," *Cell Reports Medicine* 2, no. 2 (2021): p. 100191, https://doi.org/10.1016/j.xcrm.2021.100191.

length S and nucleocapsid proteins of SARS-CoV-1 and MERS-CoV. However, considering the much lower prevalence of SARS-CoV-1 (approximately 8,000 reported cases, no new cases after 2004) and MERS-CoV (fewer than 3,000 cases since 2012) opposed to the spread of SARS-CoV-2, cross-reactivities against SARS-CoV-1 and MERS-CoV are generally not expected to bias population-scale SARS-CoV-2 testing.[119] Additionally, four more CoVs (OC43, HKU1, NL63, and 229E) circulate widely in humans, causing mild common cold-like symptoms. Cross-reactivity, to seasonal common cold CoVs, could bias results. However, protective effects toward SARS-CoV-2 of cross-reactive antibodies targeting these common CoVs are understood incompletely.[120] Systematic testing of cross-reactivity between these strains could help to resolve this issue.

- Another issue of concern with Antibody Tests is false-positive and false-negative results. Generally, high specificity of a test is critical at a low prevalence in the population (approximately <10%), otherwise the false positives may outweigh the true positives. High sensitivity is critical at high prevalence in the population, otherwise the false negatives may outweigh the true negatives.[118]
- Next point, requiring consideration is the following. A positive result of an Antibody Test, does not necessarily indicate protection against reinfection. The produced antibodies may not neutralize the virus, and very low antibody concentrations detected by sensitive tests may not be sufficient for reinfection.[121]

With the current limited understanding of immunity, prevalence of disease Antibody Testing should remain a tool of public health until more is understood about long-term impacts of SARS-CoV-2 on the immune system. When more is understood about how antibodies reflect protective immunity, how antibody responses elicited by new virus variants differ from each other, the value of antibody testing at the individual level should be reviewed.

5. Quarantine Tracking

The reason for the implementation of quarantine tracking in the generation of QR code is complex and based on a combination of different factors, such as epidemiology, disease specific factors, travel pattern, healthcare factors, economic and logistic factors.

On one hand there is the risk of infection in-flight or at airports, which airlines address with measures such as the use of filters, monitoring and testing of passengers. On the other hand, governments try to limit the risk of transporting infectious passengers from abroad or within a country with measures such as travel bans and quarantines.[122]

119. Davide F. Robbiani et al., "Convergent Antibody Responses to SARS-CoV-2 in Convalescent Individuals," *Nature* 584, no. 7821 (2020): pp. 437-442, https://doi.org/10.1038/s41586-020-2456-9.

120. Dimple D Rajgor et al., "The Many Estimates of the COVID-19 Case Fatality Rate," *The Lancet Infectious Diseases* 20, no. 7 (2020): pp. 776-777, https://doi.org/10.1016/s1473-3099(20)30244-9.

121. Ania Wajnberg et al., "Humoral Response and PCR Positivity in Patients with COVID-19 in the New York City Region, USA: an Observational Study," *The Lancet Microbe* 1, no. 7 (2020): p. e283-e289, https://doi.org/10.1016/s2666-5247(20)30120-8.

122. Michel Bielecki et al., "Air Travel and COVID-19 Prevention in the Pandemic and Peri-Pandemic Period: A Narrative Review,"

Travel restrictions and quarantine are public health tools to fight the international spread of COVID-19, although there is a lack of any international consensus regarding traveller quarantine measures, which means that approaches to quarantine and how it is implemented (voluntary, mandated, home, individual, group, etc.) will vary from country to country. Several countries combine quarantine with the testing of incoming travellers in order to reduce quarantine duration. Many have adopted quarantine as a measure for incoming travellers, assuming that some of these travellers may be incubating the disease or have the disease but are asymptomatic.

Quarantine Tracking before a flight will be important as well, for persons, who refuse vaccination for any reason, especially in areas where herd immunity has not been achieved. E.g., in April 2020, the Schengen Visa (EU passport-free zone) website had reported that once the vaccine is available, travellers would be obliged to get vaccinated in order to be eligible to enter the EU countries. An EU official had confirmed that once the COVID-19 vaccine is confirmed and available for all, visa applicants would also be required to be vaccinated in the future. If the EU obliges travellers to vaccinate, even if anti-vax travellers find a loophole in the requirement and manage to enter any of the Member States, travel insurance providers may refuse to cover them.[123]

6. Documentation of Recovery

A recent positive viral test AND a letter from a healthcare provider or a public health official stating that the individual is cleared to end isolation and therefore can travel. The letter must be dated no more than 90 days ago.

This is because people who have recovered from COVID-19 can continue to test positive for up to 3 months after their infection and retesting is not recommended within 3 months after a person with COVID-19 first developed symptoms (or the date of their first positive viral diagnostic test if their infection was asymptomatic).

But, even if a person has recovered from COVID-19, and develops symptoms of COVID-19, he/she should not travel and should seek care for testing and evaluation.[124]

7. Health Declaration

Air passengers will also be required to sign a Health Declaration form. Different countries have different Health Declaration forms, the meaning of which to emphasise the importance of not travelling with COVID-19-compatible symptoms or, not travelling if there is a identified high-risk contact of a confirmed case.

Combination of these variables will generate the QR code, and the digital Health Pass can be

Travel Medicine and Infectious Disease 39 (2021): p. 101915, https://doi.org/10.1016/j.tmaid.2020.101915.

123. "Travel Insurance Providers to Make COVID-19 Vaccination a Requirement for Coverage, If EU Makes It Obligatory First," Travel Insurance, Schengen Visa, last updated January 10, 2021, https://www.schengenvisainfo.com/news/travel-insurance-providers-to-make-covid-19-vaccination-a-requirement-for-coverage-if-eu-makes-it-obligatory-first/.

124. "Requirement for Proof of Negative COVID-19 Test or Recovery from COVID-19 for All Air Passengers Arriving in the United States," COVID-19, Centers for Disease Control and Prevention, last modified March 2, 2021, https://www.cdc.gov/coronavirus/2019-ncov/travelers/testing-international-air-travelers.html.

saved on a personal smartphone by scanning the QR code, which can serve as a valid document for entry into many countries.

3.5. COVID-19 Vaccine Passport App

A notice issued in January of 2020 warned of the potential for rapid global spread of coronavirus 2019-nCoV-19 via commercial air travel. By July, a report from the United Nations World Tourism Organization revealed 40% of all worldwide destinations were easing commercial air restrictions from the tighter restraints they had enacted earlier in the year.[125]

As of early January 2021, nearly 87 million people had been infected by SARS-CoV-2 globally. Several countries are actively considering COVID-19 immunity passports as proof of vaccination or immunity to initiate travel and commerce while palliating viral spread. Immunity to natural viral infection is mostly a sequential, multi-dimensional process that comprises a non-specific to slow the virus's progress, antibodies that specifically bind to the virus, and T-cells to remove virus-infected cells. A robust adaptive response may prevent re-infection by the same virus and may be detected by the presence of antibodies in the blood.[126]

In this day and age, research has shown pandemics primarily spread through travel and tourism. The tourism industry's impact in spreading COVID-19 was unmistakable in February of 2020 on the Diamond Princess cruise, where one passenger infected with the virus transmitted it to 619 passengers and crew. A study determined how the conditions on board amplified a highly transmittable disease and addressed how the two industries were a key sector responsible for transmitting the virus.[127]

The airline industry has made passenger safety a priority through sufficient ventilation at the gate and onboard, boarding and deplaning procedures, increased aircraft disinfection, and pre-flight screening such as temperature checks and COVID-19 testing. Enforcing face masks to be worn has significantly reduced onboard transmission. Implementing COVID-19 digital health passports may further standardize screening entry requirements at airports and borders, allowing for a safer return to travel.

The World Economic Forum launched a digital health passport in trials. This app operates as a versatile, secure platform that permits travelers to document their COVID-19 status electronically and then present it while boarding or at borders. Passengers can use the app to validate test results or vaccination status while preserving personal data privacy. It attempts to maintain an expanse of country-to-country health screening entrance specifications to be interoperable be-

125. Aisha N Khatib et al., "Navigating the Risks of Flying during COVID-19: a Review for Safe Air Travel," *Journal of Travel Medicine* 27, no. 8 (December 2020), https://doi.org/10.1093/jtm/taaa212.

126. P. Murali Doraiswamy et al., "Are We Ready for COVID-19's Golden Passport? Insights from a Global Physician Survey," 2020, https://doi.org/10.1101/2020.11.25.20234195.

127. Inmaculada Gallego and Xavier Font, "Changes in Air Passenger Demand as a Result of the COVID-19 Crisis: Using Big Data to Inform Tourism Policy," *Journal of Sustainable Tourism*, May 2020, pp. 1-20, https://doi.org/10.1080/09669582.2020.1773476.

tween and across countries and managed transparently, independently, and through a non-profit foundation. Depending on these conclusions, the pass will extend to other airlines and routes internationally.[125]

Additionally, several other large tech companies have created immunity passports. However, implementing a standardized digital health pass for COVID-19 and more robust contact tracing may be critical factors to allow for a gradual, safe return to sustainable and responsible travel. The traveler's risk may be minimized by assessing the multiple dangers of flying and using a multi-pronged policy to mitigate increasing risk.[125]

3.6. Transportation: International Air Travel

On December 28, 2020, the CDC issued orders requiring all air passengers arriving in the US from the UK to provide evidence of negative COVID-19 test results. Due to the new variants detected, they felt this was the best way to slow the spread of SARS-CoV-2. Tests need to be taken 3 days before departure and travelers must provide proof of a negative test result to the airline before boarding.[128]

To reduce the risk of spreading new variants further, the CDC issued an additional order requiring all air passengers arriving in the US from foreign countries to test negative for COVID-19 infection effective January 26, 2021. Tests need to be taken no more than 72 hours before departure. Travelers must provide the airline proof of a negative test result or documentation of recovering from COVID-19, within the last 90 days before boarding. Airlines must confirm for all passengers 2 years of age and older, or deny boarding for those that are not able to provide documentation or proof of recovery.[129]

The CDC advises all travelers to take the following precautions after traveling:

1. After travel, arrange to be tested 3-5 days later and stay home and self-quarantine for 7 days.
2. Even if your reported test results are negative, stay home and self-quarantine for the full 7 days.
3. If your test report is positive, stay in isolation to protect others from infection.
4. If you don't get tested after traveling, it's safest to stay home and self-quarantine for 10 days.
5. Suggestion: Avoid being around people who are at increased risk for severe illness for 14

128. "Testing and International Air Travel," COVID-19, Centers for Disease Control and Prevention, last modified February 23, 2021, https://www.cdc.gov/coronavirus/2019-ncov/travelers/testing-air-travel.html.

129. "COVID-19 Traveler Information," Travel advisories, Bureau of Consular Affairs, last modified January 25, 2021, https://travel.state.gov/content/travel/en/traveladvisories/ea/covid-19-information.html.

days, whether you get tested or not.[128]

The U.S. Department of State advises all travelers to be aware of COVID-19 country-specific guidelines, closures, quarantine information, entry and exit requirements, travel bans, and advisories.[128] These are updated on the U.S. Embassy COVID-19 pages.[129]

Currently, travel requirements and bans can be confusing and cause unnecessary stress for travellers. Countries vary greatly in entry requirements. When traveling trans-Pacific to Hawaii, a NAAT (Nucleic Acid Amplification Test) is required 72 hours before departure from a certified Clinical Laboratory Improvement Amendment (CLIA) lab. A negative test result is required to be uploaded to Hawaii's Safe Travels platform or printed out and be in hand before boarding the final plane to Hawaii. If test results are not available before then, the traveler must quarantine for ten days upon arrival. If negative test results are received during quarantine, the passenger must remain for the entire ten days. If positive results are received during quarantine, the traveler, and any companions, must isolate for ten days, and until there have been no symptoms for 24 hours. Passengers must also complete a mandatory State of Hawaii Travel and Health Form and pass temperature screenings at Hawaii airports. As of March 2021, proof of vaccination does not exempt a traveler from quarantine.[130]

Seychelles, in particular, is only welcoming back vaccinated tourists from a Category 1 or 2 country for 2021 or if they fly in on a private jet. If not vaccinated, they must show proof of a negative PCR test taken 72 hours prior. Once all of Seychelles' adult residents are vaccinated, all tourists will be welcome, regardless of being vaccinated, flying in on a private jet, or dependent on the Category level of their country, as long as they have received a negative COVID-19 PCR test. [131]

In order to return the global economy and our social lives back to pre-COVID-19 norms, countries need to be uniform in testing requirements to discontinue spreading COVID-19 and variants. Immunity passports can be used as a tool that is utilized to show proof of immunity or that people have a current negative COVID-19 test while protecting their personal data and others before traveling.

3.7. Privacy And Security Concerns

Mobile devices and other digital data sources for authentic, reliable data, are used during newly recognized outbreaks. Current research has demonstrated the plausibility of foreseeing the range of the COVID-19 outbreak by merging data from the Official Aviation Guide and human migration from social apps and other digital services. Previously, mobile phone data projected the expanse of cholera during the 2010 Haitian epidemic, while advanced analytic techniques demonstrated

130. "Travel Frequently Asked Questions," Info & Resources for Managing COVID-19, Hawaii State Department of Health, last modified February 25, 2021, https://hawaiicovid19.com/travel/faqs/.

131. "Seychelles Makes Itself More Accessible for Visitors," Department of Tourism, Seychelles Ministry of Foreign Affairs and Tourism, last modified January 22, 2021, http://tourism.gov.sc/2021/01/22/seychelles-makes-itself-more-accessible-for-visitors/.

to be useful during the 2014–2016 Western African Ebola crisis. However, in today's data-intensive society, it is essential to show transparency on individual data use.

Integrating electronic documentation into a smartphone app would be more impervious to fraud and more efficient in contact tracing, retesting, and updating immunity status. As reported by a New York Times article, China is reportedly applying universal sensor data and digital Health Passports to control the spread of COVID-19. There is limited transparency in how the data is verified and repurposed for surveillance goals.[132] In some Chinese provinces, QR codes on smartphones control entrance into public places based on the person's COVID-19 health status. However, these apps inform of more than COVID-19 data such as people's locations, travel history, other individuals that have come within a certain proximity, and additional health information, varying from their body temperature to whether they have had a cold lately. Taiwan and several other countries are using smartphone apps that contain alert systems connected to police departments.[133] In March of 2020, Italy's local data protection authority clarified the terms of legal data use for mitigation and containment goals, warning against the acquisition and processing of data by non-institutional actors, such as private employers.

Several weeks later, the European Data Protection Board stressed the significance of respecting and protecting personal data and highlighted various articles in the GDPR (General Data Protection Regulation) that provide legitimate grounds for obtaining personal data in the circumstances of epidemics. Article 9 authorizes the collection of personal data in the interest of public health, like guarding against dangerous transnational threats to public health unless such acquisition is equal to the pursued purpose, and upholding the basis of the right to secure data by respecting privacy and confidentiality. If data from Immunity Passports is abused, countries will lose public trust, and people will be less likely to adhere to public-health guidance.[132]

Numerous COVID-19 health passports have plans to use biometrics to protect privacy and personal data security. These safeguards have been in practice for a while. In 2005, Fitzpatrick noted in *Biometrics in Asia* that Japan was implementing biometric airport security systems after a successful trial of e-passports at Tokyo-Narita. Japan is known to be the first commercially available iris identification system, which became available in 1998. It is now at Frankfurt International. The network verifies identities by comparing iris codes captured by a camera to a previously recorded code. Other biometrics systems tested include a system that issues an electronic certificate of outline e-passports for Public Key Infrastructure verification. During this time, Hong Kong expected delivery of a facial recognition system installed in the immigration office on Shenzhen's borders in Guangdong Province.[134]

132. Marcello Ienca and Effy Vayena, "On the Responsible Use of Digital Data to Tackle the COVID-19 Pandemic," *Nature Medicine* 26, no. 4 (2020): pp. 463-464, https://doi.org/10.1038/s41591-020-0832-5.

133. Natalie Kofler and Françoise Baylis, "Ten Reasons Why Immunity Passports Are a Bad Idea," *Nature* 581, no. 7809 (2020): pp. 379-381, https://doi.org/10.1038/d41586-020-01451-0.

134. Fitzpatrick, M. 2005. "Biometrics in Asia". *AIRPORTS INTERNATIONAL*. 38 (8): 26-28.

3.8. Ethical Feasibility of Health passport

The possibility of Immunity passports, presents significant moral challenges, but assessment is a significant step in their execution. As suggested by Dr. Govind Persod, the ethical value of the immunity license ought to be evaluated, by its ability to promote fair and proper treatment and to increase social benefit. Subsequently, standardization for immunity passports should take into consideration these additional ethical values.[135]

Beriain and his colleagues claim that health passports already exist in our world, but they are named differently. The example they use is that of the vaccination certificate needed, to travel to or from certain countries. This certificate, similarly to an immunity passport, demonstrates that you have been vaccinated against some specific diseases.

Regarding the freedom to movement, the authors suggest that when an individual has been tested positive for, and recovered from the COVID-19 disease, that person has become immune to it. Therefore, they cannot be considered dangerous for the public health, and consequently the abbreviation of their basic right of freedom to movement, cannot be considered fair.

In addition, they estimate that in the next stages of the pandemic, different statuses of immunity might be at risk, as the need to classify who has the potential to spread the infection, will be increased.[136]

On 24 April 2020, the WHO expressed, "there isn't enough evidence about the effectiveness of antibody-mediated immunity to make sure the accuracy of an "Immunity passport"or "risk-free certificate."(1) This WHO announcement is assured by recent immunological studies that show asymptomatic individuals might have a weak immune response to SARS-CoV-2 infection.[60]

Additionally, some European countries are considering serological tests to issue immunity certifications (passports) that give holders certain time-limited work and social freedoms, joining larger gatherings or returning to nonessential jobs, and the US government is considering similar proposals.[137]

According to Persad and Emanuel (2020),[3] immunity passports are not to be evaluated against the criterion of normalcy, such as free movement, but in regard to the practices of strict public health restrictions or allowing activities that could lead to the spread of infection.The researchers suggest that public health should protect freedom, via the method of the "least restrictive alternative" (1), which in simple words means that individuals should be allowed to go after their life plans, unless they might end up harming public health.

And in case immunity licenses become available, it seems that they could represent that least

135. Karen W. Carroll et al., "Influences on Decision Making Identified by Parents of Children Receiving Pediatric Palliative Care," *AJOB Primary Research* 3, no. 1 (2012): pp. 1-7, https://doi.org/10.1080/21507716.2011.638019.

136. Iñigo de Miguel Beriain and Jon Rueda, "Immunity Passports, Fundamental Rights and Public Health Hazards: A Reply to Brown et Al," *Journal of Medical Ethics* 46, no. 10 (September 2020): 660–61, http://dx.doi.org/10.1136/medethics-2020-106814

137. Mark A. Hall and David M. Studdert, "Privileges and Immunity Certification during the COVID-19 Pandemic," *Jama* 323, no. 22 (September 2020): 2243–44, https://doi:org/10.1001/jama.2020.7712

restrictive alternative approach, as they can give people the opportunity to demonstrate that they are immune, and therefore could pursue the right to certain degrees of freedom.

Furthermore, Persad and his colleagues suggest that the ethics of COVID-19 passports should be considered with regard to some basic ethical principles: a) the increase of benefit, b) the priority to the vulnerable, and c) equal treatment of people.

The researchers argue that immunity licenses could potentially increase benefits, by cautiously enabling the operation of restaurants, bars, sporting events, etc. At the same time, these licenses could help prioritize the least advantaged and vulnerable populations. Through harsh public restrictions, no one could participate in social and economic activities, but in case certain activities are made possible by licensing, only those who do not possess immunity passports would be disadvantaged, compared to others.

Persad concludes that, admittedly, immunity-based licenses demand thorough implementation and scientific approval in order to be ethical in effect, but nothing makes them feel unethical in essence.[3]

3.8.1 Misinformation in Times of Covid-19

Accomplishing an extensive vaccine coverage seems to be the main issue the world is struggling with, as of the publishing of this paper. Unfortunately, this need has been met with an emergence of misleading information which according to recent studies, might negatively affect vaccine uptake. Agley, earlier this year, estimated that almost half of Americans do not intend to get vaccinated. The author suggests that this reduced willingness towards vaccination is partially due to COVID-19 misinformation being spread across media, social platforms, and by word of mouth.[138]

The levels of misinformation spreading were so high during last year, that the WHO declared that an "infodemic" takes place, alongside the pandemic.[139] Eventually, the term evolved into "misinfodemic", which intends to capture the complementary increase in misinformation regarding the virus.[140]

Additionally, Kim and his colleagues suggest that exposure to misinformation can trigger further mechanisms in individuals, making them seek supplementary data, in order to confirm the information that they consider to be false. These mechanisms urge people to search for information through their social circle in order to verify their beliefs. Interestingly, the researchers claim that exposure to misinformation or conspiracy theories, might prohibit individuals from pursuing new information, while at the same time it might act as a means of nourishment towards their pre-ex-

138. Jon Agley and Yunyu Xiao, "Misinformation about COVID-19: evidence for differential latent profiles and a strong association with trust in science," *BMC Public Health*, no 21.1 (2021): pp. 4-7, https://doi.org/10.1186/s12889-020-10103-x.

139. "Immunizing the public against misinformation," Scientific brief, World Health Organization.Last modified August 25, 2020, https://www.who.int/news-room/feature-stories/detail/immunizing-the-public-against-misinformation.

140. Nicole Krause et al., "Fact-checking as risk communication: the multi-layered risk of misinformation in times of COVID-19," *Journal of Risk Research*, no 23 (2020): pp. 1054-1056, https://doi.org/10.1080/13669877.2020.1756385.

isting beliefs.[141]

Finally, as Tasnim mentions in a recently published paper, it is reasonable that individuals living in quarantine or at the peril of a threatening disease outbreak, will probably experience higher levels of psychological distress. This fact plausibly urges them to learn more about the disease, its origin, and the effectiveness of its treatment. What is of great importance however according to the authors, is to ensure that individuals satisfy this need for facts, through a valid flow of information. It seems that this particular need has been acknowledged by the WHO, which has allied with several major social media platforms, such as Facebook, Google, and Twitter, in an attempt to filter inaccurate information and conspiracy theories spreading, while trying to promote reports from official healthcare agencies.[142]

3.9. Possible Imbalance in Health Passports

Global Inequality: It has been proven that although some wealthier countries have purchased enough doses to vaccinate their entire populations, concurrently it is estimated that almost 90% of the population in 67 countries, will not be able to receive a COVID-19 vaccine in 2021, even though the COVID-19 cases among them are relatively high.[143]

Social Inequality: It seems that unfair access to vaccinations is not limited in the global scale only. The inequality can be observed in the social sphere as well. Access to vaccination is considered relatively uneven in many other occasions, and research demonstrates poorer health outcomes for vulnerable communities and populations.[144]

Unfair access into testing procedures: Reportedly, inequality seems to have been present, since the start of the pandemic. It began to manifest itself shortly after the access into testing was made possible. With a shortage of testing systems, many populations were being left out. Reports suggest that there was or still could be an imbalance in accessing testing based on affluence.[133]

Patent rules and restrictions: Due to the pharmaceutical industry's current nature and patent requirements, there could be exclusivity demands on the market, due to the high risk and expense needed, for the patent to be finalized. Unfortunately, this specific act has its toll on low-income countries.

It is being reported that a lot of poorer countries are not able to access vaccines due to aforementioned patent restrictions, which could affect the market or set prices of vaccines, pushing

141. Hey Kyung Kim et al., "Effects of COVID-19 Misinformation on Information Seeking, Avoidance, and Processing: A Multicountry Comparative Study," *Science Communication,* no 42.5 (2020):pp. 586-595, https://doi.org/10.1177/1075547020959670.

142. Samia Tasnim et al., "Impact of rumors and misinformation on COVID-19 in social media," *Journal of preventive medicine and public health*, no 53.3 (2020): pp. 172-174, https://doi.org/10.3961/jpmph.20.094.

143. Lisa M Herzog et al., "Covax Must Go beyond Proportional Allocation of Covid Vaccines to Ensure Fair and Equitable Access," *The Bmj,* November 2020, p.2243, https://doi.org/10.1080/20477724.2017.1281374.

144. Daniele Mipatrini et al., "Vaccinations in Migrants and Refugees: A Challenge for European Health Systems. A Systematic Review of Current Scientific Evidence," *Pathogens and Global Health* 111, no. 2 (2017): 59–68, doi:10.1080/20477724.2017.1281374.

the price above mass adoption for certain countries.[145]

COVID-19 Outbreak and Persons with Disabilities: Undoubtedly, although the COVID-19 pandemic threatens all members of the society, persons with disabilities experience an unbalanced impact due to the barriers of environmental, behavioral and institutional nature. In addition, a vast majority of these individuals faces pre-existing health conditions, which make them even more vulnerable to infection, thus increasing the death rates among them.[146] According to IASC, disabled people, and their caregivers as well, face barriers that could prevent them from accessing the appropriate care and useful information in order to decrease their risk of getting infected during the pandemic.[146.]

Making equitable access to COVID-19 vaccines a reality:
Lopez and Ortega (2021)[147] suggest that the international distribution of vaccines should not be only fair, but also health-driven, taking into consideration factors such as the size, distribution, and risk profiles of each population. In addition, they believe that new production sites could be built worldwide, in order to guarantee equitable allocation.[147]

Emanuel and his colleagues (2021),[148] in a recently published paper, suggest the implementation of the Fair Priority Model, which they believe will: " (1) benefit individuals while limiting harm, (2) prioritize the disadvantaged, and (3) ensure global equal concern". (372) The authors claim that this model will progress in certain phases, where the initial purpose is to minimize premature deaths. After that, in phase 2, the allocation needs to be focused on decreasing economic hardships while restraining morbidity. Finally, in the last stage of the FPM, the goal is to diminish community transmission and to reinstate pre-pandemic interaction. At the same time, they suggest that the FPM will enhance not only the equity, but also the efficacy of vaccine distribution, in agreement with the standards set by the WHO.[148]

4. Conclusion

In this white paper, we have discussed the background of COVID-19, symptoms, immunity, testing for SARS-CoV-2 virus, and the development of various vaccines against it. We have reviewed the challenges relating to different practical considerations, fairness issues, impact on freedom of movement, personal data privacy and elaborated the tentative recommendations for Health

145. Owen Dyer, "Covid-19: Many Poor Countries Will See Almost No Vaccine next Year, Aid Groups Warn," *The BMJ,* November 2020, p. m4809, https://doi.org/10.1136/bmj.m4809.

146. "COVID-19: Who Is Protecting the People with Disabilities? – UN Rights Expert," News and Events, Office of the United Nations High Commissioner for Human Rights (OHCHR), last modified March 17, 2020, https://www.ohchr.org/EN/NewsEvents/Pages/DisplayNews.aspx?NewsID=25725.

147. Aurora del Munguía-López and José María Ponce-Ortega, "Fair Allocation of Potential COVID-19 Vaccines Using an Optimization-Based Strategy," Process Integration and Optimization for Sustainability 5, no. 1 (2021): pp. 3-12, https://doi.org/10.1007/s41660-020-00141-8.

148. Ezekiel J Emanuel et al., "Enhancing the WHO's Proposed Framework for Distributing COVID-19 Vaccines Among Countries," *American Journal of Public Health* 111, no.3 (2021):pp. 371-373, doi:10.2105/ajph.2020.306098.

Passports' ethical introduction.

Studies show that 9 out of 10 people in undeveloped countries will not receive a vaccination in the year 2021. There seem to be mixed responses to health passports' introduction from various statutory bodies and medical institutions. Since the world is gearing up for the next economic recovery and recovery from COVID-19 through vaccination, a multivariable health passport is the only way to address the multiple factors that hinder pre-pandemic interaction. Health passports might become a new normal in the future, serving as a token to access the workplace, shopping malls, hospitals, airports, and restaurants, allowing people's free movement. The primary focus in implementing health passports should be the medical, ethical, privacy, and security concerns of an individual and address those concerns while in parallel allowing selected transparency for public health.

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