

Summary of Currently Available COVID-19 Vaccines

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Summary

1. **Four** vaccines have well established safety and efficacy: two mRNA vaccines and **two** adenovirus-based vaccine. Phase 3 trials had thousands of participants: Efficacy was 95% and 94%, respectively for the two mRNA vaccines, 62% for the AstraZeneca vaccine (90% if dosing was changed) and **72% for the more recent Johnson & Johnson vaccine**. For all vaccines, serious adverse events were rare, and the incidence was similar in the two groups (vaccine and placebo recipients). Another two vaccines (from Johnson & Johnson and Novavax) have promising preliminary efficacy results (as of 29 January 2021).

Latest update of 02.02.2021: a two-dose Russian vaccine (Gam-COVID-Vac, also called Sputnik V) trial among 19,866 participants showed an efficacy of 91.6% and a good safety profile.

2. The development of the vaccines was very fast, mainly due to (i) years of previous research on corona viruses; (ii) RNA vaccines having benefited from 10–15 years of strong research; (iii) years of previous research on faster ways to manufacture vaccines; (iv) enormous funding available (including public money made available for pharmaceutical companies); (v) rapid steps from phase 1 to phase 2 to phase 3 trials, with overlapping; and (vi) regulators moving more quickly than normal.

3. **Vaccination in Switzerland (plus Liechtenstein), as of 7 March 2021: 1,307,400 doses received and 951,804 doses applied so far. This equals 11 doses per 100 persons (highest in AI, followed by NW, SH, UR, ZG and BS; in BS it was 10.6 per 100 persons). Overall, 332,585 people have received both doses (“fully vaccinated”), (3.9% of the population of Switzerland).**

The goal is that by the end of March, all high-risk patients and that by the end of June 2021, all people in Switzerland desiring the vaccination will have received it. **Over the past few weeks, between 15,000 and 26,000 doses were applied per day on average. To achieve a 70% vaccination coverage rate for the population of Switzerland by the end of June 2021, approximately 93,000 doses need to be administered per day (on average) from 8 March 2021 onwards. The main constraint is the limited number of available vaccine doses.**

4. COVAX: The Covax Facility (www.gavi.org/covax-facility#what) is a global risk-sharing procurement initiative. The goal is to pool vaccine buying power, with a target of obtaining at least 2 billion vaccine doses. So far, **190** countries have signed up to the COVAX initiative. At least ninety-two LMIC countries will have their vaccines paid for by a fund sponsored by donors. **COVAX says it has enough supply in the pipeline to inoculate 20% of the population of its member countries by the end of the year.**

Main Things to Know About COVID-19 Vaccines

1. **Four** vaccines have well established safety and efficacy: two mRNA vaccines and two adenovirus-based vaccine

A) Pfizer/BioNTech (BNT162b2)

- Primary analysis with data from 43'448 participants showed an effectiveness of 95% against COVID-19.
 - 170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group;
 - Enrollment was completed in January 2021; trial sites are in Brazil, Argentina, USA, Germany, Turkey, and South Africa.
- The safety profile of the vaccine was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache.
 - The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.
 - No serious safety concerns observed; the only Grade 3 adverse event greater than 2% in frequency was fatigue at 3.8% and headache at 2.0%.
 - Fever (temperature, $\geq 38^{\circ}\text{C}$) was rather common after the second dose when it was reported by 16% of younger vaccine recipients and by 11% of older recipients.
- Two shots are needed: the second dose given 21 to 42 days after the first dose.
- **Though clinical trial data estimated an efficacy of only 52.4% after one dose, recent findings from the UK and Israel suggest that just one shot also gives good protection (80 to 90%): www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2900448-7**
- Storage is at minus 75°C . Once thawed, vaccines must not be re-frozen, but must be used within the shelf life of 5 days at $2 - 8^{\circ}\text{C}$.
- The companies expect to produce globally up to 1.3 billion doses by the end of 2021.
- Main publication of the trial results: www.nejm.org/doi/full/10.1056/NEJMoa2034577
- There is now evidence that even one shot

B) Moderna (mRNA-1273)

- Vaccine efficacy against COVID-19 was 94.1%; vaccine efficacy against severe COVID-19 was 100% (all 30 severe cases were in the placebo group).
 - As of 30 November 2020, there were 30,420 participants (all in the USA); there were 196 cases of COVID-19; 185 cases of COVID-19 were observed in the placebo group and 11 cases in the mRNA-1273 group.
- Adverse event:
 - Serious adverse events were rare, and the incidence was similar in the two groups (grade 3 events in 1.3% among the placebo group and 1.5% in the vaccine group)
 - Solicited systemic adverse events occurred more often in the mRNA-1273 group than in the placebo group after both the first dose (54.9%, vs. 42.2%) and the second dose (79.4%, vs. 36.5%)
- Two shots are needed: the second dose given 28 to 42 days after the first dose.
- The company expects to produce at least 600 million doses in 2021, with potential to bring this figure up to 1 billion doses.
- Storage is at minus 20°C . An ampoule contains 10 doses of 0.5 ml. Thawed ampoules can be kept for 30 days at refrigerator temperatures.
- Main publication of the trial results: <https://www.nejm.org/doi/full/10.1056/NEJMoa2035389>

C) Oxford–AstraZeneca (AZD1222)

- Primary efficacy analysis with data from 11'636 participants showed an effectiveness of 62.1% against COVID-19 in participants who received two standard doses. For participants who received a low dose followed by a standard dose, efficacy was 90.0%. **There is some evidence that the vaccine offers only very limited protection against the South African variant 501.V2 (also known as B.1.351).**
- Safety profile of the vaccine: 175 severe adverse events occurred in 168 participants: 84 events in the vaccine group and 91 in the control group. Controls received the conjugate meningococcal vaccine ACWY.
- The UK Medicines and Healthcare products Regulatory Agency approved AZD1222 in late December 2020. It has not yet been approved by FDA nor by Swissmedic. It is unclear if Swissmedic approves it in February 2021.
- Two shots are needed: the second dose can be given between 4 and 12 weeks after the first dose.
- The company aims to produce globally up to 3 billion doses by the end of 2021.
- Storage: The vaccine can be stored and transported at normal refrigerated temperatures of 2 to 8°C for at least six months.
- Main publication of the trial results: [https://doi.org/10.1016/S0140-6736\(20\)32661-1](https://doi.org/10.1016/S0140-6736(20)32661-1)

D) Johnson & Johnson (Ad26.COV2.S)

- **For this vaccine, approved by the FDA on 27.2.2021, one dose (one shot) is sufficient. Data from 45'000 participants showed an effectiveness of 72% against COVID-19 in the USA, of 64% in South Africa and of 61% in Brazil.** The vaccine had 85% efficacy against severe disease anywhere in the world; this includes South Africa where almost all participants had the variant form of the virus.
- **The vaccine can be kept for up to two years when frozen at –20° C, and for up to three months when refrigerated (at 2–8° C).**
- **The US government paid for 100 million doses, expected to be fully delivered by June. With the European Union, a deal for 200 million doses was reached in October 2020. And COVAX secured 500 million doses. The company is aiming for production of a billion doses in 2021.**
- **Currently, Johnson & Johnson is conducting a second Phase 3 trial to observe the effect of two doses of their vaccine. The results are expected in late 2021.**

The following gives an overview about many vaccine candidates:

www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

2. **Two other vaccines with good efficacy (preliminary results)**

A) The Russian vaccine Gam-COVID-Vac (Sputnik V), a two-dose vaccine

- Efficacy was 91.6% based on an interim analysis, published on 2.2.2021 (www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2900234-8)
- Storage is at –18°C (though storage at 2 to 8 °C seems to be possible as well).
- Safety profile: 45 (0.3%) of 16,427 participants in the vaccine group reported serious adverse events, all of which were considered not related to the vaccine.

B) Novavax's NVX-CoV2373 vaccine

- Efficacy: 89%, based on an interim analysis of a phase 3 clinical trial conducted in the UK (data from more than 15'000 trial participants). The trial suggested 95.6% efficacy against the original coronavirus and 89.3% efficacy against the more recent UK variant (over 50% of cases were attributable to the now-predominant UK variant). 60% efficacy was seen in S-Africa (HIV-negative population only) and 49% in a mixed HIV-positive and negative population.
- The results of a larger Phase 3 trial are expected for April 2021.
- Two doses are needed
- Storage: in a regular refrigerator (2-8°C)
- Novavax reached an agreement with the Serum Institute of India, a major vaccine manufacturer, that aims at producing as many as 2 billion doses a year.

3. For how long will the vaccine-induced immunity last? **What about transmission?**

- Vaccines have their specific duration of immunity that can range from a few months to decades. Attenuated live vaccines usually have the longest immune response.
- It is not yet clear what we can expect for the COVID-19 vaccines and how long immunity lasts after infection. A small study among 100 subjects (yet to be peer reviewed) found functional SARS-CoV-2-specific T-cell responses were retained at six months following infection (Zuo et al, T-cell immunity after COVID. bioRxiv preprint, Nov. 2020).
- It is likely that for the COVID-19 vaccines, annual booster vaccinations are needed though some think that immunity may last for two to three years.
- **It is not yet fully clear if and to what degree the COVID vaccines also cut down transmission. Preliminary analyses suggest that at least some vaccines are likely to have a transmission-blocking effect.**

Main source for this section:

<https://theconversation.com/covid-19-immunity-how-long-does-it-last-152849> and www.nature.com/articles/s41586-021-03207-w

Other sources: <https://science.sciencemag.org/content/early/2021/01/06/science.abf4063> and www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-18---covid-19---immunity-after-recovery-from-covid-19.

On blocking transmission: www.nature.com/articles/d41586-021-00450-z and www.vox.com/future-perfect/22291959/covid-vaccines-transmission-protect-spread-virus-moderna-pfizer

4. Reasons why the process of finding effective vaccines was so fast

- Years of previous research on corona viruses (SARS-CoV-2 belongs to a well-studied family)
- A lot went into today's mRNA platform. The basic research on DNA vaccines began at least 25 years ago, and RNA vaccines have benefited from 10–15 years of strong research.
- Years of previous research on faster ways to manufacture vaccines
- Enormous funding made available (due to a strong sense of social and political urgency) that allowed pharma companies to run multiple trials in parallel rather than sequentially
- Medical regulators turning around their processes more rapidly than normal

- Rapid progression from phase 1 to phase 2 to phase 3 trials, with overlapping and parallel running of trials. The high incidence of COVID-10 in many countries also helped moving rapidly through phase 2 and especially phase 3.
- Pharmaceutical companies took financial risks, made easier by support through public money (MSF reports that the six front running vaccine candidates have had a total of over US\$12 billion of taxpayer and public money poured into them) and started investing in manufacturing early on, so there was no delay between completion of testing and roll-out.
- An informative publication: www.nature.com/articles/d41586-020-03626-1

5. mRNA vaccines – are they safe?

- While the technique has been around for several years, the two mRNA vaccines mark the first time this vaccine technology has been approved for use.
- mRNA vaccines = messenger RNA which is like a recipe or a template to build a protein use our body for making the viral protein itself which – once produced and secreted from the cell - triggers an immune response.
- In other words, the mRNA in the body functions like an instruction manual, telling the body how to create a piece of the “spike protein” unique to SARS-CoV-2.
- mRNA vaccine technology has been studied for decades in vaccines focused on other viruses, such as the flu, rabies and Zika. Also, human trials of cancer vaccines using the same mRNA technology have been taking place since at least 2011. If there was a problem with the technology, this would have been detected during those years.
- mRNA vaccines cannot alter one’s DNA; the (vaccine) mRNA will not enter the nucleus of the cells, where the DNA is. Once the injected mRNA enters a human cell, it degrades quickly.
- After a vaccine is given to millions of people, very rare side effects that cannot be anticipated from clinical trials might develop, so researchers and regulators will be keeping a close eye on how the vaccine roll-out goes.

Main source: <https://horizon-magazine.eu/article/five-things-you-need-know-about-mrna-vaccines.html> and <https://horizon-magazine.eu/article/five-things-you-need-know-about-mrna-vaccine-safety.html>

6. The vaccination situation in Switzerland

- The Swiss government has the following agreements in terms of number of doses:
 - Moderna: 7.5 million doses. And 6 million for the second half of 2021.
 - Pfizer/BioNTech: 3 million doses
 - AstraZeneca: 5.3 million doses
 - Novavax: 6 million doses
 - Curevac: 5 million doses (**Curevac is an mRNA vaccine; Phase 3 results are expected for late April or early May**)

With Johnson & Johnson, negotiations are currently on-going.

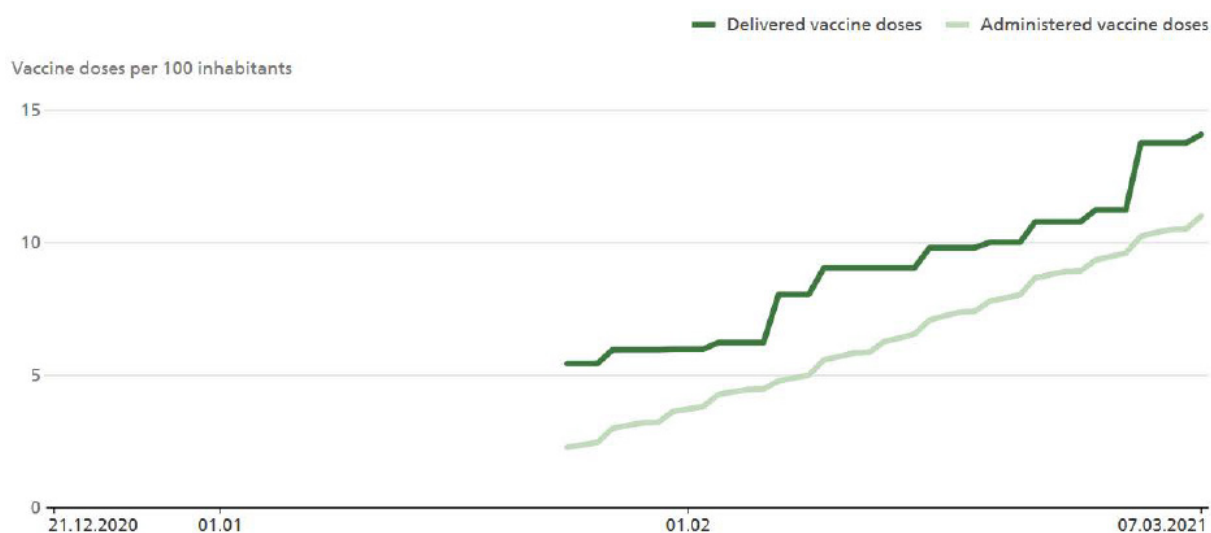
In total, the authorities have reserved a total of over 30 million vaccine doses.

- There is some uncertainty when exactly all these doses will be delivered. For February, another 650,000 doses of the two mRNA vaccines are expected. After initial production and negotiation delays more doses will become available from March/April onwards. As of mid-February, the Swiss government was confident that:

- By the end of March, all risk groups will have had the chance to get vaccinated (Berset stated on 3 Feb 2021 that in spite of challenges with the delivery of the vaccines, the goal still is that by the end of March, 1.15 million people will have received two doses).
- By the end of June, all people who want to be vaccinated should have received the vaccine.
- However, it is expected that for February, only 50% of the target of number of people vaccinated will be reached and some experts worry that the “end of June target” may be reached in autumn only. Each additional day of delay has a high socio-economic cost, calculated by the scientific task force to cost Switzerland around CHF 100 million per day.

Note: some of this information is from <https://nzzas.nzz.ch/schweiz/corona-bund-muss-impf-fahrplan-korrigieren-ld.1599250>

- The following people are being given access to vaccinations first:
 - People age 75 years and over
 - Regardless of age, people with chronic diseases or conditions (e.g. diabetes)
 - People who live in a retirement or care home. Staff who are in contact with residents of retirement and care homes also have the option of being vaccinated at the same time.
- **The number of vaccine doses given in Switzerland (plus Liechtenstein), situation per 7 March 2021, evening (source: www.covid19.admin.ch):**
 - **1,307,400 doses received so far** (the army then sends the doses to the Kantons)
 - **Of them, 951,804 doses applied so far.**
 - **“Fully vaccinated” (i.e. both doses received) were 332,585 people (3.9% of the population of Switzerland).**
 - **Coverage was highest in SH, followed by NW, UR, AI, ZG, GL and BS.**
 - During the past few weeks, the average number of applied doses per day ranged between around **15,000 and 26,000. The graph presents a wider time window** (source: www.covid19.admin.ch/en/epidemiologic/vacc-doses):



- To achieve a 70% vaccination coverage rate for the population of Switzerland by end of June 2021, approximately **93,000** doses need to be administered per day (on average) **from 8 March 2021 onwards**. The main constraint is the limited number of available vaccine doses.
- Vaccine hesitancy is decreasing but still common: a survey from January 2021 found that 41% of the respondents were fully willing to get the corona vaccine and that 34% were “not sure/waiting”. Only 24% were unwilling.

7. Some facts about COVAX and the challenges for LMIC

- The COVAX Facility (www.gavi.org/covax-facility#what) is a global risk-sharing procurement initiative. It is co-led by Gavi, the Coalition for Epidemic Preparedness Innovations (CEPI) and WHO.
- COVAX's aim is to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world. A main approach is to unite countries into one bloc so they have more power to negotiate with drug companies.
- The goal is to pool vaccine buying power, with a target of obtaining 2 billion doses to protect more than 20 percent of populations by the end of 2021. **The expectation is that by then, more than a billion high-risk and vulnerable people living in countries that would otherwise be unable to afford these vaccines, will be protected because of COVAX.**
- Ninety-two lower-income economies will be supported by the financing mechanism in COVAX and ninety-eight higher-income economies have signed up as self-financing members of the COVAX Facility.
- So far, COVAX has commitments to get the doses from five producers. For instance, Pfizer announced on 22 January 2021 an agreement to provide up to 40 million doses.
- In early January 2021, the Serum Institute of India obtained emergency use authorisation in India for AstraZeneca's COVID-19 vaccine.
- **WHO has listed two versions of the Oxford-AstraZeneca vaccine for emergency use (one produced by South Korea's SK Bioscience and one by the Serum Institute of India), giving the green light for these vaccines to be rolled out globally through COVAX. COVAX expects deliveries to start by the end of February 2021.**
- Sufficient funding and good positioning of COVAX is a challenge. In the words of the director-general of WHO: “The world is on the brink of a catastrophic moral failure”.
- **COVAX is crucial and needs to be strengthened. On February 24, 2021, the Washington Post reported that ten high-income countries have secured and administered 75% of the current global covid-19 vaccine supply. Thus, the danger that two classes emerge – a vaccinated class and an unvaccinated class (in the low and middle-income countries) – is real. A term has already been coined for this: “vaccine apartheid,” whereby countries with very limited resources remain years behind the high-income countries. This would not only be a moral failure but also economically devastating: a recent study by the International Chamber of Commerce predicted that leaving poor countries unvaccinated could deprive rich countries of \$4.5 trillion in economic activity (<https://iccwbo.org/media-wall/news-speeches/study-shows-vaccine-nationalism-could-cost-rich-countries-us4-5-trillion/>).**
- **On February 24, The Guardian reported that in mid-February, G7 countries raised their contribution to COVAX to £5.3 billion. Public health activists say the**

programme needs not just money but some of the excess vaccine doses that wealthier countries have procured (see above: Swiss authorities have reserved a total of over 30 million vaccine doses).

- By late February 2021, COVAX vaccine doses were shipped to a number of countries, with 247 million doses to reach 147 countries by the end of May. COVAX aims to distribute enough vaccines over the next six months to inoculate 3% of the population of 145 countries; this would be sufficient to cover health workers and some of the most vulnerable.
- COVAX says it has enough supply in the pipeline to inoculate 20% of the population of its member countries by the end of the year, though the Serum Institute of India – the largest supplier of vaccines.