

# COVID-19 mRNA Vaccine Safety

Version of 17 February 2021

This paper was written by Dónal O’Mathúna, PhD, Associate Professor at OSU who works in the areas of evidence-based practice and disaster ethics. This paper addresses the mRNA vaccines available from Pfizer/BioNTech and Moderna. The safety issues with other vaccines that work in different ways may be different and will be addressed as they become available.

## Did developing COVID-19 vaccines so rapidly compromise their safety?

COVID-19 vaccine development benefited from earlier research into two other coronaviruses that caused different but related diseases in recent years: MERS and SARS.[1] This gave researchers a head-start in developing COVID-19 vaccines. As vaccine candidates became available, they went through the usual 4 phases that all new vaccines go through to test for safety and efficacy (Phase 1 with dozens of volunteers; Phase 2 with hundreds; Phase 3 with at least a thousand volunteers; Phase 4 with the general public).[2]

Many factors contributed to the rapid development of the COVID-19 mRNA vaccines.[3] Governments gave large amounts of funding so that vaccine developers had more resources than usual to develop a new vaccine (and did not have to go through the lengthy fund-raising processes). The mRNA technology had been in development with other vaccines for over 20 years during which the process was improved and then adapted to COVID-19. The mRNA technology is much faster than traditional vaccine development. Phase 3 trials usually recruit 3,000 to 6,000 volunteers and can take years before enough people participate to allow statistical comparisons to be made between those who get the vaccine and those who get the placebo.[1] COVID-19 vaccines were required to recruit “well over 3,000 vaccine recipients.”[4] The Pfizer/BioNTech trial had over 43,000 participants and Moderna over 30,000. People volunteered very quickly, allowing the results to become available much faster than usual. Also, because the pandemic was so widespread, volunteers in the trials were exposed to the virus often which allowed their efficacy to be tested quickly.[3] Vaccines were manufactured in large quantities even before they were approved so they could be distributed as soon as authorized. All these factors contributed to the vaccines being tested and given emergency use authorization much more quickly than previous vaccines.

## Aren’t there safety risks since mRNA vaccines haven’t been available before?

mRNA vaccines have been under development for at least 20 years.[5] Early work with cancer and viral vaccines showed promise in animal studies, but these were much less effective when given to humans. Dozens of clinical trials of various mRNA vaccines have been completed.[5] For example, a Phase 1 trial of a rabies mRNA vaccine gave a series of 3 vaccine doses to 101 volunteers.[6] While the vaccine did not produce the desired levels of immunity, it had a good safety profile. Most people had injection-site soreness and some had short-term adverse reactions similar to those found with COVID-19 vaccines. Only 1 serious adverse effect was found, a case of Bell’s palsy which went away after 7 days. Bell’s palsy is a condition where the muscles on one side of the face become weak and the face droops. Its cause is not known.

One of the reasons why mRNA vaccines have been researched is because they can be produced more safely. Other vaccines are produced using chicken eggs, cell cultures or various biochemicals, which increase the risk of contamination and allergic reactions. These production methods are also slower. Some vaccines use viruses (killed or deactivated), which carry risks that mRNA vaccines do not have. Much of the interest in mRNA vaccines has been because they were believed to be very safe. A 2018 review of mRNA vaccines noted that Moderna and BioNTech (Pfizer's partner) have been actively involved in this research for several years.[5] These companies have a good track-record of research in this area.

### **What do we know about the short-term safety of COVID-19 vaccines?**

The Pfizer and Moderna vaccine trials reported no serious safety concerns. The safety data were monitored by independent safety monitoring boards, as well as the FDA and other expert panels. This will continue during the Emergency Use Authorization.[3]

Short-term side effects that lasted 1-2 days included pain at the injection site, fever, and muscle aches. The only severe adverse effects in the Pfizer vaccine trials were fatigue in 3.8% of those getting the vaccine, and headache in 2%. With the Moderna vaccine, severe effects were fatigue (9.7%), muscle aches (8.9%), joint aches (5.2%), headache (4.5%), pain (4.1%) and injection site pain (2.7%). While unpleasant, these sorts of side effects are indicators that someone's immune system is responding as it should and they are common with any vaccine.[7]

Allergic reactions have been reported with the vaccines. With the first 4 million doses of the Moderna vaccine, the CDC reported that 10 people had anaphylaxis, a potentially life-threatening allergic reaction.[8] This is a rate of 2.5 cases per million doses. Of the 10 people, 9 had a documented history of allergies and 5 had previously had anaphylaxis. Anaphylaxis occurred, on average, within 7.5 minutes of vaccination, and all 10 people recovered quickly because healthcare personnel were on site to respond to the anaphylaxis. Another 47 people had nonanaphylactic allergic reactions within 24 hours of receiving the vaccine.[8] In all cases for which information was available, people recovered fully. One particular batch of Moderna vaccine resulted in allergic reactions in 7 people at a drive-through clinic in California, and 1 in Oregon, leading to use of this batch being paused. An independent scientific review of these cases concluded that no vaccine recipient had anaphylaxis, and that all recovered after treatment.[9] No cause for the cluster of allergic reactions was identified. The committee concluded that the batch should continue to be used given how many other sites had used it without similar allergic reactions and the overall shortage of COVID-19 vaccines. They noted the importance of continuing to have trained staff at vaccine distribution sites to respond to adverse reactions, and that people should continue to be screened for a history of allergic reactions, and that after vaccination, people remain on site to be monitored for 15-30 minutes.

Another concern arose in Europe when Norway's health authorities announced in mid-January that 33 elderly and very frail nursing home residents had died after receiving the Pfizer vaccine. Other European countries reported similar deaths. However, on January 29<sup>th</sup>, 2021, the European Medicines Agency (the equivalent of the FDA in Europe) announced that they had studied the cases and found no link between the deaths and the vaccine.[10] The Agency noted that the people who died were very old, frail and had other serious diseases. An average of 45 people die each day in Norway's nursing homes from underlying diseases. Since Norway

focused its vaccine roll-out on nursing homes, the Agency stated that it would be normal to have some people die after receiving the vaccine. Every case in Europe is being investigated, but so far no link has been found.

### **What do we know about the long-term safety of COVID-19 vaccines?**

Information on the long-term safety of COVID-19 vaccines is sparse given that they are so new. The FDA required 2 months of follow-up data, including monitoring of side-effects, before they would grant an Emergency Use Authorization.[4] The FDA Director stated that this period was selected because most adverse effects from vaccines appear within two months.[1]

Long-term safety is one area where the unknown, potential side-effects of the vaccine have to be weighed against the known, serious effects of COVID-19. A comparison of the most serious effect may help here. From the start of the pandemic to January 21, 2021, out of the 45,940,321 people aged 25-34 years in the US, 2,278 died with COVID-19.[11] Therefore, the risk of dying from COVID-19 for 25-34 year olds was 50 out of a million. Using the same CDC database, the risk of dying with COVID-19 for those 85 or older, was 16,877 in a million. The overall risk of death from COVID-19 for all people in the US is about 1,000 in 1 million, or 1 in a 1000. This compares with the risk of life-threatening anaphylaxis from the COVID-19 vaccine being 2.5 out of a million (although no one has actually died from the vaccine). In other words, the risk of dying from COVID-19 for any American is 400 times greater than the risk of the most serious side-effect of the vaccine. For 25-34 year olds, the risk of dying from COVID-19 is 20 times higher than having anaphylaxis. This does not even take account of the serious effects some people have of contracting COVID-19. This is why authorities are saying that the known risks of getting COVID-19 far outweigh the unknown risks of the vaccine.

### **What about concerns about genetic changes and infertility?**

Claims have been made that mRNA vaccines might alter people's DNA or genetic code. DNA and RNA are the major types of genetic material in all living organisms. DNA is found in the nucleus of human cells and carries the instructions to make all our proteins. The information in DNA is copied into messenger RNA (mRNA). The mRNA leaves the nucleus and is used in another part of the cell to make a specific protein. The mRNA quickly falls apart and its pieces are recycled. This whole process goes in one direction in human cells: from DNA to RNA to protein. Some people worry that the mRNA in COVID-19 vaccines might run in reverse direction and change their DNA. This is so extremely unlikely that many researchers believe it can't occur. The vaccines contain a tiny amount of mRNA which very quickly falls apart.[12] For mRNA to affect DNA it would first have to enter the nucleus which mRNA normally can't. Even if it got in, human cells do not have the enzyme required to convert RNA into DNA. A type of virus called a retrovirus can do this, but it works on a different type of RNA, not mRNA. The COVID-19 virus is not a retrovirus. HIV is a retrovirus, and even in people who have been infected for years with this virus, RNA from other viruses has not led to changes in those people's DNA.[13] A theologian and molecular biologist recently stated that the odds of this happening are the same as someone winning the lottery 10 times—all at the same moment.

Another concern is whether COVID-19 vaccines will cause infertility. This started in December 2020 when a German physician (Wolfgang Wodarg) and Dr. Mike Yeadon (Pfizer's

former Vice President and Chief Scientist for Allergy & Respiratory<sup>1</sup>) asked the European Medicines Agency to delay approving the Pfizer vaccine.[14] They wrote that the vaccine mRNA for the spike protein was similar in structure to that for another protein called syncytin-1. This protein is important in the human placenta. They speculated that if the vaccine causes the body to make antibodies that attack the spike protein, might they also attack syncytin-1? Might that cause rejection of the placenta and make it impossible for women to complete pregnancies? It didn't help that *Utopia*, a science fiction miniseries, was airing at the time and includes a plot to fake a flu pandemic to promote a vaccine that prevents human reproduction. Getting back to vaccine science, while the mRNA for the spike protein and syncytin-1 have some similarities, they are still very different. One infectious disease specialist said it would be the same as saying that two people have similar phone numbers because they have one number in common! The German physician admitted they had no data to support their concern. Also, during the Pfizer trials, 23 women got pregnant – 12 in the vaccine group and 11 in the placebo group. The numbers are very small, but suggest the vaccine does not prevent pregnancy. In addition, if the vaccine causes infertility, COVID-19 infection would be expected to cause infertility too. However, there no evidence at this point that the pandemic has changed fertility statistics.[14]

A related question is whether pregnant women should get COVID-19 vaccines. Pregnant women were not included in the Pfizer and Moderna trials.[15] This is common practice with experimental vaccines and drugs to avoid harming fetuses. However, this leads to the current dilemma where evidence is lacking to guide people concerning the risks of the COVID-19 vaccine during pregnancy. As with the long-term safety issues, it is a matter of balancing the unknown risks from the vaccine with the known risks from COVID-19. In general, some vaccines are known to be safe during pregnancy and millions of women have received them.[16] This includes the flu vaccine. On the other hand, pregnant women who get COVID-19 are at an increased risk of severe illness (leading to hospitalization and ICU admission) compared to non-pregnant women.[17] Pregnant women may also have increased risks of adverse outcomes, such as preterm birth. Public health surveillance is ongoing to determine these risks more exactly.

### **Will anyone know if new adverse effects or safety problems develop with COVID-19 vaccines?**

A number of mechanisms exist to monitor adverse effects for any vaccine. The people enrolled in the vaccine trials will continue to be monitored for adverse effects, and other research will be conducted into this area.[4] These include the Vaccine Adverse Event Reporting System (VAERS) run by the CDC and the FDA, as well as other surveillance mechanisms.[18] The Department of Defense has an adverse event reporting system for active military personnel, and there is another for Veterans. In addition, new mechanisms were added because of the large-scale roll-out of the COVID-19 vaccines under the Emergency Use Authorization. All recipients of COVID-19 vaccines are given information on how to report adverse events.

---

<sup>1</sup> <https://www.reuters.com/investigates/special-report/health-coronavirus-vaccines-skeptic/>;  
<https://www.lifesitenews.com/news/exclusive-former-pfizer-vice-president-your-government-is-lying-to-you-in-a-way-that-could-lead-to-your-death>

These types of surveillance systems have already triggered investigations, as discussed in the section above about short-term safety issues. The concerns over allergic reactions to Moderna's vaccine in California, and to deaths of older, frail people in Norway, were noticed and investigated. In both cases, the events were determined not to be due to the vaccines, and their distribution continued. It is likely that similar reports will continue to emerge, and should be investigated. If evidence of serious adverse effects emerges, these systems will lead to changes in recommendations, changes in how the vaccines are given, or other changes.

No new treatment or vaccine comes without some level of risk or adverse effects. The evidence to date points to the COVID-19 vaccines being as safe as possible, and more effective than many other vaccines. We also know that by the middle of February 2021, almost 28 million people in the US have tested positive for the virus causing COVID-19, with almost half a million people dying.[19] Many more have suffering serious effects and may have long-term consequences. Almost 2.5 million people have died worldwide. Vaccines and other public health precautions (masking, social distancing, etc.) are the main steps we can take to bring the pandemic under control and hopefully get back to more normal living.

## References

1. Zhang S. The vaccine news that really matters. *The Atlantic*. 19 October 2020. <https://www.theatlantic.com/health/archive/2020/10/what-successful-vaccine-trial-looks-like/616775>
2. CDC. The Journey of a Vaccine. [https://covid19community.nih.gov/sites/default/files/2020-12/CEAL%20Infographics\\_Vaccine%20Journey\\_12.1.20.jpg](https://covid19community.nih.gov/sites/default/files/2020-12/CEAL%20Infographics_Vaccine%20Journey_12.1.20.jpg)
3. Maragakis LL, Kelen GD. Is the COVID-19 vaccine safe? Johns Hopkins Medicine. <https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/is-the-covid19-vaccine-safe>
4. FDA. Emergency Use Authorization for Vaccines to Prevent COVID-19 Guidance for Industry. October 2020. <https://www.fda.gov/media/142749/download>
5. Pardi N, et al. mRNA vaccines — a new era in vaccinology. *Nature Reviews Drug Discovery* 2018;17:261-279.
6. Alberer M., et al. Safety and immunogenicity of a mRNA rabies vaccine in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial. *Lancet* 2017;390(10101):1511-1520.
7. Tanula M. COVID-19 vaccine myths debunked. Mayo Clinic News Network. 9 December 2020. <https://newsnetwork.mayoclinic.org/discussion/covid-19-vaccine-myths-debunked/>
8. CDC. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021. *Morbidity and Mortality Weekly Report* 2021;70(4):125-129. <https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7004e1-H.pdf>

9. Western States Scientific Safety Workgroup. 20 January 2021. <https://bloximages.newyork1.vip.townnews.com/kptv.com/content/tncms/assets/v3/editorial/e/d6/ed62c5e8-5c58-11eb-87ac-f7d932b2e59d/600a378da62a5.pdf.pdf>
10. Georgiou A. Deaths after Pfizer COVID vaccines not linked to shots, says European Medicines Agency. *Newsweek*. 29 January 2021. <https://www.newsweek.com/pfizer-biontech-covid-vaccine-deaths-eu-medicines-agency-1565405>
11. CDC. Weekly Updates by Select Demographic and Geographic Characteristics. 21 January 2021. [https://www.cdc.gov/nchs/nvss/vsrr/covid\\_weekly/index.htm#AgeAndSex](https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm#AgeAndSex)
12. CDC and ID Society Vaccines FAQ 29 January 2021. <https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/>
13. Children's Hospital of Philadelphia. News & Views: 3 questions you will get about the new mRNA vaccines. 17 December 2020. <https://www.chop.edu/news/news-views-3-questions-you-will-get-about-new-mrna-vaccines>
14. Goodman B. Why COVID vaccines are falsely linked to infertility. *WebMD*. 12 January 2021. <https://www.webmd.com/vaccines/covid-19-vaccine/news/20210112/why-covid-vaccines-are-falsely-linked-to-infertility>
15. Gulino E. The COVID-19 vaccine won't make you infertile. *Refinery29*. 7 January 2021. <https://www.refinery29.com/en-us/2021/01/10249647/does-covid-vaccine-cause-infertility-side-effects?>
16. CDC. Vaccines during pregnancy FAQs. <https://www.cdc.gov/vaccinesafety/concerns/vaccines-during-pregnancy.html>
17. CDC. Investigating the impact of COVID-19 during pregnancy. 4 February 2021. <https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19/what-cdc-is-doing.html>
18. CDC. Ensuring COVID-19 vaccine safety in the US. 15 February 2021. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html>
19. Johns Hopkins University. COVID-19 dashboard. <https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>
20. Prentice D, Sander T. What you need to know about the COVID-19 vaccines. 8 December 2020. <https://lozierinstitute.org/what-you-need-to-know-about-the-covid-19-vaccine/>