THE UNIVERSITY OF BRITISH COLUMBIA

Dr. Steven Pelech
[redacted]

To the Editors
Winnipeg Free Press
letters@freepress.mb.ca

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Re: **The efficacy and safety of COVID-19 vaccines**

In response to "The Unwelcome Unvaxxed" by Patricia Dawn Robertson

I have been contacted by some of your readers to respond to the misinformation that Ms. Robertson expressed in her recent article in your publication today. I believe that she is highly ignorant about the situation with respect to COVID-19, and the growing recognition amongst many qualified scientists and physicians about the poor efficacy and the unacceptable harms that are now recognized as associated with COVID-19 genetic vaccines. The publication of such trite and hateful commentary will certainly tarnish the reputation of your organization if not retracted. I am providing you with some information that will be appearing as a small part of an upcoming book from the former Canadian COVID Care Alliance (CCCA), in which I am the vice-president. I am an editor of co-author of this book. I hope that you or one of your investigative reporters will carefully consider the information contained with this letter.

First in Part 1, I will introduce myself to establish my credentials and then expertise. My full name is Steven Pelech, and I reside [redacted] British Columbia, Canada. My Ph.D. and post-doctoral training is in the area of biochemistry, and I have been on the faculty of the University of British Columbia as a professor in the Department of Medicine for over 35 years.

I have been asked in over 16 court cases to provide expert opinion reports regarding the efficacy and safety of COVID-19 genetic vaccines. In doing so, I have also read through expert reports provided by

other scientists and doctors across Canada that have advocated mass COVID-19 vaccination, and I have found them highly wanting and deficient.

In brief, I have worked with viruses in a research setting ever since I undertook my Ph.D. studies. At that time, I had worked with the Semliki Forest virus in the laboratory of Dr. Dennis Vance to examine its effects on the synthesis of phosphatidylcholine, one of the major lipids inside of cells. This is a positive-sense, singled-stranded RNA virus, like the SARS-CoV-2 virus, and it is known to cause disease in animals and humans. As an undergraduate student at the University of British Columbia, I took second, third and fourth year lecture and laboratory courses in Microbiology and Immunology, including in Virology. I teach such material in my own lectures over the last 35 years. Recently, I have been actively involved in COVID-19 research for over 3 and a half years, especially with respect to the replication of the SARS-CoV-2 virus, and the production of antibodies against this virus in people who have been infected by this virus and/or have been vaccinated against this virus. I have been involved in the development of serological tests for SARS-CoV-2 directed antibodies, and the application of these tests to evaluate natural and COVID-19 vaccine-induced immunity in a 4,500-person clinical study that I led.

I have read over two thousand publications in the scientific literature, regularly accessed the websites of several Canadian provincial and federal government health agencies as well as those in other countries. I have written several manuscripts related to COVID-19 and SARS-CoV-2 from my original research, and I am an editor and major author of two books on COVID-19 that are presently under review by Skyhorse Publishing. This has informed my opinions about the effectiveness of strategies for prevention and treatment of COVID-19, and the risks and benefits of these interventions.

Throughout this letter in Part 2, I have identified many of the key primary publications in the scientific literature and government websites that addresses these matters and these are cited as footnotes. I recognize that much of what I have written is very technical in nature. However, I have made a concerted effort to permit those not skilled in biochemistry, immunology and virology to comprehend the complexities related to assessing the effectiveness and safety of COVID-19 vaccines and natural immunity to control infectious viral pathogens. After you have read this letter, assuming that you are intrigued enough to do so, I am happy to speak with one of your editors on this matter, and if desired prepare a rebuttal opinion piece to Ms. Robertson's Opinion piece that you published. Better yet, I

hope that your organization has the guts to actually investigate the narrative espoused by public health authorities and parroted by legacy media that COVID-19 genetic vaccines are safe and effective and that booster vaccination is necessary.

Part 1: My Qualifications and Acknowledgements as an Expert on COVID-19

I am a full Professor in the Department of Medicine and Division of Neurology at the University of British Columbia (UBC), where I have been on faculty since 1988. I was one of the founding senior scientists of The Biomedical Research Centre at UBC in 1987. I hold B.Sc. Honours (1979) and Ph.D. (1982) degrees in Biochemistry from UBC. My post-doctoral training was at the University of Dundee with Sir Philip Cohen, and at the University of Washington in Seattle with Nobel laureate Dr. Edwin Krebs.

I have previously completed several courses in microbiology, immunology and virology during my B.Sc. undergraduate training, and I was a founding and senior scientist for six years at The Biomedical Research Centre, which was an immunology-focused institute located at UBC, where I have remained on faculty as a professor in the Department of Medicine for over 35 years. Over a dozen of my scientific research articles have appeared in specialty immunology journals, including the *Journal of Immunology, Blood, Molecular Immunology, Immunology, Infectious Immunology, Cancer Immunology and Immunotherapy*, *International Journal of Vaccine Theory, Practice and Research* and *Vaccines*. These studies document some of my work to understand the molecular mechanisms by which different immune cells, including macrophages, T and B cells become activated. My lectures in formal graduate level courses include teaching in immunology and virology at UBC. I have presented my research at over 100 national and international scientific conferences. My UBC lab and spin-out companies have been engaged in the production and testing of over 1600 antibodies for our internal research programs and for commercial sale for over 30 years. My research as an independent investigator has routinely involved for over 36 years, the use of standard and novel immunological techniques developed in my lab, such as Western blotting, dot blotting, antibody microarrays, reverse lysate microarrays and epitope mapping for determination of where antibodies specifically bind their targets.

I have authored over 250 scientific publications in peer-reviewed journals and book chapters about cell communication systems important for cell survival and function and implicated in the pathology of

cancer, diabetes, neurological and immunology-related diseases. My accolades include the 1993 Martin F. Hoffman Award for Research at UBC, and the 1993 Merck Frosst Canada Prize from the Canadian Society of Biochemistry and Molecular Biology. I was the 2001 Distinguished Lecturer for the Faculty of Medicine at UBC for the Basic Sciences. I have served on grant review panels for the US National Institutes of Health, the Canadian Institutes for Health Research, the National Research Council of Canada, the Michael Smith Health Research Foundation, Genome Alberta, Genome Prairie, the Canadian National Cancer Institute, the Canadian Heart and Stroke Foundation and the American Heart Association, and I have acted as an external reviewer for 22 other agencies including the U.S. National Science Foundation and the Israel Science Foundation. I have also been an external reviewer for 28 different scientific journals, including those that are focused on immunology and vaccines.

I was the founder and president of Kinetek Pharmaceuticals Inc. from 1992 to 1998, and the founder, president and chief scientific officer of Kinexus Bioinformatics Corporation from 1999 to the present. Kinetek was engaged in the development of drugs that inhibit protein kinases, primarily for oncology application and diabetes. Kinexus has produced over 1,600 antibody products against cell regulatory proteins, and employs these antibodies in novel, immunology-based, high throughput methods such as antibody microarrays to monitor cell communication systems in biological specimens from over 2000 academic and industrial clients in over 35 countries over the last 22 years. These antibody products include those that specifically recognize parts of the Spike, Nucleocapsid, Membrane and other SARS-CoV-2 proteins encoded by the genome of this virus.

My expertise has been sought specifically with respect to understanding the immunological mechanisms by which a natural immune response is elicited by SARS-CoV-2, the causative agent of COVID-19, and the immunity afforded by the lipid nanoparticle Spike RNA- and adenovirus Spike DNA-based COVID-19 vaccines. This has been informed, in part, by clinical studies undertaken in the last three years at my company Kinexus in which we have investigated the nature and production of antibodies against the 28 different proteins that are encoded by the genome in the SARS-CoV-2 virus, by examination of blood samples from over 4500 participants from across Canada. In this independent ethics review board approved clinical study, I am the lead investigator, and I have been in direct communication with all of the participants. Some of our preliminary findings have already been published in *JCI Insights*, which is the flagship journal of the American Society for Clinical Investigation

in 2021.[1] Additional manuscripts that document our SARS-CoV-2 antibody testing study are currently in preparation, and we have recently completed a second antibody testing study to determine the extent of immunity against the Omicron variants and the duration effectiveness of the COVID-19 vaccines.

I have also been investigating the use of drugs to inhibit the replication of the SARS-CoV-2 virus in infected host cells. My expertise on enzymes known as protein kinases has permitted me to predict and then verify that compounds that inhibit a protein kinase known as GSK3-beta can block the production of the Spike of the virus, and assembly of SARS-CoV-2 virus particles. A provisional patent based on this work was filed with the University of British Columbia (UBC) and a manuscript that describes this work has been accepted for publication.[2] I have also spearheaded the development commercial antibodies against many of the SARS-CoV-2 proteins and verified their utility in another published scientific article in the peer-reviewed journal Microbial Factories.[3]

In addition to the direct study of the SARS-CoV-2 and immune responses to this virus in people, I am also a co-founder and vice president of the Canadian Covid Care Alliance (CCCA) and very active within this organization. Recently, the CCCA has been renamed the Canadian Citizens Care Alliance. The CCCA's membership include over 600 biomedical scientists, medical doctors and other health practitioners, and the CCCA examines the scientific literature and data from public health authorities to ascertain the threat of COVID-19 and the various strategies available to mitigate its effects. In my capacity as the co-chair of the Scientific and Medical Advisory Committee (SMAC) of the CCCA, I oversee the activities of a panel of 36 scientists and medical doctors that seeks to provide a scientific evidence-based and balanced, independent, but critical assessment of health care policies related to COVID-19. This Committee has met weekly over the last two years by Zoom, but typically has daily

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1 Majdoubi, A., Michalski, C., O'Connell, S.E., Dada, S., Narpala, S. *et al*. (2021) A majority of uninfected adults show pre-existing antibody reactivity against SARS-CoV-2. JCI Insight. 6(8): e14631. doi:10.1172/jci.insight.146316

2 Shapira, T., Rens, C., Pichler, V., Rees, W., Steiner, T., Jean, F., Winkler, D.F.H., Sarai, I., Pelech, S., Av-Gay, Y. (2022) Inhibition of glycogen synthase kinase-3-beta (GSK3β) blocks nucleocapsid phosphorylation and SARS-CoV-2 replication. Molecular Biomedicine. 3, 43. doi:10.1186/s43556-022-00111-1

3 McGuire, B.E., Mela, J.E., Thompson, V.C., Cucksey, L.R., Stevens, C.E., McWhinnie, R.L., Winkler, D.F.H., Pelech, S., Nano, F.E. (2022) *Escherichia coli* recombinant expression of SARS-CoV-2 protein fragments. Microbial Cell Factories. 21:21. doi:10.1186/s12934-022-01753-0. bioRxiv pre-print. doi:10.1101/2021.06.22.449540

correspondences by e-mails. The fruits of our efforts are published on the CCCA website (www.canadiancovidcarealliance.org) and in peer-reviewed scientific journals. In particular, I was a coauthor on a CCCA report that critiqued the original 6-months clinical study performed by Pfizer/BioNTech on their BNT162b2 RNA vaccine,[4] a published review about COVID-19 vaccines and pregnancy in the peer-reviewed journal *Vaccines*,[5] and another manuscript published in the peer-reviewed journal *International Journal of Vaccine Theory, Practice and Research*.[6] In addition, I am a coauthor on several other publications that have been posted on the CCCA website that relate to the manufacturing and quality issues associated with the BNT162b2 mRNA COVID-19 vaccine,[7] the efficacy and safety of the BNT162b2 mRNA COVID-19 vaccine based on Phase 3 trial results,[8] and the vaccination of children with COVID-19 vaccines.[9] I have been the Senior editor and author of a book about the science underlying the SARS-CoV-2 virus, COVID-19, vaccines, therapeutics and masks, which is currently in press.[10] I am also a Senior editor and author of a second book that examines Canada's

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4 Bridle, B.W., Martins, I., Mallard, B.A., Karrow, N.A., Speicher, D.J., Chaufan, C., Northey, J.G.B., Pelech, S., Shaw, C.A., Halgas, O. (2021) Concerns regarding the efficacy and safety for BNT162b2 mRNA coronavirus disease (COVID-19) vaccine through six months. www.CanadianCovidCareAlliance.org (January 10, 2022) 1-10 https://www.canadiancovidcarealliance.org/wp-content/uploads/2022/01/Final-CCCA-Critique-Thomas-COVID-19-Vaccines-6-months-NEJM-Jan-10-22.pdf

5 Karrow, N.A., Shandilya, U.K., Pelech, S., Wagter-Lesperance, L., McLeod, D., Bridle, B, Mallard, B.A. (2021) COVID-19 vaccination and potential impact on fetal and neonatal development. *Vaccines.* 2021, *9*, x. doi:10.3390/xxxxx

6 McLeod, D., Martins, I., Pelech, S., Beck, C., Shaw. C.A. (2022) Dispelling the myth of a pandemic of the unvaccinated. *Int. J. Vaccine Theory Practice Res.* 2(1):267-286.

7 Gutchi, M., Speicher, D. J., Natsheh, S., Oldfield, P., Britz-McKibbon, P., Palmer, M., Karrow, N., Massie, B., Mallard, B., Chan, G. Pelech, S. (2022) An independent analysis of the manufacturing and quality control issues of the BNT162b BioNTech/Pfizer vaccine identified by the European Medicine Agency. www.Canadian Covid Care Alliance.org (October 29, 2022) 1-5 https://www.canadiancovidcarealliance.org/wp-content/uploads/2022/11/22OC29_EMA-Analysis-of-BNT162b-Manufacture.pdf

8 Bridle, B.W., Martins, I., Mallard, B.A., Karrow, N.A., Speicher, D.J., Chaufan, C., Northey, J.G.B., Pelech, S., Shaw, C.A., Halgas, O. (2021) Concerns regarding the efficacy and safety for BNT162b2 mRNA coronavirus disease (COVID-19) vaccine through six months. www.CanadianCovidCareAlliance.org (January 10, 2022) 1-10 https://www.canadiancovidcarealliance.org/wp-content/uploads/2022/01/Final-CCCA-Critique-Thomas-COVID-19-Vaccines-6-months-NEJM-Jan-10-22.pdf

9 Payne, E., Rennebohm, R., Bridle, B., Mallard, B., Karrow, N., Massie, B., Northey, K., Shoemaker, C., Pelech, S., Chaufan C., McLeod, D., Hardie, J., Pinto, C., Britz-McKibbin, P., Shaw, C. (2022) Request to halt vaccinations of children. www.CanadianCovidCareAlliance.org (July 14, 2022) 1-28 https://www.canadiancovidcarealliance.org/wp-content/uploads/2022/07/CCCA-Halt-vaccination-of-children-Officials-Letter-Jul-14-22.pdf

10 Pelech, S. & Shaw, C.A. (ed.) (2024) Down the COVID-19 rabbit hole: Independent scientists and physicians unmask the pandemic. Skyhorse Publishing. (in press)

response to the COVID-19 pandemic.[11] These books have over 1700 primary citations.

I believe that my formal training, experience and published research, demonstrates my expertise in immunology, and my recent activities specifically related to SARS-CoV-2 over the last three years, places me in an excellent situation to comment upon related matters. Consequently, I have been sought as an Expert Witness for over a dozen court challenges with respect to government and private employer mandated vaccination and family disputes over the vaccination of children. In particular, I have been accepted as an expert witness and provided cross-examination in other disciplinary hearings with the British Columbia College of Physicians and Surgeons, the British Columbia College of Nurses and Midwives, and the College of Nurses in Ontario.

Part 2: The Efficacy and Safety of COVID-19 Vaccine Verses Natural Immunity

Table of Contents

[11] Pelech, S. & Shaw, C.A. (ed.) (2024) COVID-19 Pandemonium: A pandemic of ignorance, fear and greed. The capture of our institutions. (in preparation)

2.1. Summary Overview

The crux of the matter is whether the risks of no intervention and infection with the SARS-CoV-2 and subsequent acquisition of natural immune are greater than the risks posed by taking an experimental vaccine to prevent COVID-19. To answer this question, it is necessary to assess the risks of illness and death from COVID-19, and the efficacy and safety of COVID-19 genetic vaccines. As it turns out, the answer to this question is complicated, because the risks of severe COVID-19 and death are very dependent on age and the presence of co-morbidities as will be presented. The efficacy and safety of COVID-19 vaccines is also very dependent on their production and quality control.

In my learned opinion, the key questions and short answers are:

a. *Are COVID-19 vaccine experimental?* Yes. The underlying technology is novel and new information continued to be reported that documents unexpected issues with efficacy and safety in the scientific literature.

b. *Are the COVID-19 genetic vaccines effective in reducing infection and transmission of COVID-19, and reducing the incidence of severe COVID-19 and death?* These do not, beyond a short period of a few months, prevent infection with SARS-CoV-2, and those vaccinated individuals that get COVID-19 are just as infectious and likely to transmit the virus as non-vaccinated individuals. **There are no Phase 3 clinical studies that demonstrate severity and risk of death is lower in vaccinated individuals**. This is hard to evaluate, since most people have natural immunity and the virus has evolved through mutation to much more less virulent forms.

c. *Are there issues with the way COVID-19 genetic vaccines work that would lead to theoretical concerns?* Yes. There are four facts that together are extremely worrisome. 1) With COVID-19 vaccines, tens of trillions of lipid nanoparticles are injected in the deltoid muscle with each inoculation. 2) Around three-quarters of the lipid nanoparticles leave the site of injection and travel around the body within 2 days. 3) Uptake of the lipid nanoparticles is not directed and they can enter into any cell type. 4) In order to elicit an immune response, it is necessary for immune cells to attack, damage and potentially kill cells that expressed the Spike protein on their surface

after they have taken up the Spike RNA in the lipid nanoparticles. These inflammatory attacks may damage and weaken tissues and organs.

d. *Are there demonstrated adverse reactions to COVID-19 genetic vaccines in clinical studies and following post-marketing approval?* Yes. The original Phase 3 clinical trials, post-marketing data accumulated by Pfizer, and vaccine injury reports all demonstrate an unprecedented number of vaccine injury reports for COVID-19 vaccines.

e. *In particular, are there theoretical concerns or demonstrated evidence that COVID-19 vaccines may affect female fertility and the health of a developing fetus?* The ovaries are amongst the major organs to which the lipid nanoparticles are known to concentrate in. An inflammatory attack against the ovaries might damage oocytes in ovaries, and cause a reduction of their numbers. Changes in menstrual cycles in vaccinated women implicate disruption of the production of female hormones that control menstrual periods, which are produced in part by ovaries. While COVID-19 vaccination during the second and third trimesters of pregnancy do not appear to significantly affect birth weight and basic physiology of newborns, it is impossible to ascertain the long-term effects at this time. The effect of vaccination on fetus viability in the first trimester is also difficult to estimate due to a significant rate of miscarriages that occur independent of vaccination status.

f. *Are there greater risks of thrombosis, myocarditis and myopericarditis with COVID-19 vaccines than from SARS-CoV-2 infection, and is this serious?* For particularly males aged 12 to 29 years of age, there is an unacceptable high rate of myocarditis and myopericarditis, which can have persistent symptoms and be lethal. By contrast, in this demographic, the risk of myocarditis and myopericarditis from COVID-19 is 10- to 100-fold lower.

g. *Do vaccinated people present a health danger to unvaccinated people? Does vaccine shedding exist?* If COVID-19 vaccination with booster shots leads to immune tolerance, new strains of SARS-CoV-2 may evolve that could infect a person with natural immunity from a previous SARS-CoV-2 infection, as apparently did happen with the Omicron variants. The phenomenon of vaccine shedding remains mysterious, but might arising from shedding of SARS-CoV-2 virus, shedding of vaccine lipid nanoparticles, and/or shedding of exosomes that contain Spike RNA and/or Spike

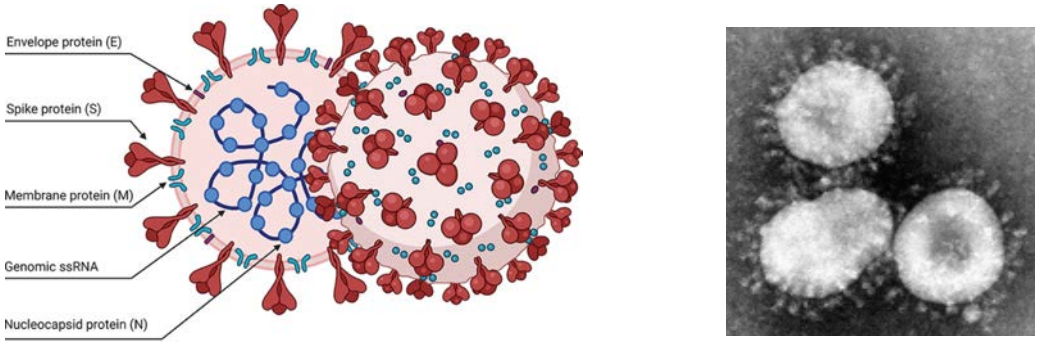
protein. At this time, I do not see this as a major risk for unvaccinated individuals, which are already likely to have effective natural immunity, and new variants of SARS-CoV-2 are relatively benign for the vast majority of people.

In the rest of Part 2, I will provide a sampling of the scientific data that supports my above conclusions. I will commence with a quick review of how natural immunity develops after infection with a virus.

2.2. *Comparison of Natural and COVID-19 Vaccine-induced Immunity*

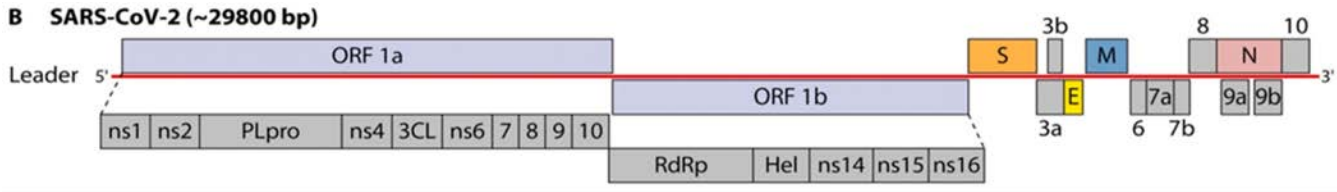
The SARS-CoV-2 virus as a small (~0.15 micron-wide) particle that features on its surface the Spike protein complex (a trimer), Membrane and Envelope proteins, and in its interior, Nucleocapid proteins that are bound to a single strand of sense-RNA. This RNA permits the product of all of these four proteins as well as at least 24 other non-structural (NSP) or ancillary proteins, which are required for replication of the virus in infected cells. The basic structure of SARS-CoV-2 virus is very similar to SARS-CoV-1, MERS and other coronaviruses, four of which cause a large portion of common colds. It gains entry into host cells by binding via the Spike protein to host proteins on the surface of cells, most notably angiotensin-converting enzyme 2 (ACE2) and neuropilin. The basic structure of the SARS-CoV-2 virus is shown in Figure 1. Figure 2 illustrates the arrangement of the viral genes in the SARS-CoV-2 virus genome. The Spike protein is the largest protein on the surface of the coronavirus, and accounts for their crown-like appearance in electron microscope-derived images.

Figure 1. Structure of the SARS-CoV-2 virus particle. Adapted from Fig. 1 of Pizzato *et al.* (2022).[16] Right panel shows an electron microscope image of the SARS-CoV-2 virus particle.



[16] Pizzato, M., Baraldi, C., Sopetto, G.B., Finozzi, D., Gentile, C., *et al.* (2022) SARS-CoV-2 and the host cell: A tale of interactions. Front. Virol. 1: 1-29. https://www.frontiersin.org/articles/10.3389/fviro.2021.815388/full

Figure 2. Location of protein-encoding genes in SARS-CoV-2 genome. Of particular relevance are the Spike (S), Membrane (M), Envelope (E) and Nucleocapsid (N) proteins. Adapted from Figure 2 of Tali *et al.* (2021).[17]



Antibodies are produced by immune B-cells in response to a natural infection with a respiratory virus like SARS-CoV-2. In particular, the virus enters the body through the mouth and nose (as well as eyes and ears) and infects cells of the nasopharyngeal cavity and lungs. Cells of the innate immune system, such as macrophages, neutrophils and dendritic cells engulf and then digest the virus particles with the production of pieces of the Spike, Membrane, Envelope and Nucleocapsid proteins. In addition, fragments of the other SARS-CoV-2 nonstructural and ancillary proteins may be produced from cells that are successfully infected by the virus, but undergo subsequent attacked by these innate immune cells as well as T-cells of the adaptive immune system. These viral protein fragments become complexed with immune cell proteins called major histocompatibility (MHC) antigens, where they are presented on the surfaces of macrophages, neutrophils and dendritic cells (antigen-presenting immune cells (APC)). When these migrating APC's encounter in the lymph nodes, T- and B-cells that happen to possess a high binding affinity for a fragment of a viral protein presented with an MHC antigen, they are stimulated to grow and divide into expanded colonies of identical cells. In the case of B-cells, they produce antibodies of the IgM and IgA classes primarily in the mouth and airways. Notably, these are secreted antibodies into the mucosa lining the airways. In the case of T-cells, these seeks out and destroy virus-infected cells that produce viral protein fragments that are complexed with MHC antigens. After the viral threat is mitigated, a portion of the B- and T-cells that are specific for recognizing the viral proteins are converted to memory or plasma cells. These adaptive immune cells are quickly reactivated should there be a reinfection at a later date. Memory and plasma B- and T-cells can remain viable for decades. As the natural immune response is directed against almost all of the

[17] Tali, S.H.S., LeBlanc, J.J., Sadiq, Z., Oyewunmi, O.D., Camargo, C. *et al.* (2021) Tools and techniques for severe acute respiratory Syndrome Coronavirus 2 (SARS-CoV-2)/COVID-19 detection. Clinical Microbiol. 34 (3): 1-63. doi:10.1128/cmr.00228-20

viral proteins in an infected person, it is able to efficiently deal with the original virus as well as highly related viruses that might be encountered at a later date.

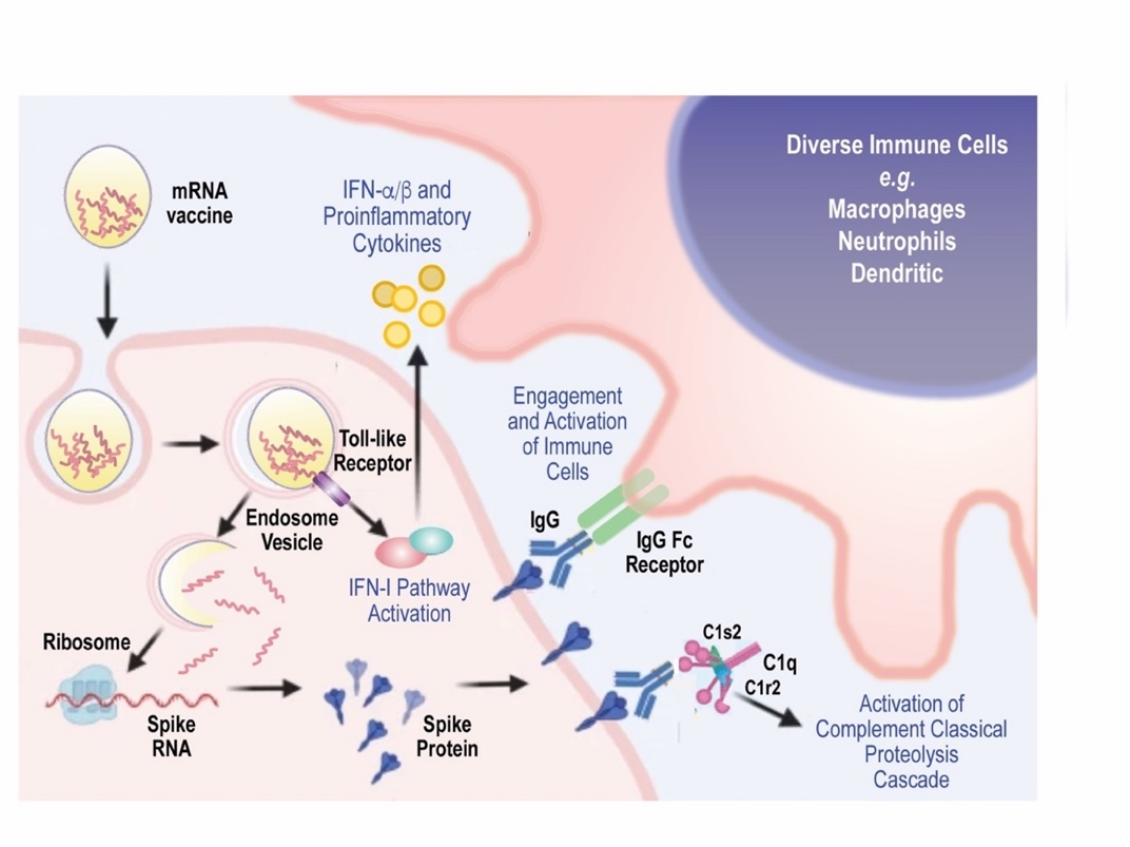
The mechanism by which immune protection is conferred by the COVID-19 genetic vaccines is very different from natural immunity, and unfortunately the mechanism is often misunderstood by those not very familiar with immunology. Likewise, the type of immune protection produced from these vaccines is also very different.

The COVID-19 vaccines mRNA are specifically for the Spike protein, and due to genetic manipulation, which includes N1-methypseudo-uridine substitution for uridine in the RNA, they are stable for weeks and even months as explained later. However, the main point here is that only a tiny portion of the lipid nanoparticles are directly taken up by antigen presenting cells, and the vast majority of the tens of trillions of lipid nanoparticles enter into other cells. Moreover, the main way the lipid nanoparticles would be taken up by macrophages would be via phagocytosis processes, which would be directed to the lysosomes of these cells, where they and their RNA content would be digested before the Spike mRNA can be translated into making Spike protein. For the small amount of the lipid nanoparticles that are able to deliver their mRNA cargo into the cytoplasm of the cell, it is feasible that the Spike mRNA can be used by the ribosomes to produce Spike protein, but this should be mostly directed into the luminal side of the endoplasmic reticulum. The upshot is this Spike protein is likely to be transported to the outer surface of the intact and remain anchored, but not bound up with MHC antigens. Figure 3 shows the scenario that is likely with any cell that takes up any COVID-19 vaccine lipid nanoparticles with RNA. The important lesson here is that in order to elicit an immune response, the recruited immune cells have to attacked, damage and, to an unclear extent, destroy the cells that present the foreign Spike protein on their surfaces. When small vesicular bits of cells known exosomes are produced during the immune cell attack, these can feature the Spike protein, and when taken up by phagocytosis by antigen-presenting cells, and can be partially digested, so that Spike fragments can be complexed with MHC antigens on their surface.

The presence of antibodies against the Spike protein produced from a previous infection of SARS-CoV-2 or related coronavirus will evoke an even stronger immune reaction against the vaccinated cells that took up the lipid nanoparticles and expressed the Spike protein. Those immune cells that were transfected with the lipid nanoparticles and produced Spike protein are more likely to be destroyed by

other immune cells, then to be able to act as antigen presenting cells to stimulate specific B- and T-cells for recognition of the Spike protein as an antigen.

Figure 3. Mechanisms of RNA vaccine action. Toll-like receptors (TLR) sense non-natural lipids present in the lipid nanoparticles and induce the release of cytokines that recruit immune cells to the site of the transfected host cell. Existing anti-Spike antibodies may react with the produced Spike protein that is expressed on the surface of the lipid nanoparticle-transfected host cell. Innate immune cells that express a receptor (IgG Fc receptor) that recognize the common portion (Fc) of the IgG class antibodies allows the immune cells to attach and attack the transfected host cell, and generate small pieces of the host cell called exosomes. These exosomes are coated by Spike protein (along with other host cell proteins), and are engulfed and digested by the innate immune cells. Exosomes are a known result of transfection with gene therapy products and are normally assessed for potential excretion into the environment under gene therapy regulations. Fragments of the Spike protein that are generated in the innate immune cells are presented with major histocompatibility antigens (MHCs) by these cells to T-cells and B-cells in lymph nodes and other locations where these adaptive immune cells reside. In addition, antibody-bound Spike proteins on host cells recruit the activation of proteins of the Complement system, leading to formation of holes and destruction of the host cell.



As the COVID-19 vaccines are injected into the upper arm into the deltoid muscle, the immune response is mediated in the blood circulation. The primary antibody response is the production of IgG

class antibodies, primarily of the IgG1 and IgG3 types, which are very proinflammatory. These are very high affinity and durable antibodies (typically lasting for about 3 weeks) before they are replaced by the production of more antibodies from B-cells if the need persists for more to fight an infection. However, these antibodies (described as bivalent) are not as effective as IgA and IgM secreted antibodies (described as multivalent), which are much more efficient for binding up virus particles. Furthermore, unlike IgA and IgM antibodies, the amounts of IgG antibodies are very low in the nasopharyngeal captivity and the upper lungs. With repeated boosting the COVID-19 vaccines, there is also the switching of the IgG antibodies to the IgG2 and IgG4 types, which are much less efficient than the IgG1 and IgG3 antibody types, which facilitates the development of immune tolerance, i.e., the immune system down-regulates its response to a foreign antigen that appears to be a common part of the environment or human body. Finally, because the immune response is directed against only one of the SARS-CoV-2 proteins, which has an appreciable rate of mutation, the antibody and T-cell responses are much more restricted than the natural immunity response to the whole virus.

2.3. Historical Vaccine Development

The body has evolved a highly sophisticated and effective immune system that learns to recognize and specifically counteract novel infectious pathogens. In particular, the adaptive immune system relies on the combined actions of B-cells that produce specific antibodies and T-cells that attack pathogen-infected cells. Such recognition depends on the ability of these lymphocytes to target tiny portions of a pathogen called epitopes. Some parts of a pathogen are very immunogenic, *i.e.,* elicit a strong immune response, whereas other portions are ignored by the immune system. Infectious pathogens such as viruses, bacteria, and fungi are constantly evolving, and previous exposure to an earlier version of the pathogen can provide immune protection against future infections, including other highly related pathogens.

The development of vaccines goes back over two hundred years ago, when English physician and scientist Edward Jenner developed the first smallpox vaccine from preparations of cowpox in 1796.[18] There the introduction of a related or less virulent form of an infectious pathogen became a standard way of conferring resistance to future infections with deadly pathogens. Before there were methods

[18] (2023) About Edward Jenner. The Jenner Institute. Retrieved from https://www.jenner.ac.uk/about/edward-jenner#

to artificially produce the proteins of these pathogens for direct injection into vaccine recipients, the use of weakened, attenuated strains elicited an immune response with much lower risks of severe disease.

Heat or chemical inactivated preparations of a pathogen may be used for such vaccines, but this has the disadvantage that the level of pathogen is restricted to what was injected. With a live pathogen that has retained its ability to multiple, ideally very slowly to give the immune system time to develop counter-defenses before the pathogen can do too much damage, stronger immunity can be achieved. This is why traditional vaccines have typically used inoculants that have from a few dozen copies to thousands of copies of a particular pathogen.

With the advent of recombinant DNA technology in the 1970's, it became feasible to isolate the genes that encoded the proteins of pathogens and start to produce them in larger quantities in bacteria like *Escherichia coli* (*E. coli*) and later eukaryotic cells such as the popular Sf9 (*Spodoptera frugiperda*) caterpillar cells, human embryonic kidney cells (*e.g.,* HEK-293 cells), or yeast (*e.g.,* budding yeast *Saccharomyces cerevisiae*). Injection of purified preparations of these recombinantly produced pathogen proteins or short artificial pieces of these proteins created by chemical synthesis in the laboratory, provided for large quantities of antigens that could be injected into animals to induce antibody production against the foreign proteins. However, the immune response would be focused on the specific proteins that were inoculated into the animals and not the whole pathogen, which results in a narrower degree of immune protection. Nevertheless, a polyclonal antibody response would be induced, because a population of different B-cells would be stimulated to produce different antibodies against different parts (*i.e.,* epitopes) of an injected protein or peptide fragment. Incidentally, preparations of monoclonal antibodies can be developed by creation of hybridoma cells where an antibody producing B-cell is fused with a cancer cell, isolated and then repeatedly propagated to give rise to a pure population of identical cells that generate exactly the same antibody specific for a single epitope. Such monoclonal antibodies can be effective therapeutics when they target specific oncoproteins on cancer cells or proteins on the surface of pathogens.

2.4. COVID-19 Vaccine Development

Over 200 COVID-19 vaccines have been in development, with over 71 in Phase 3 trials, and at least 38 approved.[194] The Chinese Sinovac (CoronaVac) and Sinopharm vaccines, which use inactivated whole SARS-CoV-2 virus for injection, are essentially traditional vaccines. However, most of the COVID-19 vaccines used in North America and Europe exclusively target the Spike protein of the SARS-CoV-2 virus as the sole antigen to evoke an immune response to achieve immunity. In these latter vaccines, either the inoculation features the Spike protein or it contains messenger-RNA (mRNA) or DNA to instruct infected cells to manufacture the viral protein inside of the cells of the vaccine recipient. The Novavax's Nuvaxovid (also known as Covovax) and Medicago's Corifenz vaccines are protein subunit vaccines that use recombinant purified Spike protein as the antigen. Such preparations of Spike protein may be about 95% pure, as achieved with the histidine-tagged Spike protein in the Novavax product (the other 5% are Sf9 insect proteins). It is possible that the contaminating proteins can also elicit an immune response. All of the aforementioned COVID-19 vaccines have tended to offer poorer initial efficacy for production of anti-Spike protein antibodies than achieved with COVID-19 genetic vaccines.[4] This is likely due to the inability of these vaccines to generate as high levels of the antigens as possible with the lipid nanoparticle (LPN)/mRNA or adenovirus/DNA-based vaccines.

The Russian Sputnik V COVID-19 vaccine, AstraZeneca's Vaxzevria, and Janssen's Jcovden (Johnson & Johnson) vaccines, are adenovirus preparations that contain Spike DNA, which provides for Spike messenger-RNA production to then permit biosynthesis of the Spike protein. They use modified adenoviruses to deliver the DNA for the Spike protein into infected cells. Adenoviruses can cause colds and even cancer, but the versions used as delivery vehicles are genetically engineered so as not to replicate and not to cause cancer by removal of viral genes that are necessary for these outcomes.[19] A significant advantage of these adenovirus-based vaccines is that the DNA is fairly stable, and multiple copies of RNA can be produced from each Spike DNA molecule. Multiple copies of each Spike protein can then be generated from a single Spike mRNA molecule. However, the mRNA that is produced is very labile, and the production of Spike protein from that mRNA is presumed to be transient. Moreover,

[19] Khoshnood, S., Ghanavati, R., Shirani, M., Ghahramanpour, H., Sholeh, M., *et al.* (2022) Viral vector and nucleic acid vaccines against COVID-19: A narrative review. Front Microbiol. 13:984536. doi:10.3389/fmicb.2022.984536

there still remains the chance of integration of the DNA into the host cell genome, which is an alternative mechanism by which cells can become cancerous if the integration is near cancer-related genes (known as proto-oncogenes or tumor suppressor protein genes) in the genome. The risk for this may be low, and such cells are likely destroyed by the immune system. Another disadvantage of this type of vaccine is that the immune system also learns to recognize the adenovirus vector with its own viral proteins. Consequently, a different strain of the delivery adenovirus may be required for booster shots, since the immune system can produce antibodies that may inactivate the ability of the adenovirus to enter into cells or facilitate the adenovirus's removal by innate immune cells. This may be alleviated by inoculation of the delivery adenovirus through the mucosal route, either in the airway or by intrarectal administration.

Pfizer-BioNTech's BNT162b2 (later named Comirnaty) and Moderna's mRNA-1273 (later named Spikevax) are mRNA-containing vaccines that deliver a genetically modified mRNA (modRNA) gene for production of the Spike protein. These modifications permit high stability of the mRNA through the incorporation of non-natural nucleotides (*i.e.,* N1-methyl pseudouridine for uridine) and an altered nucleic acid sequence, particularly to increase the nucleotide base content in the RNA for more cytidine and guanidine nucleotides. Cytidine and guanidine nucleotides pairs with greater affinity for each other than does adenine and uracil (or N1-methyl pseudouridine) pairs in double-stranded nucleic acids. Higher cytidine and guanidine nucleotides can improve the stability of the RNA. Despite the different RNA sequence from the original Spike gene, the resultant Spike protein should be identical due to the redundancy of the genetic code.

The genetic COVID-19 vaccines work to produce an immune response through very different mechanisms of action from traditional vaccines, and while there is overlap in many of the intervening steps, the differences have profound implications for the efficacy and safety of these products. As outlined in Section 2.2, in the case of the traditional COVID-19 vaccines, innate immune cells directly consume and digest the Spike protein, and then present pieces to T-cells and antibody producing B-cells. By contrast, the COVID-19 genetic vaccines penetrate into normal body cells, which produce and then present the Spike proteins on their surfaces. Then the immune cells attack and damage the Spike protein-producing cells. The debris produced from the damaged or destroyed cells, known as exosomes, are then engulfed by immune cells and degraded into pieces of the Spike protein, which are

complexed on their surfaces with MHC antigens for presentation to T-cells and B-cells. These immune cells are located in lymph nodes and the spleen. Memory B-cells are also widely distributed in the bone marrow, Peyers' patches, gingiva (gums), mucosal epithelium of tonsils, the lamina propria of the gastro-intestinal tract, and in the circulation.

In the typical descriptions of how the COVID-19 genetic vaccines work, it has been suggested that the lipid nanoparticles or adenovirus in these vaccines are directly taken up by host innate immune cells such as dendritic cells and macrophages. However, as the LPNs used in the Pfizer/BioNTech and Moderna RNA vaccines have no targeting proteins on their surface, they will fuse with any cell membrane that they encounter. Likewise, the adenovirus-based COVID-19 vaccines can bind to a wide variety of different cell surface receptors to gain entry into diverse cell types. Only a very tiny portion of the LPNs or adenoviruses in the COVID-19 vaccines would be expected to end up in immune cells directly. The more likely scenario is presented in Figure 3., where almost any cell could be penetrated by an LPN or adenovirus. It should be appreciated that pre-existing antibodies to the Spike proteins of other coronaviruses or anti-Spike antibodies generated from the first inoculation with a COVID-19 vaccine will elicit a more powerful inflammatory and destructive response with booster injections, unless the mechanisms of immune tolerance are induced.

2.5. COVID-19 Genetic Vaccines Production

Large scale production of vaccines comes with major challenges to ensure consistency in the final product to maintain batch stability, efficacy and safety. Since the Pfizer/BioNTech COVID-19 vaccine is the most commonly used vaccine in Canada and the US, the next few subsections provide a summary of the main findings of a more detailed technical assessment concerning the development and manufacturing of BNT162b.[20] A number of deficiencies in the product's development were identified by regulatory agencies and appear to have either been ignored or glossed over. Substantial differences in Pfizer's manufacturing (Process 1 versus Process 2) led to worrisome quality differences between the clinical trials (manufactured with Process 1) and what most people received in the commercial rollout of the Pfizer vaccine (manufactured with Process 2). Vaccine approval for the declared COVID-19 pandemic was given ‘fast-track ’conditional approval to address ‘‘*a seriously debilitating, rare or*

[20] Gutschi, LM. (2022) Quality issues with mRNA Covid vaccine production. Bitchute. Retrieved from https://www.bitchute.com/video/muB0nrznCAC4/

life-threatening disease devoid of a viable treatment" and approval was granted on the condition that additional information would be forthcoming after the vaccine was rolled out. Much of these data have not been fully provided to date.

Data for the following portion of this section was primarily obtained from the European Medicines Agency European Public Assessment Report (EPAR) for the BioNTech/Pfizer vaccine.[21] Additional information was obtained through email leaks from December, 2020 that were released to journalists and to the *British Medical Journal*.[22, 23] It should be appreciated that the information provided to the EMA by Pfizer was very similar to what was provided to other health regulatory agencies, including Health Canada and the US FDA.

As mentioned earlier, traditional vaccines contain a known amount of the target antigens found in attenuated or dead versions of pathogens or proteins derived from them to evoke an immune response. They do not require a person's cells to manufacture and present them on their membrane surface at an uncontrolled rate and level. It is this very difference that has been overlooked when assessing the safety, dosage, and pharmacokinetics of BNT162b2 (Pfizer-BioNTech mRNA vaccine) and its by-products, including the mRNA-encoded Spike protein. Therefore, BNT162b2 and the other COVID-19 genetic vaccines are not like any other vaccine that has ever been used successfully in the past as the innate immune response is initially targeted directly against one's own cells rather than against the invading pathogen. Unlike traditional vaccines, in which the formulation contains a known concentration of viral antigen, BNT162b2 does not contain the viral antigen that triggers the immune response. Instead, the mRNA directs the body's cells to manufacture the viral spike protein *in vivo* at levels that may vary over 100-fold or more amongst vaccinees, and it is that very difference that has been overlooked when assessing the safety and pharmacokinetics of BNT162b2 and its components and derivatives. Individuals produce variable amounts of Spike protein due to their genetics, age, hormonal, and nutritional status, which batch of vaccine they receive, and so on. Therefore, since the

[21] (2020) Comirnaty European Public Assessment Report. Dec. 21, 2020. European Medicines Agency. Retrieved from https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf

[22] Tinari, S. (2021) The EMA COVID-19 data leak, and what it tells us about mRNA instability. BMJ. 372:n627. doi:10.1136/bmj.n627

[23] (2021) Rappaport Rolling Review Report overview LoQ-COVID-19 mRNA vaccine BioNTec, 2020. COVID Truths. Retrieved from https://www.covidtruths.co.uk/2021/04/ema-leaked-papers/

Spike protein is not part of the BNT162b2 formulation but is in fact the active component of the vaccine, *i.e.*, the actual immunogen, it should have been assessed as a gene therapy product.

2.5.1. Are modRNA Product Vaccines or Gene Therapies?

One might have thought *a priori* that mRNA vaccines would be regulated as gene therapy products to which they objectively correspond to. This would require even more testing than traditional vaccines or even drug. When injecting nucleic acids including mRNA, there are potential safety concerns specific to gene therapy products, such as genomic effects or immunological responses that may require additional regulatory assessment of safety risks for these products. However, nucleic acid vaccines have been subject to complex, contradictory and unclear regulatory guidance such that no specific regulatory guidance for these products were available at the time the mRNA vaccines received their Interim Order from the Minister of Health in Canada on December 9, 2020.[24]

Of note, BioNTech and Moderna originally expected to see their products regulated as gene therapies. For example, Moderna's statement in their second quarter 2020 Securities and Exchange Commission (SEC) filing *"Currently, mRNA is considered a gene therapy product by the FDA"* is all the more curious given that Moderna had likely already filed an IND (Investigational New Drug) application to FDA to begin clinical trials.[25] The genome sequence for the SARS-CoV-2 virus only become available in mid-January 2020 a few months before.

In 2008, the EMA amended its definition of gene therapy products to state, *"Gene therapy medicinal products (GTMPs) shall not include vaccines against infectious diseases."* As a result, the non-clinical requirements and controls as described in the EMA's Guidance for GTMPs would no longer apply, but no rationale was provided for this amendment. These controls include studies on biodistribution, dose response, potential targets of toxicity, identification of the target organ for biological activity, potential of integration into the genome and transmission in the germ line, toxicity related to the expression of

[24] (2020) Media Advisory. Health Canada authorizes first COVID-19 vaccine. Government of Canada. Retrieved from https://www.canada.ca/en/health-canada/news/2020/12/health-canada-authorizes-first-covid-19-vaccine.html

[25] (2020) Moderna. Quarterly Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Moderna, Ed.; Securities and Exchange Commission. Retrieved from https://www.sec.gov/Archives/edgar/data/1682852/000168285220000017/mrna-20200630.htm

structurally altered proteins, reproductive toxicity, tumorigenicity, repeated dose toxicity, and excretion into the environment.[2611]

Similarly, in 2013, the FDA guidance on gene therapy products, without explanation, excluded from its scope vaccines for infectious disease:

> *"This guidance does not apply to therapeutic vaccines for infectious disease indications that are typically reviewed in CBER/Office of Vaccines Research and Review (OVRR)."*[27] [12]

This exclusion serves only regulatory purposes. It does not change the US FDA biological definition of gene therapy products which remains as:

> *"Gene therapy products are all products that mediate their effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and that are administered as nucleic acids, viruses, or genetically engineered microorganisms."*[28]

It is the 2005 WHO Guidelines that grants nucleic acid vaccines, including mRNA vaccines, the status of a vaccine: antigens produced *in vivo* in the vaccinated host following administration of a live vector such as an adenovirus or nucleic acid or antigens produced by chemical synthesis *in vitro* and must comply with this international regulation concerning Good Manufacturing Practices (GMP), including demonstration of the purity and quality of the starting material.[29] The WHO Expert Committee on Biological Standardization provided Guidelines specifically for mRNA vaccines in April 2022, updated

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[26] (2008) Guideline on the non-clinical studies required before first clinical use of gene therapy medicines. CHMP, Ed. European Medicines Agency. Vol. EMEA/CHMP/GTWP/125459/2006. Retrieved from https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-non-clinical-studies-required-first-clinical-use-gene-therapy-medicinal-products_en.pdf

[27] (2013) Preclinical assessment of investigational cellular and gene therapy products. CBER, Ed.; U.S. Federal Drug Administration. Vol. FDA-2012-D-1038. Retrieved from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/preclinical-assessment-investigational-cellular-and-gene-therapy-products

[28] (2015) Design and analysis of shedding studies for virus or bacteria-based gene therapy and oncolytic products. Research, C. f. B. E. a., Ed. US Federal Drug Administration. Retrieved from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/design-and-analysis-shedding-studies-virus-or-bacteria-based-gene-therapy-and-oncolytic-products

[29] (2005) WHO guidelines on non-clinical evaluation of vaccines TRS No 927. World Health Organization. Vol. Annex 1. Retrieved from https://www.who.int/publications/m/item/nonclinical-evaluation-of-vaccines-annex-1-trs-no-927

from the draft guidance document of 2020.[30] These advisory guidelines updated the information and regulatory considerations for modRNA and self-amplifying mRNA vaccine products, addressed development, manufacturing and control of the vaccine, and clarified the requirements for non-clinical evaluation. However, modRNA vaccines remain regulated as vaccine products and not as gene therapy products.

2.5.2. Long-Term Follow-up After Administration of Gene Therapy Products

Despite the exclusion of vaccines from gene therapy guidance, the US FDA has active programs in infectious diseases within its Office of Tissues and Advanced Therapies including laboratory research on replication deficient (adenovirus) and replication competent viral vector (measles, vaccinia).[31] Health Canada does not have specific guidelines or regulations relating to gene therapies; these products are regarded as biological drugs as are vaccines.[32] However, the US FDA provides guidance on the long-term follow-up of gene therapy products, such as viral vectors, which requires the manufacturers to systematically record delayed adverse events.[33] Specifically, the emergence of new clinical conditions such as "*a new malignancy, new incidence or exacerbation of a pre-existing neurological disorder, a new incidence or exacerbation of a prior rheumatological or autoimmune disorder, a new incidence of a hematological disorder and new infections especially those potentially product-related*", are to be recorded annually for a minimum of 5 years, followed by up to 10 years of observation. However, these requirements are not imposed on biological or nucleic acid products reviewed under vaccine guidance.

[30] (2022) Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: Regulatory considerations. World Health Organization. Annex 3, TRS No 1039, WHO, Ed. Retrieved from https://www.who.int/publications/m/item/annex-3-mRNA-vaccines-trs-no-1039

[31] Oh, S.S. (2022) Cellular, Tissue, and Gene Therapy Advisory Committee Meeting. Review of Intramural Research Program – Gene Transfer and Immunogenicity Branch, March 10, 2022. US Food and Drug Administration. Retrieved from https://www.fda.gov/media/156771/download

[32] Viswanathan, S., Bubela, T. (2015) Current practices and reform proposals for the regulation of advanced medicinal products in Canada. Regen Med. 10(5):647–663. doi:10.2217/rme.15.28

[33] (2020) Long term follow-up after administration of human gene therapy products: Guidance for industry. Retrieved from https://www.fda.gov/media/113768/download

Questions remain regarding the regulatory approval process for mRNA vaccines, specifically those regarding the pharmacological, pharmacodynamic characteristics and safety risks unique to nucleic acid medicinal products, which are further reviewed by Banoun (2023).[34]

2.5.3. Manufacturing and Quality

Chemistry, Manufacturing and Control (CMC) are processes to ensure that quality manufacturing standards have been established for the finished product. This is to ensure consistency in identity, safety, quality, stability and strength between the product used in the clinical trials and individual lots produced for commercial purposes. For modRNA commercial vaccines this would include creation of master and working cell banks, test method development and stability testing, process development, qualification and validations as well as quality assurance processes and techniques.[35] However, the modRNA platform was a novel manufacturing platform requiring novel control and analytical technology and thus knowledge from prior platforms for similar products/vaccines were limited and could not be leveraged for quality control.

2.5.4. BNT162b2 modRNA Structure

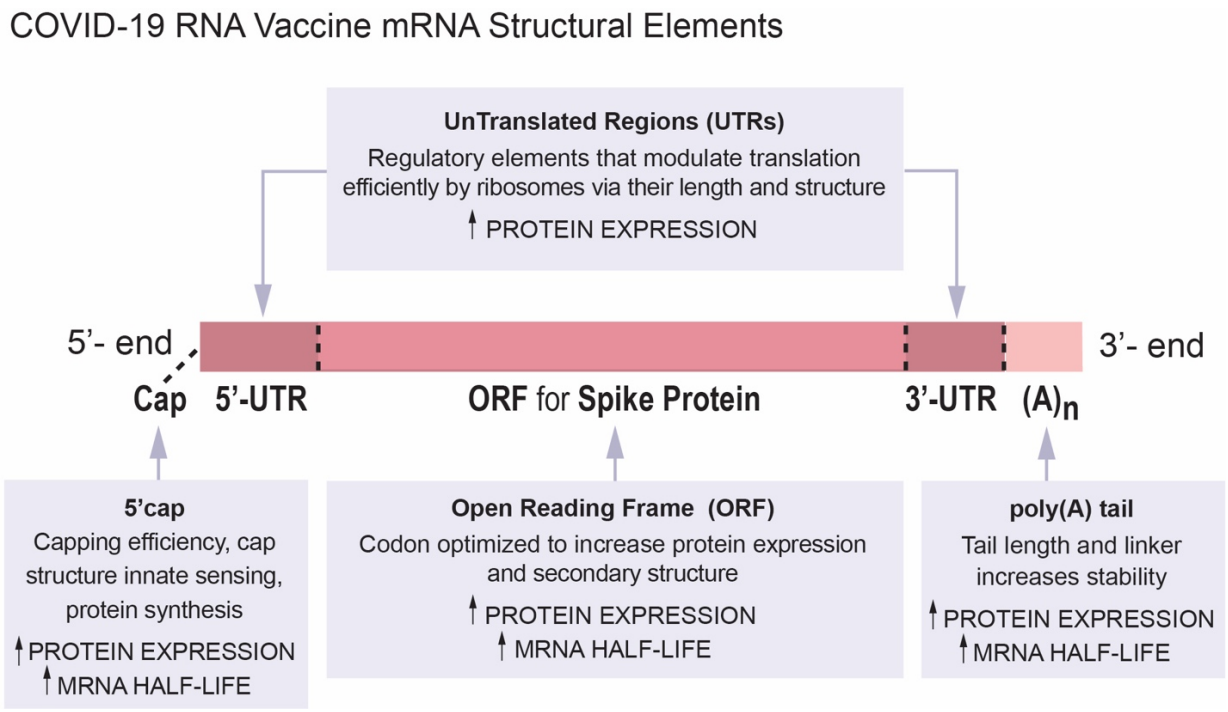
In the Pfizer/BioNTech vaccine, the modRNA has been altered from the mRNA sequence of the Spike protein of the SARS-CoV-2 coronavirus by: (a) including mutations to replace two adjacent lysine and valine amino acids with two prolines instead, to ensure an antigenically optimal pre-fusion conformation and reduced the risk of any released Spike protein entering into other cells; (b) replacing all uridine bases with N1-methylpseudouridine to evade defenses against foreign RNA;[35] (c) including human-derived 5' and 3' UTRs (untranslated regions) and a poly-adenine (A) tail with a 30A segment, a linker, and a 70A segment, to enhance translation; and (d) optimizing codon use by selecting synonymous codons that will optimize expression (*i.e.,* replacement of adenine and thymidine nucleotide bases with cytidine and guanidine nucleotide bases in the RNA, while still retaining the final

[34] Banoun, H. (2023) mRNA: Vaccine or gene therapy? The safety regulatory issues. Int J Mol Sci. 24(13):10514. doi:10.3390/ijms241310514

[35] Whitley, J., Zwolinski, C., Denis, C., Maughan, M., Hayles, L., *et al.* (2022) Development of mRNA manufacturing for vaccines and therapeutics: mRNA platform requirements and development of a scalable production process to support early phase clinical trials. Transl Res. 242:38-55. doi:10.1016/j.trsl.2021.11.009

Spike protein amino acid sequence) (Figure 4). The design of the sequence was facilitated by *in silico* methods. Since this mRNA is bioengineered, its non-proprietary name is tozinameran, and Comirnaty is the proprietary name for the Pfizer/BioNTech product. BNT162b2 was the laboratory identifier used to describe the modRNA during its development and testing.

Figure 4. mRNA structural elements that control the structure and stability of mRNA and the protein product.[35] In the cases of the Pfizer/BioNTech and Moderna COVID-19 mRNA vaccines, codon optimization involves use of codon triplicates that favor use of guanidine and cytidine nucleotide bases (but still specify the correct amino acids), replacement of uridine bases with 1-N-methyl-pseudouridine (m1Ψ), and the mutation of Lysine-986 and Valine-987 to Proline-986 and Proline-987, which inhibits the fusion of the resultant Spike protein with membranes following engagement with host cell receptors.



In a seminal article written in 2014 by BioNTech founders Drs. Ugur Sahin and Özlem Türeci, along with Dr. Katalin Karikó, they noted that *in vitro* transcribed mRNA represents a new class of drugs to deliver genetic information into cells.[36] The complex pharmacology of mRNA and issues with delivery to achieve sufficient levels of encoded protein and to reach a high number of cells were discussed. Safety considerations of mRNA-mediated activation of immune mechanisms, potential mitochondrial

[36] Sahin, U., Karikó, K., Türeci, Ö. (2014) mRNA-based therapeutics – developing a new class of drugs. Nat Rev Drug Discov. 13(10):759–780. doi:10.1038/nrd4278

toxicities associated with non-natural nucleotides and prolonged treatment, dosing, and tissue targeting were also identified. Many of these issues remain unsolved, which exemplifies their experimental nature even today.

2.5.5. modRNA Effects in Human Cells

While this genetic engineering of the viral mRNA results in high levels of Spike protein production, it is now known that this modRNA can persist for days, weeks and possibly months in humans,[37] as can the Spike protein itself.[38]

The genetic engineering of the mRNA may result in aberrant protein production. The various modifications made to the mRNA may be prone to errors when translated in cells and this may generate variations in the resulting Spike proteins when compared to the Wuhan Spike protein. For instance, differences in folding of the Spike protein[39] and generation of other antibodies with unknown effects may occur.[40] Abnormal Spike protein and fragments following vaccination have been documented.[41, 42] Interestingly, when the BNT162b2 was used to transfect cells in culture, the resultant Spike protein was observed to be larger than predicted by its amino acid sequence, and this was assumed to be due to the attachment of complex polymers of sugar molecules (*i.e*., glycosylation) of the protein, but never confirmed experimentally. This was originally flagged by the EMA as one of its initial concerns and

[37] Röltgen, K., Nielsen, S., Silva, O., Younes, S.F., Zaslavasky, M., *et al.* (2022) Immune imprinting, breadth of variant recognition, and germinal center response in human SARS-CoV-2 infection and vaccination. Cell. 185(6):1025–1040.e14. doi:10.1016/j.cell.2022.01.018

[38] Bansal, S., Perincheri, S., Fleming, T., Poulson, C., Tiffany, B., *et al.* (2021) Cutting edge: Circulating exosomes with COVID spike protein are induced by BNT162b2 (Pfizer-BioNTech) vaccination prior to development of antibodies: A novel mechanism for immune activation by mRNA vaccines. J Immunol. 207(10):2405–2410. doi:10.4049/jimmunol.2100637

[39] McKernan, K., Kyriakopoulos, A.M., McCullough, P. (2021) Differences in vaccine and SARS-CoV2 replication derived mRNA. Implications for cell biology and future diseases. OSF Preprints. doi:10.31219/osf.io/bcsa6

[40] Seneff, S., Nigh, G., Kyriakopoulos, A.M., McCullough, P. (2022) Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and microRNAs. Food Chem Toxicol. 164:113008. doi:10.1016/j.fct.2022.113008

[41] Patterson, B.K., Francisco, E.B., Yogendra, R., Long, E., Pise, A., *et al.* (2022) SARS-CoV-2 S1 protein persistence in SARS-CoV-2 negative post-vaccination individuals with Long Covid/PASC-like symptoms. Research Square (Preprint). Retrieved from https://www.researchsquare.com/article/rs-1844677/latest

[42] Magen, E., Mukherjee, S., Bhattacharya, M., Detroja, R., Merzon, E., *et al.* (2022) Clinical and molecular characterization of a rare case of BNT162b2 mRNA COVID-19 vaccine associated myositis. Vaccines (Basel). 10(7):1135. doi:10.3390/vaccines10071135

assigned as Specific Obligation-1 (SO1) for Pfizer to address.[21] As it stands, it is still unclear if these mutant Spike proteins may be associated with unwanted and adverse events as has been demonstrated with other codon-optimized proteins.

The exact features of the Spike protein produced by the synthetic mRNA are unclear, especially with the bivalent Wuhan/Omicron BA.4/5 and the latest monovalent XBB1.5 COVID-19 vaccines. It is not known how the Spike protein translated from the modified mRNA fully compares to the original Wuhan virus version. It is assumed the genetic engineering of the nucleotide sequence as undertaken with the COVID-19 vaccines would not alter the Spike protein amino acid sequence. However, depending where the Spike protein is produced, this alone might give rise to different glycosylation compositions in this highly sugar-coated protein.

There is a lack of clarity regarding the Spike protein characterization despite several requests for such data from the EMA. A full comparison of the Spike protein made by the mRNA in the vaccine to the natural virus has not been performed to date. Although the amino acid sequence of the Spike protein produced by the engineered mRNA in the COVID-19 vaccines is currently unknown, thousands of distinct gene sequences for the Spike protein are publicly available from direct gene sequencing of the SARS-CoV-2 virus and its variants. These concerns are further compounded for the 'bivalent' modified mRNA injectable formulations released in the Fall 2022 that encoded two distinct Spike proteins, namely the original ancestral Wuhan strain and a combination of BA.4/BA.5 Omicron sub-variants. This allowed for formation of unnatural trimeric complexes with novel mixes of Spike proteins from both versions of the SARS-CoV-2 virus.

On December 6, 2021, at a meeting held by WHO,[43] vaccinologist Professor Florian Kramer anticipated heterotrimer formation with bivalent vaccines, questioning if this could "lead to problems in protein folding?"[44] Presumably this concern was raised because protein folding differences could alter the

[43] (2021) WHO consultation on COVID-19 vaccine research: How can vaccine research further contribute to achieve the control of the pandemic everywhere? World Health Organization. Retrieved from https://www.who.int/news-room/events/detail/2021/12/06/default-calendar/who-consultation-on-covid-19-vaccines-research-how-can-vaccine-research-further-contribute-to-achieve-the-control-of-the-pandemic-everywhere

[44] Krammeer, F. (2021) Challenges to develop and assess variant-specific vaccines. Cdn.who.int. Retrieved from https://cdn.who.int/media/docs/default-source/blue-print/florian-krammer_3_anticipated-challenges_vrconsultation_6.12.2021.pdf

safety and efficacy profile of the vaccine. However, if heterotrimer formation leads to an improved immunological response as Moderna claimed in its submission to the FDA at the CDC meeting on September 1, 2022,[45] it is reasonable to ask if there are also different toxicological or immunological responses that are currently unknown. This issue is less problematic with the more recently released monovalent COVID-19 vaccine with only the XBB.1.5 Omicron subvariant.

2.5.6. modRNA Production: Process 1 vs Process 2

The manufacturing process of the modRNA was changed substantially for the commercial scale-up lots (Process 2) from the pilot-scale process used to produce the BNT162b2 vaccine candidate for the clinical trials (Process 1). This had implications for GMP, risked Marketing Authorization, and has implications clinically.

The modRNA drug substance in BNT162b2 is produced by *in vitro* transcription from a DNA template. The DNA template defines the sequence of the modRNA, but it is not supposed to be part of the final pro-vaccine product.

Process 1 was used to produce modRNA evaluated in the clinical trials. Using a cell free method, linear DNA was amplified using the polymerase chain reaction. This results in a linear template including the open reading frame (ORF) for the S1/S2 protein, and the 3' and 5' UTRs. The 5-prime cap was added enzymatically as was the poly(A) tail.[46] However, this technique does not produce sufficient modRNA for commercialization for billions of doses in the time frame and fidelity required as is possible from a plasmid DNA.[47]

Process 2 was used for commercial scale production of BNT162b2 vaccine. Using genetic engineering techniques, DNA containing a Kozak sequence (for direct binding of translated RNA to ribosomes), untranslated regions (UTRs), viral Spike protein sequence, and a poly(A) tail (to protect the translated

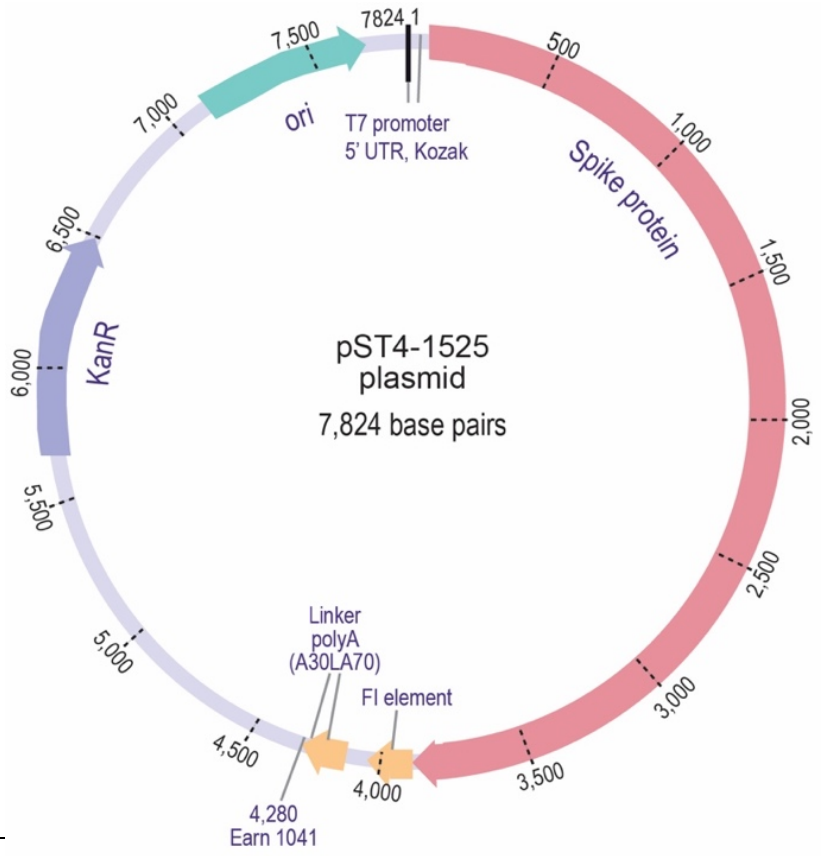
[45] (2022) September 1, 2022 ACIP Meeting – Booster doses of Moderna; Prizer/BioNTech COVID-19 Omicron-modified. YouTube. Retrieved from https://www.youtube.com/watch?v=i34wDDfhRpg&t=2176s

[46] Rosa, S.S., Prazeres, D.M.F., Azevedo, A.M., Marques, M.P.C. (2021) mRNA vaccines manufacturing: Challenges and bottlenecks. Vaccine. 39(16):2190–2200. doi:10.1016/j.vaccine.2021.03.038

[47] Ouranidis, A., Vavilis, T., Mandala, E., Davidopoulou, C., Stamoula, E., *et al.* (2022) mRNA therapeutic modalities design, formulation and manufacturing under Pharma 4.0 Principles. Biomedicines. 10(1):50. doi:10.3390/biomedicines10010050

RNA from degradation and aid in transcription termination), was inserted into a plasmid, which is a circular piece of DNA. In this case, plasmid pST4-1525 was used (Figure 5), which has 7,824 base pairs including a promoter for the T7 RNA polymerase, the recognition sequence for the endonuclease used for linearization of the DNA, a kanamycin resistance gene, and an origin of replication (ORI). The plasmid was taken into *E. coli* bacterial cells. As the *E. coli cells* grow and multiply in the presence of kanamycin (to ensure that only those particular *E. coli* that received the plasmid produce the Spike RNA can survive and proliferate), the plasmid multiplies along with them. *E. coli* is then harvested and chemically lysed to recover the plasmid DNA, which is then further purified. Subsequently, the circular plasmid DNA is linearized by cutting it using a restriction endonuclease enzyme (Eam1104I) and purified by ultrafiltration and Diafiltration (UFDF).[48]

Figure 5. pST4-1525 plasmid map. Adapted from Josephson *et al.* (2020).[49]



[48] (2023) Ultrafiltration and Diafiltration (UF/DF). Unchained Labs. Retrieved from https://www.unchainedlabs.com/ultrafiltration-diafiltration-uf-df/

[49] Josephson, F. (2020) Rapporteur's Rolling Review assessment report. Committee for Medicinal Products for Human Use. EMEA/H/C/005735/RR. Retrieved from https://covidvaccinereactions.com/ema-pfizer-leak/

The DNA template in both processes is then used as the starting material for the modRNA production. *In vitro* translation (IVT) transcription is an enzymatic reaction requiring an RNA polymerase, nucleotide triphosphate substrates (substituting N1-methylpseudouridine for uridine), the polymerase cofactor magnesium chloride ($MgCl_2$), and a pH buffer containing polyamide and antioxidants. Like Moderna, Pfizer/BioNTech used the T7 RNA polymerase (derived from the T7 bacteriophage), which binds to a cognate *promoter* sequence likewise derived from T7 that has also been engineered into the DNA plasmid upstream of the gene for the Spike protein. Only a few hours are needed to produce the modRNA and the process can be standardized.[46] The 5-prime cap is also added during the IVT reaction for both processes. Rather than adding the poly(A) tail enzymatically as in Process 1, in Process 2 it is already encoded for in the plasmid.

At the completion of IVT using plasmid DNA as used in Process 2, several impurities may be present, notably host cell genomic DNA from *E. coli*, RNA, proteins, endotoxins (bacterial cell wall components from the *E. coli* cells) and isoforms of the plasmid DNA.[49, 50] These were quantified routinely.

Manufacturers of biotechnological and biological products including vaccines, often make changes to the manufacturing process including increasing the scale of production, product stability and any changes imposed by regulatory authorities, both during development and post-approval. The manufacturers must demonstrate that the relevant quality attributes do not adversely impact safety or efficacy of these changes. Although there are no specific guidelines for changes in manufacturing processes specific to nucleic acid products, the International Council on Harmonization Q5E[51] did anticipate that: "*The principles outlined in this document might also apply to other product types such as proteins and polypeptides isolated from tissues and body fluids*" which would therefore include nucleic acids.

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[50] Banoun, H. (2022) Current state of knowledge on the excretion of mRNA and spike produced by anti-COVID-19 mRNA vaccines; possibility of contamination of the entourage of those vaccinated by these products. Infect Dis Res. 3(4):22. doi:10.53388/IDR20221125022

[51] (2005) ICH Topic Q 5 E. Comparability of Biotechnological/Biological products. European Medicines Agency. Retrieved from https://www.ema.europa.eu/en/documents/scientific-guideline/ich-q-5-e-comparability-biotechnological/biological-products-step-5_en.pdf

In particular, requirements for clinical comparative efficacy and safety studies are dependent on the stage of development and the type of change involved. If changes are made after the confirmatory clinical trials, as was done with the Pfizer/BioNTech vaccine, a thorough comparability assessment is generally required including:

> *"…physicochemical and biological in vitro studies, and may include clinical pharmacokinetic and/or pharmacodynamic comparability studies. If this comparability exercise cannot rule out an impact on the efficacy and safety profile of the drug, additional clinical study* (ies) *may have to be performed*."[52]

In its rolling review in November 2020, the EMA noted that there was a decrease in the purity of the mRNA. In the clinical trial batches, the intact mRNA was 78-83% pure, which was much higher than in the commercial batches at 60%.[37] Side-to-side comparisons based on analytical testing and biological assays demonstrated significant differences in the purity and amount of intact mRNA with the Process 2 batches. This may indicate notable physical, chemical and biological differences, warranting further comparative clinical studies. Emails from the EMA leak/hack showed that the EMA's Head of Pharmaceutical Quality, Dr. Jekerle Veronika, discussed the "differences in the level of mRNA integrity" between clinical and commercial material. It was hoped than an approval by the end of 2020 could be possible if the mRNA integrity issue (and 2 other major objections) were to be resolved.[53]

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[52] (2007) European Medicines Agency. Guideline on comparability of biotechnology-derived medicinal products after a change in the manufacturing process. Vol. EMEA/CHMP/BMWP/101695/2006. CHMP, Ed. European Medicines Agency. Retrieved from https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-comparability-biotechnology-derived-medicinal-products-after-change-manufacturing-process_en.pdf

[53] Veronika, J. (2020) E-mail dated November 24, 2020, to Dr. Evdokia Korakianiti of the EMA. EMA Leaks\09.png. Retrieved from https://covidvaccinereactions.com/wp-content/uploads/2021/04/EMA-Docs-and-CVR-Edits.zip

A protocol amendment to the pivotal trial was therefore added,[54] which required 252 patients receiving Process 2 lots to be compared to patients in the clinical trials receiving Process 1 lots for comparable safety and efficacy. To date, this data is unavailable.[55]

Most recently, a Freedom of Information (FOIA) request to the UK Regulator (Medicines and Healthcare Products Regulatory Agency) obtained by the *Daily Skeptic* revealed, *"This exploratory objective was removed and documented in protocol amendment 20 in September 2022 due to the extensive usage of vaccines manufactured via "Process 2." Thus, this process comparison was not conducted as part of the formal documentation within the protocol amendment*." Therefore, clinical comparability between these two manufacturing processes cannot be assumed and thus represents a new biological product, which is not comparable to the product in the clinical trials for safety and efficacy.[56] In essence, the UK regulator used 'real world evidence' to support compatibility of the two processes, in contradiction to the original accepted method of a small, randomized trial.

2.5.7. Impurities Identified in Process 2 Batches

2.5.7.1. Truncated and Fragmented modRNA

As discussed above, impurities in Process 2 lots included fragmented mRNA considered a critical quality attribute but it is not yet known what effects these smaller mRNA fragments (impurities) have in the body. These shorter Spike protein fragments may be released more readily into the circulation from vaccine transfected cells. Such truncated fragments may lack the transmembrane domain and attached palmitate fatty acids at the back end of the Spike protein, which would normally anchor them to the cell membrane. At the time of conditional approval, the allowable limits for fragmented mRNA were up to 45% in the final product.[37] Despite alteration of the sequence in the Spike protein with two amino acid residues replaced by two proline residues from mutation of the mRNA sequence, which locks the

[54] Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., *et al.* (2020) C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med. 383(27):2603–2615. doi:10.1056/NEJMoa2034577

[55] Block, J. (2022) COVID-19: Researchers face wait for patient level data from Pfizer and Moderna vaccine trials. BMJ. 378:o1731. doi:10.1136/bmj.o1731

[56] The Information Commissioner's Office. (2023) Internal review of FOI 23/510. Medicines and Healthcare Products Regulatory Agency. Retrieved from https://dailysceptic.org/wp-content/uploads/2023/09/IR-23-510.pdf

Spike protein in a prefusion state, the Spike protein should still be able to engage angiotensin-converting enzyme 2 (ACE2) and other Spike receptors that are expressed on cells of the body. ACE2 is important for reducing blood pressure through its ability to degrade the hormone angiotensin 2. The Spike protein binds to ACE2,[57] TMEM16F,[58] and CD42b receptors on platelets, and stimulates their activation and aggregation,[59] and contributes to thrombosis (blood clotting) and thrombocytopenia (reduction of production of platelets), which are known risks associated with COVID-19 vaccines.[60]

70. There is also little data on whether these fragmented mRNA pieces result in harmful proteins or peptides (small proteins) or if they induce autoimmunity (cause the body to attack itself). For example, there can be as much as a 30% amino acid similarity between the Spike protein and a human protein called Syncytin-1. Although cross-reactivity of anti-Spike antibodies produced in vaccinated individuals has not yet been reported that is directed towards Syncytin-1,[61, 62, 63] autoimmunity often takes years before its manifests overtly in people.

2.5.7.2. Double-stranded RNA (dsRNA)

Other impurities in the BNT162b2 included dsRNA, which occurs secondarily to the *in vitro* transcription process that can generate dsRNA by-products.[6452] dsRNA can induce pro-inflammatory cytokines such as type 1 interferon, trigger Toll-like receptor 3 and separately affect

[57] Zhang, S., Liu, Y., Wang, X., Yang, L., Li, H., *et al.* (2020) SARS-CoV-2 binds platelet ACE2 to enhance thrombosis in COVID-19. J Hematol Oncol. 13(1):120. doi:10.1186/s13045-020-00954-7

[58] Cappelletto, A., Allan, H.E., Cresente, M., Schneider, E., Bussani, R., *et al.* (2021) SARS-CoV-2 spike protein activates TMEM16F-mediated platelet pro-coagulant activity. BioRxiv (preprint). doi:10.1101/2021.12.14.472668

[59] Li, T., Yang, Y., Li, Y., Wang, Z., Ma, F., *et al.* (2020) Platelets mediate inflammatory monocyte activation by SARS-CoV-2 spike protein. J Clin Invest. 132(4):e150101. doi:10.1172/JCI150101

[60] Cox, D. (2021) Targeting SARS-CoV-2-platelet interactions in COVID-19 and vaccine-related thrombosis. Front. Pharmacol. 12:708665. doi:10.3389/fphar.2021.708665

[61] Prasad, M., Lin, J.L., Gu, Y., Gupta, R., Macary, P., Schwarz, H. (2021) No crossreactivity of anti-SARS-CoV-2 Spike protein antibodies with Syncytin-1. Cell Mol Immunol. 18(11):2566–2568. doi:10.1038/s41423-021-00773-x

[62] Mattar, C.N.Z., Koh, W., Seow, Y., Hoon, S., Venkatesh, A., *et al.* (2022) BNT162B2 COVID-19 mRNA vaccination did not promote substantial anti-syncytin-1 antibody production nor mRNA transfer to breast milk in an exploratory pilot study. Ann Acad Med Singap. 51(5):309–312. doi:10.47102/annals-acadmedsg.2021447

[63] Pelech, S., Winkler, D. (2023) personal communication.

[64] Baiersdörfer, M., Boros, G., Muramatsu, H., Mahiny, A., Vlatkovic, I., *et al.* (2019) A facile method for the removal of dsRNA contaminant from *in vitro*-transcribed mRNA. Mol Ther Nucleic Acids. 15:26–35. doi:10.1016/j.omtn.2019.02.018

expression/translation of Spike protein.[65] Removal of dsRNA is at best, 90%, which indicate that short segments of dsRNA may remain and has been hypothesized to contribute to immune-inflammatory reactions such as myocarditis.[66] When present in LPNs, dsRNA will also be transfected into macrophages and dendritic cells.[67] Dendritic cells trigger immune responses in lymphoid tissues upon early sensing of infectious pathogens and communicate with immature dendritic cells present in peripheral tissues such as the myocardium which may result in an autoimmune attack and myocarditis.

It is worth noting that due to the optimization of a high cytidine and guanidine content from gene-editing of the RNA to make the Spike protein in both the Pfizer/BioNTech and Moderna COVID-19 vaccines, this will produce tighter binding and stability of the dsRNA. This may facilitate more prolonged stimulation of cellular responses to perceived viral infection of cells, since dsRNA is not normally produced in healthy cells.

2.5.7.3. Endotoxin

Endotoxin can be introduced into the modRNA drug substance primarily from the *E. coli* used in the DNA template production but also from large volume buffers used in purification and from raw materials used in the manufacturing of the mRNA vaccines.[35] Endotoxin is difficult to remove due to its ubiquity, high heat stability, and hydrophobic properties.[68] Lipopolysaccharides (LPS) from endotoxin can bind both the S1 and S2 subunits of the Spike protein, which may result in enhanced inflammatory responses.[69] Endotoxin is a very potent stimulus of macrophages and monocytes even at picogram levels (a picogram is a trillionth of a gram).[70] Some researchers have suggested Spike protein is not pro-

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[65] Nelson, J., Sorensen, E.W., Mintri, S., Rabideau, A.E., Zheng, W., *et al.* (2020) Impact of mRNA chemistry and manufacturing process on innate immune activation. Sci Adv. 6(26):eaaz6893. doi:10.1126/sciadv.aaz6893

[66] Milano, G., Gal, J., Creisson, A., Chamorey, E. (2021) Myocarditis and COVID-19 mRNA vaccines: A mechanistic hypothesis involving dsRNA. Future Virol. 10.2217/fvl-2021-0280. doi:10.2217/fvl-2021-0280

[67] Kranz, L.M., Diken, M., Haas, H., Kreiter, S., Loquai, C., *et al.* (2016) Systemic RNA delivery to dendritic cells exploits antiviral defence for cancer immunotherapy. Nature. 534(7607):396–401. doi:10.1038/nature18300

[68] Li, Y., Fujita, M., Boraschi, D. (2017) Endotoxin contamination in nanomaterials leads to the misinterpretation of immunosafety results. Front Immunol. 8:472. doi:10.3389/fimmu.2017.00472

[69] Samsudin, F., Raghuvamsi, P., Petruk, G., Puthia, M., Petrlova, J., *et al.* (2023) SARS-CoV-2 spike protein as a bacterial lipopolysaccharide delivery system in an overzealous inflammatory cascade. J Mol Cell Biol. 14(9):mjac058. doi:10.1093/jmcb/mjac058

[70] Munford, R.S. (2016) Endotoxemia-menace, marker, or mistake? J Leukoc Biol. 100 (4):687–698. doi:10.1189/jlb.3RU0316-151R

inflammatory on its own in macrophages, except in the presence of endotoxin or lack of glycosylation.[71] LNPs with or without modRNA can induce exacerbated inflammation in the presence of pre-existing inflammation due to endotoxin,[72] and concerns have been raised that the unrecognized contamination of nanoparticles with endotoxin may be associated with toxicity.[68] In view of the high level of DNA plasmids in the BNT162b2 vaccine as discussed in the next subsection, it is feasible that endotoxin levels may also exceed current regulatory limits.[73]

2.5.7.4. Plasmid Vector DNA

As mentioned above, to produce the mRNA that is encapsulated in LPNs that are used as COVID-19 vaccines, both Pfizer/BioNTech and Moderna utilize DNA copies of the Spike gene that are incorporated into plasmids. These plasmids or vectors were used to transfect *E. coli* bacterial cells for high production of modRNA copies, which were subsequently purified from lysed bacteria. The purification protocols should have removed the plasmid DNA along with bacterial endotoxins and LPS. However, several laboratories have independently confirmed the substantial presence, as much as 35% or more, of the

[71] Cinquegrani, G., Spigoni, V., Iannozzi, N.T., Parello, V., Bonadonna, R.C., Dei Cas, A. (2022) SARS-CoV-2 spike protein is not pro-inflammatory in human primary macrophages: Endotoxin contamination and lack of protein glycosylation as possible confounders. Cell Biol Toxicol. 38(4):667–678. doi:10.1007/s10565-021-09693-y

[72] Parhiz, H., Brenner, J.S., Patel, P.N., Papp, T.E., Shahnawaz, H., *et al.* (2022) Added to pre-existing inflammation, mRNA-lipid nanoparticles induce inflammation exacerbation (IE). J Control Release. 344:50–61. doi:10.1016/j.jconrel.2021.12.027

[73] USP-NF. (2023) Analytical procedures for mRNA vaccine quality (Draft Guidelines) – 2nd Edition. United States Pharmacopoeia-National Formular. Retrieved from https://www.uspnf.com/notices/analytical-procedures-mrna-vaccines-20230428

nucleic acid in the COVID-19 mRNA vaccines as DNA.[74, 75, 76, 77, 78] The contamination appears to be higher in the Moderna vaccine than the Pfizer/BioNTech product, but most of the DNA fragments are much smaller and less than 200 base pairs in length.

A recent preprint by Canadian Citizens Care Alliance scientists and others showed that around 1.9 – 3.7 µg/dose of DNA by fluorometry appears to be typically found in vials of BNT162b2b that are supposed to contain 30 µg of Spike RNA, and 3.3 to 5.1 µg/dose for the Moderna product.[78] This would correspond to around 100 billion or more DNA molecules in each injection and represent contamination levels that exceed 3.33 µg/mg of RNA. However, the DNA contamination in these COVID-19 vaccines meets the European Medicines Agency (EMA) 0.33 µg/mg requirement,[49] and the FDA's 0.010 µg/dose requirements using the qPCR method for quantitation.[79] The large differences in residual DNA levels found between fluorometry and qPCR measurements maybe due to the fact that qPCR cannot quantitate molecules smaller than the size of the amplicon (105-114 base-pairs). Therefore, qPCR underestimates the total DNA in each vaccine and this raises questions of analytical methods recommended by regulatory agencies for modRNA vaccines. Health Canada, the US FDA and the European Medicine Agency have acknowledged the high degree of DNA that contaminated the Pfizer/BioNTech and Moderna vaccines, but have dismissed this and still consider the vaccines to be

[74] Palmer, M., Gilthorpe, J. (2023) COVID-19 mRNA vaccines contain excessive quantities of bacterial DNA: Evidence and implications. Doctors for COVID Ethics. Retrieved from https://doctors4covidethics.org/covid-19-mrna-vaccines-contain-excessive-quantities-of-bacterial-dna-evidence-and-implications/

[75] McKernan, K., Helbert, Y., Kane, L.T., McLaughlin, S. (2023) Sequencing of bivalent Moderna and Pfizer mRNA vaccines reveals nanogram to microgram quantities of expression vector dsDNA peer dose. ResearchGate. doi:10.31219/osf.io/b9t7m Retrieved from https://www.researchgate.net/publication/369967228_Sequencing_of_bivalent_Moderna_and_Pfizer_mRNA_vaccines_reveals_nanogram_to_microgram_quantities_of_expression_vector_dsDNA_per_dose

[76] Buckhaults, P. (2023) Testimony before South Carolina Senate Medical Affairs Ad-Hoc Committee on DHEC. Retrieved from https://www.youtube.com/watch?v=IEWHhrHiiTY

[77] (2023) Urgent expert hearing on reports of cancer-promoting DNA contamination in C-19 mRNA vaccines. World Council for Health. Retrieved from https://worldcouncilforhealth.org/multimedia/urgent-hearing-dna-contamination-mrna-vaccines/

[78] Speicher, D.J., Rose, J., Gutschi, L.M., Wiseman, D.M., McKernan, K. (2023) DNA fragments detected in monovalent and Pfizer/BioNTech and Moderna modRNA COVID-19 vaccines from Ontario, Canada: Exploratory dose response relationship with serious adverse events. OSF Preprints. Retrieved from https://osf.io/mjc97/

[79] Sheng-Fowler, L., Lewis, A.M. Jr, Peden, K. (2009) Issues associated with residual cell-substrate DNA in viral vaccines. Biologicals. 37(3):190–195. doi:10.1016/j.biologicals.2009.02.015

safe.[78,80, 81, 82, 83] In the recent testing of 27 mRNA Pfizer/BioNTech and Moderna vaccine vials obtained in Canada, "*all vaccines exceeded the guidelines for residual DNA set by the FDA and WHO of* [0.010 µg]/*dose by 188-509-fold*."[78] However, the transfection of these plasmid DNA contaminants using LPNs warrants reconsideration of the current regulatory limits, since these limits are based on injecting naked DNA directed into plasma where it may be rapidly destroyed.

Residual DNA can result in type 1 interferon responses and poses a risk to genomic integration. One of the mechanisms that Pfizer/BioNTech took to reduce the amount of plasmid Spike DNA was to digest it into smaller pieces with enzymes called nucleases. The consequence of this may be to further increase the probability of a piece of the DNA integrating into and disrupting the genomes of cells that take up the LPNs, and this has been explained by South Carolina University professor Dr. Philip Buckhaults when he gave a speech to a South Carolina Senate Medical Affairs Ad-Hoc Committee.[76] This situation can lead to "insertional oncogenesis," which is when foreign DNA gets integrated next to critical growth control genes, known as oncogenes or tumor suppressor genes and interferes with their normal regulation, thereby driving cancer cell proliferation. When DNA is circularized as it is in an intact plasmid, it is less likely to integrate into the genome. However, when it is cut into linear fragments with nucleases, the probability of integration into host cell DNA increases.[84] Even fragments of DNA as little as 7 bp have been shown to disrupt rates of DNA integration or recombination.[85] Some LPNs have been

[80] Horwood, M., Chartier, N. (2023) Exclusive: Health Canada not concerned about scientists' finding of plasmid DNA contamination in COVID shots. Epoch Times. Retrieved from https://www.theepochtimes.com/world/exclusive-health-canada-not-concerned-about-scientists-finding-of-plasmid-dna-contamination-in-covid-shots-5449394

[81] Phillips, J. (2023) FDA responds to reports of DNA contamination in COVID vaccines. Epoch Times. Retrieved from https://www.theepochtimes.com/article/fda-responds-to-reports-of-dna-contamination-in-covid-vaccines-5496717

[82] Demasi, M. (2023) Exclusive: An interview with Buckhaults about DNA contamination in COVID vaccines…and the FDA responds. MaryAnne Demasi Substack. Retrieved from https://maryannedemasi.substack.com/p/exclusive-an-interview-with-buckhaults

[83] Stieber, Z. (2023) European regulator confirms BioNTech did not highlight DNA sequence in COVID-19 vaccine. Epoch Times. Retrieved from https://www.theepochtimes.com/health/european-regulator-confirms-pfizer-did-not-highlight-dna-sequence-in-covid-19-vaccine-5519668?utm

[84] Lim, S., Yocum, R.R., Silver, P.A., Way, J.C. (2023) High spontaneous integration rates of end-modified linear DNAs upon mammalian cell transfection. Sci Rep. 13:6835. doi:10.1038/s41598-023-33862-0

[85] Ledwith, B.J., Manam, S., Troilo, P.J., Barnum, A.B., Pauley, C.J., *et al.* (2000) Plasmid DNA vaccines: Assay for integration into host genomic DNA. Dev Biol (Basel). 104:33–43.

developed to further improve on the delivery of DNA contents into the nucleus of cells, where the genome is normally present.[86]

Another problematic aspect of the Pfizer/BioNTech vaccine is that the DNA plasmid includes an SV40 promoter/enhancer/*ori* element, which is the portion of SV40 virus genome that drives the production of flanking genes. This inclusion was not originally disclosed to the EMA, nor to Health Canada, raising questions of adulteration and intention to deceive the regulatory agencies.[81, 87] Health Canada has recently confirmed the presence of the SV40 promoter/enhancer in the Pfizer/BioNTech vaccine after this was brought to their attention, but they have concluded that the risk/benefit profile continues to support the use of the Pfizer/BioNTech vaccine.[88]

This SV40 promoter might have been originally included to increase the rate of Spike RNA production from the DNA plasmid during the production phase. However, if portions of the contaminating plasmid integrate into a cell's genome, this could result in increased rates of mRNA production of genes next to the SV40 virus promoter/enhancer elements, which again can potentially contribute to driving oncogenesis. Moreover, the SV40 virus promoter/enhancer features a DNA nuclear targeting sequence.[89] The SV40 virus was a common contaminant in inactivated polio vaccines that were offered from 1955 to 1963, so a substantial portion of the population over 60 years of age may have persistent SV40 infections.[90] The Large T antigen produced from the SV40 virus, which may be present in 10-20% of the population, can bind to SV40 virus promoter/enhancer elements, which could lead to even higher mRNA production of cellular genes at sites of genome integration. However, the risk of this is

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[86] Nie, Y., Fu, G., Leng, Y. (2023) Nuclear delivery of nanoparticle-based drug delivery systems by nuclear localization signals. Cells. 12(12):1637. doi:10.3390/cells12121637

[87] Chartier, N. (2023) Here are the four e-mails from Health Canada which underpin our work on DNA plasmid contamination and the undisclosed presence of Simian Virus 40 enhancer-promoter. X Retrieved from https://twitter.com/nchartieret/status/1716579403243634922?s=46&t=fHNy04S5p-78vK_ah9g3hw

[88] Horwood, M. (2023) Exclusive: Health Canada confirms undisclosed presence of DNA sequence in Pfizer shot. Epoch Times. Retrieved from https://www.theepochtimes.com/world/exclusive-health-canada-confirms-undisclosed-presence-of-dna-sequence-in-pfizer-shot-5513277

[89] Bai, H., Lester, G.M.S., Petishnok, L.C., Dean, D.A. (2017) Cytoplasmic transport and nuclear import of plasmid DNA. Biosci Rep. 37(6):BSR20160616. doi:10.1042/BSR2016061

[90] Institute of Medicine (US) Immunization Safety Review Committee (2002) Immunization Safety Review: SV40 contamination of polio vaccine and cancer. Stratton, K., Almario, D.A., McCormick, M.C., editors. Washington (DC): National Academies Press (US). doi:10.17226/10534

unclear at this time. The DNA plasmid used to manufacture the RNA in the Moderna COVID-19 vaccine did not include an SV40 promoter.[75]

Finally, it should also be appreciated that the RNA in the COVID-19 vaccines may also be converted back into a DNA copy through the action of RNA reverse transcriptases in host cells such as LINE-1.[91] Such a conversion of Spike RNA into stable DNA in the nucleus of a liver cell line by LINE-1 was independently confirmed.[92] Liver is one of the major organs that accumulates the Pfizer/BioNTech vaccine LPNs,[21] and it is feasible that the DNA copy may permit more sustained production of more Spike RNA molecules, and more Spike protein copies.

2.5.8. Lipid Nanoparticles in COVID-19 RNA Vaccines

The lipid nanoparticles for use in vaccines are novel for use in humans and have not undergone rigorous safety assessments. The LNPs are semi-spheres made of fat (lipids) that protect the mRNA from decaying (degrading) and also carry the mRNA into cells. They contain PEGylated lipid (ALC-0159) and the cationic lipid (ALC-0315), *neither of which have been used in humans before*. PEGylation refers to the addition of polyethylene glycol as a component of a lipid or a protein, and in the case of LPNs, it reduces the rate of their clearance from the circulation by certain organs such as the kidneys. Normally, approval for such novel ingredients would require a full independent review for pharmacology and toxicity. These safety studies appear to be incomplete.

Cationic (positively-charged) lipids are known to cause inflammation (both with and without mRNA cargo inside them) and can be directly toxic to cells.[93] PEGylated nanoparticles can also cause significant allergic reactions.[94] There is limited data both on the metabolism and distribution of these

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[91] Zhang, L., Richards, A., Barrasa, M.I., Hughes, S.H., Young, R.A., Jaenisch, R. (2021) Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. Proc Natl Acad Sci USA. 118(21):e2105968118. doi:10.1073/pnas.2105968118

[92] Aldén, M., Olofsson Falla, F., Yang, D., Barghouth, M., Luan, C., *et al.* (2022) Intracellular reverse transcription of Pfizer BioNTech COVID-19 mRNA vaccine BNT162b2 *in vitro* in human liver cell line. Curr Issues Mol Biol. 2022 Feb 25;44(3):1115–1126. doi:10.3390/cimb44030073

[93] Ndeupen, S., Qin, Z., Jacobsen, S., Bouteau, A., Estanbouli, H., Igyártó, B.Z. (2021) The mRNA-LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory. iScience. 24(12):103479. doi:10.1016/j.isci.2021.103479

[94] Moghimi, S.M. (2021) Allergic reactions and anaphylaxis to LNP-Based COVID-19 vaccines. Mol Ther. 29(3):898–900. doi:10.1016/j.ymthe.2021.01.030

lipids, and it is not known how much ends up in each organ. There is no formal, controlled clinical data to support the safety of repeated exposures to the LNPs in humans beyond two inoculations.

2.5.9. Analytical Procedures for modRNA Vaccine Quality

Due to the rapid development and newness of the mRNA platform compendial standards were lacking. These are official quality standards contained in a pharmaceutical compendium such as the United Stated Pharmacopeia-National Formulary (USP-NF) or the European Pharmacopoeia (Ph Eur). The Ph. Eur standards for the assays used for the pro-vaccines are currently being developed, which will include mRNA-LNP medicinal products as well as the DNA template used for the preparation of the mRNA transcript.[95] The USP-NF developed a second draft of their analytical procedures for modRNA vaccine quality.[73]

It is important to note that compendial standards define a common set of methods to determine mRNA vaccine quality but do not enforce those standards or determine the acceptance criteria for quality and purity, which is under the purview of regulatory agencies. The updated WHO 2022 guidelines for mRNA vaccines also noted that "*detailed production and control procedures, controls were not yet standardized*" and certain details are not in the public domain and may be considered proprietary and confidential.[30] No specific numerical limit for dsRNA, DNA, plasmid purity and other process related impurities were stated in the WHO 2022 guidelines. The WHO guidelines also stated testing for process or product related impurities "*may be reduced or discontinued once production consistency has been demonstrated*," if the national regulatory agency is in agreement.

The United States Pharmacopoeia (USP) Draft Guidelines recommends more sensitive methods for analysis of the modRNA particularly for poly(A) integrity and 5' cap analysis than what was used by the manufacturer for Process 2 lots. Further, more in-depth analysis of purity of the modRNA drug substance such as nucleoside and residual T7 polymerase are additional proposed quality attributes.

[95] (2023) Ph. Eur. Commission kicks off elaboration of three general texts on mRNA vaccines and components. Council of Europe. Retrieved from https://www.edqm.eu/en/-/ph.-eur.-commission-kicks-off-elaboration-of-three-general-texts-on-mrna-vaccines-and-components

These are both welcome additions to detect and quantify these impurities since oxidized nucleotides are associated with age-related, especially neurodegenerative diseases.[96]

As noted earlier, residual dsRNA is a major contaminant of the modRNA drug substance secondary to the IVT process. dsRNA by-products such as runoff transcripts or an antisense RNA molecule similar in size to the desired mRNA can occur but require various analytical procedures for determining purity and quality. Immunoblot or ELISA analysis used by the manufacturer may not detect these types of dsRNA contamination and are difficult to quantify.[97] Analytical tools such as native and gel electrophoresis were not included to determine these critical quality attributes by the manufacturer or in the draft USP Guidelines.

Finally, RNA sequencing for confirming the expected mRNA sequence in addition to RT-PCR, and a full plethora of DNA plasmid testing including sequencing, is also proposed by USP.[73] These proposed compendial standards provide a more sensitive and thorough analysis for purity and safety than were used for either Process 1 or Process 2 lots raising questions of safety and purity for the early and current vaccine product. In particular, the sequencing of the DNA starting material which identifies the mRNA sequence performed for Process 1 lots was replaced with qPCR of the RNA for Process 2 lots,[49] a less sensitive method. This raises troubling questions about the fidelity of transcription during IVT and risks for aberrant protein production that were not identified in safety or analytical testing**.**

Specifications for quality attributes and testing for the final drug product includes LPNs and their lipid contents, appearance, sterility and selected attributes, which are included in the requirements for final drug product lot testing.

Importantly, subdivisible particles were noted in the Process 2 lots but were not described for Process 1 lots. These particles represent impurities and may have toxicological and clinical implications.[98] These impurities may have occurred due to instability of the buffer used in the initial process 2 lots and were

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[96] Li, Z., Malla, S., Shin, B., Li, J.M. (2014) Battle against RNA oxidation: Molecular mechanisms for reducing oxidized RNA to protect cells. Wiley Interdiscip Rev RNA. 5(3):335–346. doi:10.1002/wrna.1214

[97] Jacobsen, E. (2022) Quality control in mRNA vaccine manufacturing – The critical path. Future Lab, Biocompare. Retrieved from https://www.biocompare.com/Editorial-Articles/592381-Quality-Control-in-mRNA-Vaccine-Manufacturing-The-Critical-Path/

[98] Segalla, G. (2023) Chemical-physical criticality and toxicological potential of lipid nanomaterials contained in a COVID-19 mRNA vaccine. Int J Vac Theor Prac Res. 3(1):787–817. doi:10.56098/ijvtpr.v3i1.68

likely due to the fact that Process 1 lots had not been previously frozen and were in fact flown to the clinical sites by private jets as needed.[99] On October 29, 2021, the US FDA authorized two presentations representing a manufacturing change from the phosphate-saline/sucrose buffer found in the original purple-topped vials to a Tris/sucrose buffer; the grey topped monovalent adult vaccine and an orange topped vaccine for those aged 6-11 years for increased stability, simpler storage requirements and a ready-to-use formulation.[100] This may be viewed as a tacit admission that the stability of the initial lots of the Process 2 batches were suboptimal with unknown safety and efficacy effects.

2.5.10. Additional Issues

A high degree of variability in biodistribution of the COVID-19 vaccines can result from how they are inoculated into the deltoid muscles of recipients. A standard protocol of 'aspiration' during intramuscular injection of COVID-19 vaccines was generally abandoned, since it can slightly increase the chances of pain during administration.[101] As a consequence, about 2% or more of the vaccinations would result in delivery of the COVID-19 vaccine LPNs or adenoviruses directly into the bloodstream. This could account in part for why a small portion of vaccines recipients have much more severe adverse effects than most others.[102]

No one knows the potency, quantity, or duration of the Spike protein produced in different organs and the endothelium (*i.e.,* lining of blood vessel walls) given widespread biodistribution. There is no control of the amount of Spike protein is produced by transfected cells or duration of production. Tens of trillions of LPNs are injected with each vaccination. It is not known how age, sex, weight or other characteristics affect the potency of the vaccine. It is unknown how much Spike protein is made in each

[99] Lewis, L.M., Badkar, A.V., Cirelli, D., Combs, R., Lerch, T.F. (2023) The race to develop the Pfizer-BioNTech COVID-19 vaccine: From the pharmaceutical scientists' perspective. J Pharm Sci. 112(3):640–647. doi:10.1016/j.xphs.2022.09.014

[100] (2021) Emergency Use Authorization (EUA) for an unapproved product review memorandum. U.S. Food and Drug Administration. Retrieved from https://www.fda.gov/media/153947/download

[101] Rzymski, P., Fal, A. (2022) To aspirate or not to aspirate? Considerations for the COVID-19 vaccines. Pharmacol Rep. 74(6):1223–1227. doi:10.1007/s43440-022-00361-4

[102] Brail, S. (2022) Marc Girardot's unified theory of vaccine injury. Wholistic Substack. Retrieved from https://wholistic.substack.com/p/marc-girardots-unified-theory-of-vaccine-injury

organ in humans that takes up the synthetic mRNA. Evidence appears to indicate that small amounts of LNPs may result in large amounts of Spike protein being produced in particular organs.[103]

Mulroney *et al.* (2023)[104] recently noted that N1-methylpseudouridylation of mRNA occasionally causes +1 ribosomal frameshifting in mice and humans with the Pfizer/BioNTech COVID-19 vaccine. This results in production of off-target "Spike" proteins that can feature different amino acid sequences after the frameshift, with the potential for eliciting "off-target" immune responses.[105] The degree to which such novel chimeric proteins are created in COVID-19 RNA vaccinated individuals remains unclear as does the consequences of antibodies that may be produced against the novel sequences and their reactivities with human proteins.

Basic pharmacological data of the optimal dose, its range, and upper toxicity thresholds are lacking. By not performing pharmacokinetic and distribution studies of the encoded Spike protein, which was already known to be toxic and bioactive (off-target effects), the regulatory submissions for the COVID-19 genetic vaccines were incomplete. From the very start, the nonclinical safety studies were designed in order to provide data that would put the manufacturers' products in a "good light." The critical flaw here was that the guidance documents used by Health Canada were only applicable to traditional vaccines, and not vaccines using gene therapy technology.

Overall, mRNA vaccine quality has been questionable and variable. There appears to be substantial differences in the mRNA vaccines between batches and even between vials. This may be due to variations in handling, freezing/thawing/dilution requirements, and manufacturing variability. Stainless steel particles seen with the naked eye in some Moderna vials should have forced a larger

[103] Di, J., Du, Z., Wu, K., Jin, S., Wang, X., *et al.* (2022) Biodistribution and non-linear gene expression of mRNA LNPs affected by delivery route and particle size. Pharm Res. 39(1):105–114. doi:10.1007/s11095-022-03166-5

[104] Mulroney, T.E., Pöyry, T., Yam-Puc, J., Rust, M., Harvey, R.F., *et al.* (2023) (N)1-methylpseudouridylation of mRNA causes +1 ribosomal frameshifting. Nature. e-publication December 6, 2023. doi: 10.1038/s41586-023-06800-3

[105] Wiseman, D., Gutschi, L.M., Speicher, D.J., Rose, J., McKernan (2023) Ribosomal frameshifting and misreading of mRNA in COVID-19 vaccines produces "off-target" proteins and immune responses eliciting safety concerns: Comment on UK study by Mulroney *et al*. Retrieved from osf.io/nt8jh. doi:10.31219/osf.io/nt8jh

product review - but this was limited to particular lots.[106] A broad range of limits for purity and quality was permitted in the commercial production of the vaccines. Large manufacturing variability between batches plus patient-to-patient variability likely resulted in different levels of Spike production and response to the vaccine product.[107]

There has been significant variability in the severity of adverse events, including lethality, with other COVID-19 vaccines by vaccine maker and batch number. For example, in the UK, a freedom of information request about adverse reactions with COVID-19 vaccines indicated for the ten most reported batches up to April 24, 2022, the number of Yellow Card vaccine injury reports varied from 1-7 reports per 1000 doses; this included 45,320 reports for the AstraZeneca, 32,766 reports for the Pfizer/BioNTech, and 12,550 reports for the Moderna vaccines.[108] Contamination has also been an issue, for example, with the AstraZeneca vaccines (which although manufactured by Emergent Biosolutions in Baltimore, U.S.A., were never approved for use by the FDA, but were exported to Canada and Mexico).[109] More than half of Canada's supply of the AstraZeneca came from the Baltimore plant, until these vaccines were pulled on May 11, 2021 from the Canadian market.[110] Some of the problem involved cross-contamination with Johnston and Johnson COVID-19 adenovirus vaccine. Likewise, there was a major issue with batches of the Moderna COVID-19 vaccines in Japan.[111] Two Japanese men died after receipt of the second dose of the same batch of a Moderna COVID-19 vaccine, and subsequent testing found black substances in a few millimeters in size in 40 of vials of a different

[106] (2021) Moderna COVID-19 vaccine recall investigation report. Takeda Pharmaceuticals. Retrieved from https://www.takeda.com/ja-jp/announcements/statement-regarding-moderna-covid-19-vaccine-recall-investigation-report--october-2021

[107] Schmeling, M., Manniche, V., Hansen, P.R. (2023) Batch-dependent safety of the BNT162b2 mRNA COVID-19 vaccine. Eur J Clin Invest. 53(8):e13998. doi:10.1111/eci.13998

[108] FOI Team (2022) Freedom of Information request on specific batch numbers on the adverse reactions reported following the COVID-19 vaccinations (FOI release 22/661). Medicines and Health Products Regulatory Agency. Retrieved from https://www.gov.uk/government/publications/freedom-of-information-responses-from-the-mhra-week-commencing-6-june-2022/freedom-of-information-request-on-specific-batch-numbers-on-the-adverse-reactions-reported-following-the-covid-19-vaccinations-foi-22661

[109] Fenton, N.E. (2023) The scandal of the Astrazeneca vaccine from the Emergent Biosolutions plant in Baltimore. Substack. Retrieved from https://wherearethenumbers.substack.com/p/the-scandal-of-the-astrazeneca-vaccine

[110] Blackwell, T. (2021) More than half Canada's AstraZeneca vaccine came from U.S. plant accused of quality-control problems. National Post. Retrieved from https://nationalpost.com/news/canada/more-than-half-canadas-astrazeneca-vaccine-came-from-u-s-plant-accused-by-fda-of-quality-control-problems

[111] Chooi, W.H., Ng, P.W., Hussain, Z., Ming, L.C., Ibrahim, B., Koh, D. (2022) Vaccine contamination: Causes and control. Vaccine. 40(12):1699–1701. doi:10.1016/j.vaccine.2022.02.034

batch of the Moderna COVID-19 vaccine. About half a million people in Japan were inoculated with three batches of the Moderna vaccine before 1.63 million doses were recalled by Moderna Inc, Takeda Pharmaceuticals Co Ltd and the Japanese authorities.

Another retrospective study of 66,587 suspected adverse effects (SAE) across 52 specific batches of Pfizer/BioNTech BNT162b2 administered to 4,026,575 people in Denmark between December 27, 2020 and January 11, 2022, revealed large variations in the reported SAE.[107] The SAE rates were lower in the larger vaccine batches, and there were batch-dependent differences in the seriousness of the SAE. Certain smaller batches (representing 4.2% of all the vaccine doses) were associated with 71% of all SAEs, 27.5% of all serious SAEs and 47% of all SAE-related deaths in the Danish study.

2.5.11. WHO Guidelines on Vaccine Evaluation.

With regard to Health Canada's approval of the Pfizer COVID-19 vaccines. Both Pfizer and Health Canada followed the internationally accepted guidelines from the WHO for vaccine evaluation stating that the "*Pharmacokinetic studies (e.g., determining serum or tissue concentrations of vaccine components) are normally not needed."*

With respect to scope, a WHO 2005 document states: "*For the purposes of this document, vaccines are considered to be a heterogeneous class of medicinal products containing immunogenic substances capable of inducing specific, active and protective host immunity against infectious disease.*" BNT162b2 does not contain immunogenic substances capable of inducing specific, active, and protective host immunity against infectious disease.[112]

The WHO 2014 Annex 2 guidelines states when it comes to scope: "*This document addresses regulatory considerations related to the nonclinical and initial clinical evaluation of adjuvanted vaccines*." BNT162b2 does not contain an adjuvant, although the LPNs do cause inflammation. Essentially, the

[112] (2005) Annex 1 WHO guidelines on nonclinical evaluation of vaccines. World Health Organization. Retrieved from https://www.who.int/biologicals/publications/trs/areas/vaccines/nonclinical_evaluation/ANNEX%201Nonclinical.P31-63.pdf?ua=1

WHO publications are only applicable to traditional vaccines, and not vaccines using gene therapy technology.[113]

In a December 2020 draft document on regulatory evaluation,[112] WHO admitted that detailed information was not available for the production of the COVID-19 mRNA vaccines. The WHO confirmed that controls for safety and efficacy of gene-based mRNA vaccine biologic products were not standardized. Certain details of vaccine components remain proprietary and were not publicly disclosed. In light of these unknowns, the WHO conceded that it was not feasible to develop specific international regulatory guidelines or recommendations, and strict adherence to normal regulatory guidance may not be possible.

It appears that there is insufficient evidence that these vaccine products meet the quality required of pharmaceutical products, raising concerns about their safety and efficacy. Regulatory assessment using current vaccine guidance is likely inadequate to determine safety and efficacy for a genetic product.[34] Assessment using a comprehensive gene therapy guidance may have been more appropriate given the nature of transfection with a nucleic acid, but currently is *not required* if the *use* of the product is for prevention of infectious diseases such as a vaccine.[114] Real-world data falsifies the original claim that mRNA-based COVID-19 biologics function as authentic vaccines for preventing viral infection and transmission rather than short-term gene-based therapeutic agents that might at best alleviate symptom severity.

2.5.12. Concluding Remarks About COVID-19 mRNA Vaccine Production

Based on the regulatory assessment of the mRNA vaccines, the following can be reasonably concluded:

a. These products are genetic therapy products that were not fully assessed by regulatory authorities under the guidance and controls required for such products. Although indicated for the prevention of an infectious disease and are used as a vaccine, under new definitions by the CDC and WHO, the mode of action of these products is based on transfection of a nucleic acid

[113] (2014) Annex 2 Guidelines on the Nonclinical Evaluation of Vaccine Adjuvants and Adjuvanted Vaccines. World Health Organization. Retrieved from https://www.who.int/publications/m/item/nonclinical-evaluation-of-vaccine-adjuvants-and-adjuvanted-vaccines-annex-2-trs-no-987

[114] (2020) Human therapy for rare diseases. Guidance for industry. Food and Drug Administration Center for Biologics Evaluation and Research. Retrieved from https://www.fda.gov/media/113807/download

containing genetic information, but the appropriate regulatory controls and long-term safety studies were not performed.[34]

b. These products are mislabeled and adulterated. The label does not specify these are bioengineered nucleic acid mRNA, nor include the LNPs which may act as an adjuvant and provide for biodistribution throughout the body. These products are contaminated with small amounts of endotoxin, dsRNA, and significant contamination with plasmid DNA from the template produced by *E. coli.* Residual dsDNA poses particular oncological infectious risks.[79] Furthermore, the frameshifting in the reading of N1-methylpseudouridylated Spike mRNA by ribosomes generates highly mutated forms of the Spike protein that may interfere with the formation of the Spike trimers in cells.

One of the main mechanisms to consider with the dsDNA is insertional mutagenesis, although this is not a prerequisite for limiting dsDNA in medicinal products approved for human use. Firstly, DNA and RNA can enter spermatozoa and be transmitted to the next generation, along with the traits they encode for, without chromosomal integration.[115]

Secondly, a related phenomenon is that of episomal expression, which has been used in the development of gene therapy to achieve genetic modification without altering the chromosomal DNA. Other aspects of how DNA limits were to be assessed, such as those found in FDA guidelines were not addressed.[116]

c. The US FDA proposed that any DNA contaminants smaller than about 200 bp is unlikely to act as a functional gene sequence, but specific types of contaminating sequences require particular scrutiny, including the SV40 promoter/enhancer sequence containing two 72 bp repeats, as this sequence is a known nuclear localization sequence that can ferry DNA into the nucleus of cells.[117] The commercial product was produced with a sufficiently different manufacturing process

[115] Spadafora, C. (2017) Sperm-mediated transgenerational inheritance. Front Microbiol. 8:2401. doi:10.3389/fmicb.2017.02401

[116] (2020) Chemistry, manufacturing, and control (CMC) information for human gene therapy investigational new drug applications (INDs). CBER, Ed.. USFDA. US Department of Health and Human Services. Retrieved from https://www.fda.gov/media/113760/download

[117] Dean, D.A., Dean, B.S., Muller, S., Smith, L.C. (1999) Sequence requirements for plasmid nuclear import. Exp Cell Res. 253(2):713–722. doi:10.1006/excr.1999.4716

(Process 2) requiring verification of clinical comparability for efficacy and safety. This data does not appear to be available. This is a not a theoretical concern since a similar issue arose from the 1976 Swine flu inoculations, where the original influenza vaccine had been field tested but upon the declaration of a pandemic, the updated influenza vaccines were made without any confirmatory comparability testing.[118]

d. Several cases of Guillain-Barré syndrome were associated with this vaccine, and issues with manufacturing such as endotoxin contamination were considered a potential cause.[119]

Real-world data falsifies the original claim that mRNA-based COVID-19 biologics function as an authentic vaccine for preventing viral infection and transmission rather than as a short-term gene-based therapeutic agent that might alleviate at best, symptom severity.

2.6. Effectiveness of COVID-19 Vaccines

2.6.1. Approved COVID-19 Vaccines in Canada under Interim Order

Four COVID-19 vaccines, all targeting the Spike protein on the surface of the SARS-CoV-2 virus, were approved for use in Canada in 2021 under Interim Order: Pfizer-BioNTech BNT162b2 (later named Comirnaty) and Moderna mRNA-1273 (later named Spikevax), which are both vaccines that deliver RNA for production of the Spike protein; and AstraZeneca's Vaxzevria and Janssen's Jcovden (Johnson & Johnson (J&J)) vaccines, which are both adenovirus preparations that contain DNA that provide for RNA production to then permit the biosynthesis of the Spike protein. In 2022, Novavax's Nuvaxovid and Medicago's Corifenz were also approved by Health Canada. These latter vaccines used preparations of Spike protein that were purified from genetically engineered caterpillar cells and tobacco leaf cells, respectively, and delivered in a lipid nanoparticle along with a novel adjuvant to stimulate an immune reaction; each Nuvaxovid vaccine dose contained about 5 microgram (μg) of

[118] Sencer, D., Millar, J.D. (2006) Reflections on the 1976 swine flu vaccination program. Emerg Infect Dis. 12(1):29–33. doi:10.3201/eid1201.051007

[119] Evans, D., Cauchemez, S., Hayden, F.G. (2009) "Prepandemic" immunization for novel influenza viruses, "swine flu" vaccine, Guillain-Barré syndrome, and the detection of rare severe adverse events. J Infect Dis. 200(3):321–328. doi:10.1086/603560

Spike protein, and Corifenz vaccine dose about 3.75 μg of a lipid membrane-encapsulated virus-like particle that is enriched in Spike protein. (1 μg is 1 millionth of a gram)

The first two doses for those over 12 years of age of the Moderna vaccine had 100 μg of the RNA for the Spike protein, compared to 30 μg of the RNA for the same protein in the first two adult doses of the Pfizer-BioNTech vaccine. After 6 months, booster shots were recommended for those 12 years of age or older with the Pfizer-BioNTech vaccine (30 μg/dose) and for those over 18 years of age with the Moderna vaccine (50 μg/dose).[120]

For the COVID-19 vaccination of children 6 months and older, only the Pfizer-BioNTech and Moderna RNA vaccines have been approved by Health Canada.[120] The Moderna product was approved for 6-month to 5-year-olds with a 2-dose regimen (25 μg/dose one month apart), whereas the Pfizer product was approved with a 3-dose regiment) (3 μg/dose at an interval of three weeks between the first and second doses, with eight weeks between the second and third dose). For 5- to 11-year-olds, the Pfizer-BioNTech vaccine was used at a dosage that was one third of the teen and adult dose (10 μg/dose),[121] whereas the Moderna vaccine was used at half the adult dose (50 μg/dose) for 5- to 11-year-olds,[122] and a quarter of the adult dose for 6-months to 4-years old children (25 μg/dose). Therefore, a 5-year-old child received 5-times higher levels of the Spike mRNA with the pediatric dose of the Moderna vaccine when compared to the Pfizer-BioNTech product. A 6-month-old child received an 8-times higher level of the Spike mRNA with the pediatric dose of the Moderna vaccine when compared to the Pfizer-BioNTech product. Normally, a dose of a vaccine would roughly be related to body weight, but it is quite evident that this was largely ignored with the dispensing of the COVID-19 vaccines.

Based on the doses of Spike protein mRNA that have been used in these vaccines, it can be estimated that a single 100 μg inoculation may contain over 30 trillion lipid nanoparticles that typically feature around 5 to 10 copies of the Spike protein gene. The whole SARS-CoV-2 RNA is close to 30,000

[120] (2023) Approved COVID-19 vaccines. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines.html

[121] (2023) Pfizer/BioNTech Comirnaty COVID-19 vaccine. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/pfizer-biontech.html

[122] (2023) Moderna Spikevax COVID-19 vaccines. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/vaccines/moderna.html

nucleotides long and is single-stranded, but the Spike gene is only around 4,000 nucleotides long. It is calculated that the human genome, with 2,900,000,000 nucleotides per strand weighs about 0.855 picogram per strand. (A pictogram is a trillionth of a gram) Therefore 4,000 nucleotides would weigh around 0.00000118 picograms or 0.00000000000118 µg per 4,000 nucleotide RNA molecules. With 100 µg of RNA in one vaccine inoculation, this works out to about 85 trillion RNA molecules by this calculation. (As mentioned earlier, there is also some contaminating plasmid DNA with the RNA so the final number of RNA molecules may be slightly less.) From each genetically modified RNA molecule, it is feasible that hundreds of copies of the Spike protein can be produced.

Traditional vaccines with attenuated, weakened strains of a pathogenic virus typically range from as low as 50 to a few thousand virus particles in an inoculation, with each virus having only one copy of each viral gene. Consequently, the COVID-19 genetic vaccines permit the generation of Spike proteins in vaccine recipients that are at levels that could never be achieved with previous vaccines or even a natural infection without causing severe disease or death. This incredible capacity of these RNA and adenovirus vaccines to produce such high levels of Spike protein accounts for their ability to elicit strong immune responses, but also their higher potential for vaccine injury.

As mentioned above, the four COVID-19 genetic vaccines that were offered in Canada were RNA-based using lipid nanoparticle carriers (*i.e.*, Pfizer-BioNTech and Moderna) or DNA-based using adenovirus carriers (*i.e.*, AstraZeneca and J&J). In each case, these particular vaccines deliver genetic instructions for the production of the Spike protein of the SARS-CoV-2 virus inside of the host cells that take up these vaccines (initially at the site of the injection in the deltoid muscle region of the arm). The Spike protein is then presented on the surface of these cells to elicit an inflammatory immune response that culminates in the stimulation and proliferation of T-cells and B-cells, the latter producing antibodies that specifically target epitopes on the Spike protein. However, to produce the activation of T- and B-cells, this necessitates the damage and likely destruction of the Spike-presenting transfected cells. This is particularly problematic for neurons and cardiac muscle cells (cardiomyocytes), which do not regenerate in adults.

Lipid nanoparticles and adenoviruses have been used previously to deliver drugs and toxins into animals for therapeutic purposes, and even to elicit immune responses.[123] lipid nanoparticles or genetically engineered adenoviruses normally present the antigen of the pathogen on their surfaces. However, the combination of the lipid nanoparticles to get production of a target pathogen's protein on the surface of the body's own cells to elicit an immune response against that target remains experimental, especially since new information continues to accrue about the unexpected consequences of this novel method of antibody production.

In a sense, the genetic vaccines are "pro-drugs", which require further processing to produce active ingredients. Unfortunately, the production of the Spike protein is very host cell-dependent, and this processing is influenced by many different factors, including vaccine dose to body size ratio, cell type taking up the vaccine, health, nutritional, hormonal, and pharmacological status.[124] Consequently, the levels of Spike protein could potentially vary by up to two orders of magnitude (*i.e.,* 100-fold) or more. This can lead to marked variations in vaccine efficacy and injury from person to person.

Prior to the approvals of these vaccine formulations for human use by the US FDA and Health Canada at the end of 2020, no such lipid nanoparticles or adenoviruses had ever been approved for any RNA- or DNA-based vaccine to produce immunity against a pathogen's proteins by specifying their production within the body's own cells. It should be noted that the European Medicines Agency did approve Zabdeno, an adenovirus-based vaccine for prevention of Ebola virus disease, under Emergency Use Authorization in 2020. However, this vaccine was only about 50% effective in tested animals, and its efficacy in humans still remains to be determined in a formal clinical trial, since ethically it would be wrong to test such vaccines in healthy volunteers with such a high failure rate in animal trials.[125] Zabdeno was not marketed in Canada or the US.

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[123] Dolgin, E. (2021) The tangled history of mRNA vaccines. Nature. 597(7876):318-–324. doi:10.1038/d41586-021-02483-w

[124] Gutchi, L., Speicher, D.J., Natsheh, S., Oldfield, P., Britz-McKibbon, P., *et al.* (2022) An independent analysis of the manufacturing and quality issues of the BNT162b BioNtech/Pfizer quasi-vaccine based on the European Medicines Agency's Public Assessment Report (EPAR). Canadian Covid Care Alliance. Retrieved from https://www.canadiancovidcarealliance.org/wp-content/uploads/2022/11/22OC29_EMA-Analysis-of-BNT162b-Manufacture.pdf

[125] (2020) Summary of product characteristics: Zabdeno suspension for injection. European Medicines Agency. Retrieved from https://www.ema.europa.eu/en/documents/product-information/zabdeno-epar-product-information_en.pdf

To counteract the COVID-19 pandemic crisis, the four COVID-19 genetic vaccines were first released for general use in the Canadian population starting in mid-December 2020 under an Interim Order. In the US, only three of these vaccines (AstraZeneca's adenovirus vaccine was not approved) were authorized for general use through Emergency Use Authorization (EUA). It is noteworthy that EUA approval is normally granted only if there are no alternative treatments for a disease, although technically dexamethasone had already been shown to effectively treat many cases of hospitalized COVID-19 patients that require supplemental oxygen.[126]

In Canada, the US and elsewhere, these vaccines were still technically in Phase 3 clinical trials in early 2023. For example, the Pfizer-BioNTech COVID-19 vaccine, which is the most widely used, was in Phase 3 trials that were not scheduled to be completed until July 30, 2023.[127] The approvals provided by Health Canada and the FDA remain contingent on active and passive monitoring of the efficacy and safety of these non-traditional vaccines. Consequently, these COVID-19 vaccines are still regarded by many as highly experimental in nature. The fact that billions of people have been inoculated with these vaccines does not mean that they are not still experimental as their efficacy and safety remain topics of intense biomedical research, which will be evident later starting in Section 2.7.

The testing of drugs and vaccines by manufacturers normally requires pre-clinical trials in at least two different animal models to provide initial efficacy and safety data. Phase 1 trials are performed on healthy volunteers to evaluate initial safety concerns. Phase 2 trials are then undertaken with the main targeted participants (*i.e.,* those most vulnerable to a disease) with different concentrations of the drug or vaccine to establish an optimum dose to elicit a desired therapeutic or immune response as appropriate. Phase 3 trials are subsequently conducted on usually thousands of targeted participants in multiple centers to investigate the longer-term efficacy and safety of the tested drug or vaccine at the optimal dose.

[126] RECOVERY Collaborative Group; Horby, P., Lim, W.S., Emberson, J.R., Mafham, M., Bell, J.L., *et al.* (2021) Dexamethasone in hospitalized patients with COVID-19. N Engl J Med 384(8):693–704. doi:10.1056/NEJMoa2021436

[127] (2021) Pfizer-BioNTech COVID-19 BNT162b2 Vaccine effectiveness study – Kaiser Permanente Southern California. U.S. National Library of Medicine. Retrieved from https://clinicaltrials.gov/ct2/show/NCT04848584

The importance of continuing Phase 3 studies with COVID-19 vaccines has been prompted by several factors, including an unprecedented shortening of the typical testing period (5 to 10 years) of a vaccine before approval for general release to under a single year with "Operation Warp Speed" in the US. This was achieved by reducing the number of many cell and animal preclinical trials with the vaccines that are normally undertaken over 1 to 3 years down to a couple of months and running them in parallel with Phase 1 and 2 human trials. Of particular concern, many of the safety studies were performed in rats or mice, which is problematic, because these rodents do not feature ACE2 receptors that bind to the original Wuhan SARS-CoV-2 Spike protein. Phase 2 and 3 trials, which instead of being conducted over the usual 3 to 5 years, were combined, and based on just 2 months of testing, were approved for dissemination to the general population with an Interim Order in Canada and an Emergency Use Authorization in the US. For example, the Phase 3 clinical studies with the Pfizer-BioNTech vaccine commenced on July 27th, 2020, and the vaccine was approved for general use for those over 18 years of age by early December of 2020. **Ultimately, these novel genetic vaccines were approved for wide-spread use in about a tenth of the time as compared to traditional vaccines**.

It should be appreciated that the RNA- and adenovirus-based genetic vaccines did not satisfy the US CDC's original definition of a "vaccine," which was previously described as "*a product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease.*"[128] Later, on September 1, 2021, the definition of vaccine was simplified to "*a preparation that is used to stimulate the body's immune response against diseases*." The new definition of "*immunity*" was also problematic with "*protection from an infectious disease*." The CDC states that "*If you are immune to a disease, you can be exposed to it without becoming infected*."[129] Obviously, this must be false, because the actual infection with the virus still proceeds, but ideally, the immune system is able to eradicate the virus before it can evoke the symptoms of disease. It is amply clear that one can still become infected with SARS-CoV-2 after vaccination, but the claims were later adjusted to suggest that protection is provided to reduce the severity of the illness, but not necessarily to prevent infection.

[128] (2018) Vaccines and Immunizations. Immunizations: The basics. Centers for Disease Control and Prevention. Retrieved from http://web.archive.org/web/20200317214611/https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm

[129] (2022) Vaccines and Immunizations. Immunizations: The basics. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm? Sourced September 10, 2022.

This means that one can still become infected, and still transmit the pathogen after they are vaccinated for COVID-19.

The COVID-19 RNA and adenovirus "vaccines" are more like genetic therapy, because they do not contain the actual immunogen to elicit an antibody response but rather provide genetic instructions for the body to produce the immunogen. Normally, the use of genetic therapy products commands a much higher level of testing than traditional drugs or vaccines. It is also noteworthy that vaccines do not carry the same degree of liability to manufacturers for injury from these products in the US compared with other drugs.[130]

As mentioned earlier, all COVID-19 vaccines were approved under Interim Order in Canada, and under Emergency Use Authorization in the US. Most people would be surprised to learn that the efficacy and safety requirements for approval of a medication or device under Interim Order are minimal and contrary to popular belief, even amongst health professionals, vaccines and drugs can be approved with little or even no evidence of efficacy and safety under Interim Order, as stipulated in Section 30.1 of the Food and Drugs Act, R.S.C., 1985, c. F-27.[131] This is apparently what happened with Health Canada's approval of the COVID-19 genetic vaccines starting in December 2020. This does not mean that these experimental COVID-19 vaccines were known to be efficacious and safe at the time of their approval. As noted in lawyer Shawn Buckley's discussion publication:[131]

> *"For COVID-19 vaccines, there were the following major legal changes to deliberately circumvent the normal protections in our drug approval law:*
>
> *a) The normal drug approval process requires objective proof of:*
>
> *i. safety;*
>
> *ii. efficacy; and*

[130] 42 U.S. Code § 300aa-22 – Standards of responsibility. LII Legal Information Institute. Cornell Law School. Retrieved from https://www.law.cornell.edu/uscode/text/42/300aa-22

[131] Buckley, S. (2023) Changes to the drug approval test for COVID-19 vaccines: Permitted vaccines to be approved without objective proof of (1) safety, (2) efficacy, or (3) the benefits outweighing the risks. Natural Health Products Protection Association. Retrieved from https://nhppa.org/wp-content/uploads/2023/03/NHPPA-Discussion-Paper-COVID-19-Vaccine-Test-March-17-2023.pdf

iii. benefit outweighing risk.

COVID-19 vaccines were exempted from this normal drug approval process.

COVID-19 vaccines were approved under a subjective test which mandated that approval must be granted if the argument could be made that the benefits outweighed the risk. No actual proof of safety, efficacy or benefit outweighing risk was required.

b) The law was changed so that the approval of a COVID-19 vaccine could not be revoked:

i. due to evidence the vaccine was unsafe or not-effective;

ii. due to assessments the benefits did not outweigh the risks.

These legal changes were in force from September 16, 2020 to:

i. September 15,2021, for the Pfizer and Moderna vaccines;
ii. November 18, 2021, for the AstraZeneca vaccine; and
iii. November 22, 2021 for the Johnson and Johnson vaccine.

c) A classic conflict of interest was created where the Government was allowed to purchase and import unapproved vaccines while the Government waited for itself to approve the vaccines." [131]

2.6.2. Relative and Absolute Risk Reduction with COVID-19 Vaccines

Drugs and vaccines are "normally" expected to undergo a rigorous testing process, first in animals and then in people. This is not what happened with the COVID-19 vaccines. Animal trials, when actually performed, were conducted in parallel with human trials, and the Phase 3 human trials were predominantly carried out on healthy people or those who had only one co-morbidity and were mainly working age adults. Normally, Phase 3 trials are carried out on those that would most benefit from a treatment.

Before reviewing the Phase 3 clinical trials with COVID-19 vaccines that were used to justify the Interim Order approval in Canada and equivalent approvals by regulatory agencies in other countries, it is instructive to understand the difference between "relative risk reduction" (RRR) and "absolute risk reduction" (ARR) in monitoring the effectiveness of a medical treatment. The ARR is the absolute difference in rates of an event (*e.g.*, infection) between the experimental group and the control group. It is calculated by subtracting the experimental group event rate (ER) from the control group event rate (CR) and is usually expressed as a percentage. In contrast, the relative risk reduction (RRR), or vaccine efficacy (VE), represents the relative decrease in the risk of an adverse event in the experimental group compared to the control group. It is calculated as the relative risk of the rate of the experimental group (ER) minus the rate of the control group (CR) divided by rate of the control group (CR), and, as with the ARR, is usually expressed as a percentage.

To illustrate this, consider a trial with 200 participants (100 allocated to the experimental group and 100 allocated to the control group); if one of the experimental participants becomes ill (rate 1/100 = 0.01), compared with two in the control group (rate 2/100 = 0.02) who become ill, the RRR of the vaccine is 50% (=(0.01-0.02)/0.02) x 100%), a potentially attractive reduction likely to persuade users to accept the treatment. In contrast, the ARR is merely 1% (= (0.02 – 0.01) x 100%), which means that most of the individuals who did not take the 'vaccine' are still likely to remain free from the "disease" 98% of the time, as opposed to 99% of the time if they took the vaccine. This may give pause to patients and health professionals when considering the desirability of accepting a new treatment, especially considering the scant safety data.[132] Of note, while the RRR of the first Pfizer-BioNTech Phase 3 trial was 95%, the ARR was only 0.8%, which was calculated by independent investigators but not reported in the original peer-reviewed publication (although the raw data was available in the Supplemental section to permit such calculations).[133]

Because communicating relative risk can be so misleading, not only to the public but also to health professionals, in a 2011 report entitled "Communicating Risks and Benefits: A User's Guide", the US

[132] Brown, R.B. (2021) Outcome reporting bias in COVID-19 mRNA vaccine clinical trials. Medicina (Mex). 57(3):199. doi:10.3390/medicina57030199

[133] Thomas, S.J., Moreira, E.D., Kitchin, N., Absalon, J., Gurtman, A., *et al.* (2021) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine through 6 months. N Engl J Med. 385:1761–1773. doi:10.1056/NEJMoa2110345

FDA instructed investigators to "*provide absolute risks, not just relative risks,*" noting (on page 60) that "*Patients are unduly influenced when risk information is presented using a relative risk approach; this can result in suboptimal decisions. Thus, an absolute risk format should be used.*"[134] To put this into perspective, based on the COVID-19 RNA vaccine Phase 3 trial data in a 6-month period (the duration of the clinical study to generate this data), vaccinating everyone in the vaccine group only reduced COVID-19 incidence by less than 1% compared to no vaccination, despite the RRR of 95%.[133] This was because the overall risks of getting symptomatic COVID-19 that was confirmed by PCR testing in the unvaccinated group during the 6-months period was only about 4%.

2.6.3. Distinguishing between the Unvaccinated and Vaccinated in Clinical Studies

It should be appreciated that vaccine efficacy estimates that have been published in clinical trial reports of Phase 3 clinical trials with COVID-19 vaccines and highly quoted by public health officials have been RRR and not ARR values. In the Phase 3 clinical trials to ascertain whether the COVID-19 vaccines reduced the actual occurrence of SARS-CoV-2 infection and COVID-19 symptoms, there have been numerous deficiencies in the haste to get these vaccines to market. **These clinical trials did not assess whether the vaccines reduced transmission, severity, hospitalizations, or deaths.** Moreover, they poorly evaluated whether COVID-19 vaccines reduced occurrence of the disease in segments of the population that are at greatest risk, namely the very elderly, obese or those with comorbidities such as diabetes.

The preclinical, Phase 1, Phase 2 and Phase 3 trials were all accelerated for these vaccines, and the formal Phase 3 clinical trials never tested end points such as protection from COVID-19-induced death or transmissibility of the virus. Nor were biochemical studies of blood samples performed, such as D-dimer analyses to detect potential blood clotting, C-reactive protein for inflammation, and troponin for heart damage. In the absence of properly matched placebo controls, these deficiencies may not be clear from the post-marketing safety studies of the COVID-19 vaccines following their release to the public. Instead, the post-marketing, Phase 4 studies were relied upon to learn more about the benefits, limitations, and risks of the COVID-19 vaccines, for example, on pregnancy outcomes. For all intents

[134] Fischhoff, B., Brewer, N.T., Downs, J.S., eds. (2011) FDA. Communicating risks and benefits: An evidence-based user's guide, 242. Retrieved from https://www.fda.gov/about-fda/reports/communicating-risks-and-benefits-evidence-based-users-guide

and purposes, these novel RNA and adenovirus vaccines remained “experimental” after their approvals. Ironically, as data accumulate regarding their clinical outcomes, regulations governing their use are constantly being refined. As highlighted in the next few paragraphs, the term “unvaccinated” is very problematic, and can cause significant misrepresentation of the COVID-19 data on public health websites.

In consideration of all the epidemiological studies that benchmark the risk reduction of the acquiring COVID-19 with the vaccines relative to “unvaccinated” individuals, irrespective of whether such comparisons are made in the clinical trials or the post-approval release of these vaccines, the following are significant and common issues that must be appreciated:

a. A higher testing bias by PCR or rapid antigen testing of unvaccinated people occurred, especially since the adoption of vaccine passports, where workplace testing was usually focused, or even restricted to those that were unvaccinated (for example, at the University of British Columbia);

b. Very frail and elderly people, who are also at greatest risk of requiring hospitalization due to their fragile condition, were often not vaccinated in some places like Quebec for fear of vaccine-induced injury from mounting overly strong immune responses;

c. The definition of the “vaccinated” included only those who were 2- to 3-weeks after their vaccination (depending on the province in Canada; 3 weeks in British Columbia). Hence, for statistical purposes, patients who were actually vaccinated but developed COVID-19 within the first 2- to 3-weeks post vaccination were categorized as unvaccinated. This is particularly problematic, because vaccination appeared to initially increase the risk of acquiring COVID-19, especially when this was performed during a wave of COVID-19 cases (see later in para. 127);

d. The over-reporting of hospital cases, intensive care units (ICU) admissions and deaths of individuals with COVID-19 under circumstances where the original hospitalizations were due to other reasons independent of having a SARS-CoV-2 infection, *i.e.,* the individuals had an existing comorbidity or death from other causes but happened to test positive for SARS-CoV-2 at the time of admission or during their stay in hospital. By April, 2022, only 46% of recorded COVID-19 cases

in Ontario hospitals had COVID-19 symptoms at the time of admittance. [135] Likewise, in British Columbia by the end of January 2022, only about 40% of all of the COVID-19 cases were symptomatic at admission;[136] and

e. Many of the "vaccinated" and "unvaccinated" cases already had immunity from natural infection with SARS-CoV-2. This was especially evident in children, most of whom were asymptomatic for COVID-19.

With respect to Point b above, data from Scotland revealed that at the time of triple vaccination of the elderly, there were increased COVID-19 case numbers in the elderly as shown in a report provide by Public Health Scotland.[137] This was attributed to vaccination "*and the prioritisation of the booster/third dose to the clinically extremely vulnerable at the beginning of the booster programme*." However, as further explained below, due to the extremely high production of Spike protein with each vaccination, the capacity of the highly mobile immune system may be overwhelmed initially with massive appearance of Spike protein on body cells and is unable to also deal with SARS-CoV-2 virus particles that meanwhile enter into the respiratory system. Facing less resistance in the upper airways and lungs by a diverted immune system, these viruses can propagate sufficiently to then produce illness. This is why vaccination during a COVID-19 wave with increased cases is not advised, because it may actually increase the spread of the disease.

With respect to Point c above, one of the reasons why the aggregation of COVID-19 cases diagnosed within 2 weeks of injection together with the unvaccinated is very problematic becomes apparent upon the analyses of epidemiological data that was provided by the Alberta

[135] (2022) Ontario's COVID-19 hospitalizations rise to 1,730, most since mid-February. Canadian Broadcasting Corporation News. Retrieved from https://www.cbc.ca/news/canada/toronto/covid-19-ontario-april-26-2022-hospitalizations-1.6431094

[136] Carrigg, D. (2022) Majority of new COVID-19 hospitalizations in B.C. among people admitted for other reasons. The Vancouver Sun. Retrieved from https://vancouversun.com/news/local-news/majority-of-new-covid-19-hospitalizations-among-people-admitted-for-other-reasons

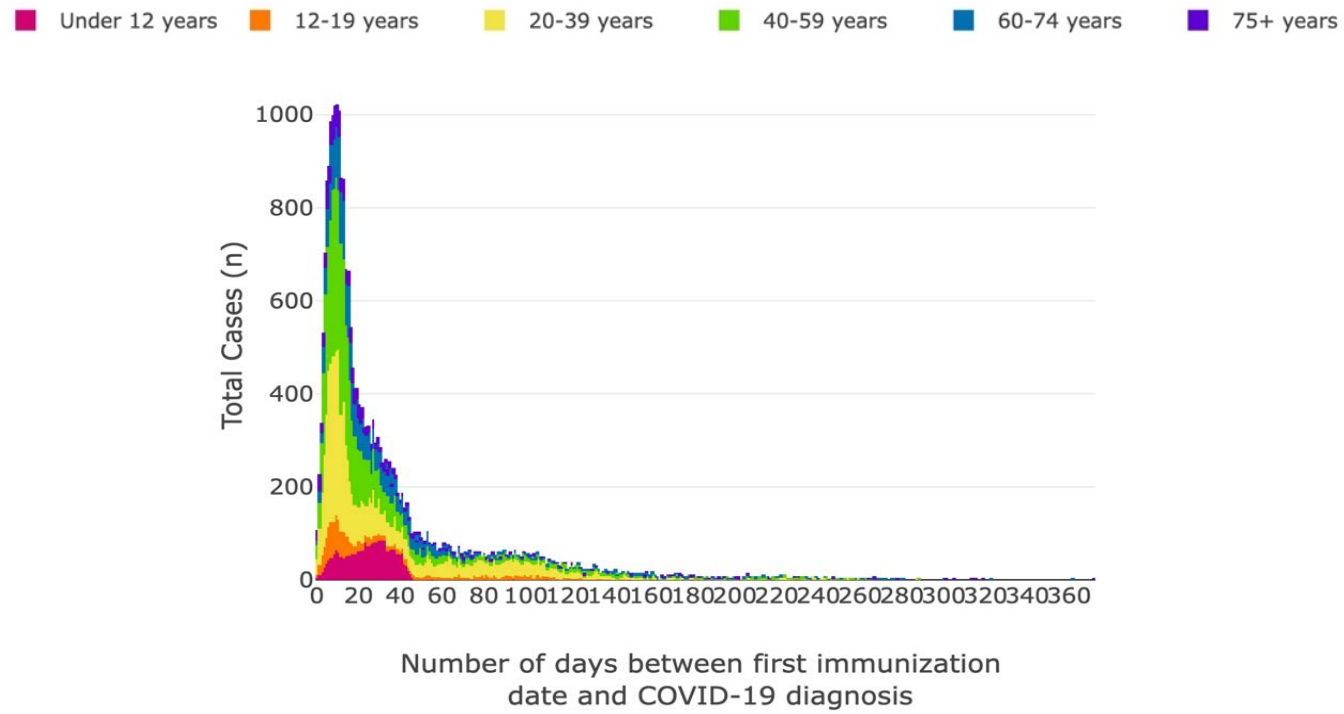
[137] (2022) Public Health Scotland COVID-19 and Winter Statistical Report. As at 14 February 2020. See Figure 16. Retrieved from https://www.publichealthscotland.scot/media/11916/22-02-16-covid19-winter_publication_report.pdf

Health website.[138] Data in tabular and graphic forms were provided for the occurrence of COVID-19 in vaccinated individuals as a function of time following vaccination that was available between August 11, 2021 and January 11, 2022 on-line. One of these figures (Figure 6 below) showed the timing of COVID-19 infections in people that were vaccinated only once. Note that this data must be recovered using the Way Back Machine website[139] as it was removed on January 11, 2022. This figure revealed a dramatic rise in COVID-19 cases in the first seven days post-inoculation. After about 9 days, the number of COVID-19 cases started to decline. It is clear that vaccination actually increased the chances of getting COVID-19 during the first two weeks. If it did not, then the rate of COVID-19 should have remained unchanged for about a week, and then it should have dropped with the development of immunity. In view of this vaccine-induced increase in COVID-19 cases within the first two weeks of the first vaccination, it is highly inappropriate to include these cases with the unvaccinated cases was routinely done by public health authorities. It renders case counts, hospital admissions, and deaths higher than they should be for the unvaccinated and makes the single vaccinated data look more favorable for vaccine-induced protection from SARS-CoV-2 infection and COVID-19 disease with vaccines. The high levels of Spike production during this initial period places a burden on the immune system that may divert it from an effective response to an actual SARS-CoV-2 infection in the airways. Antibodies and T-cells that could recognize the Spike protein, rather than targeted incoming SARS-CoV-2 virus particles, are instead preoccupied with attacking the vaccinated cells that are actively producing the Spike protein throughout the entire body.

[138] (2022) COVID-19 Alberta statistics. Interactive aggregate data on COVID-19 cases in Alberta. Government of Alberta. Retrieved for January 11, 2022 from https://web.archive.org/web/20220111010547/https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#vaccine-outcomes

[139] (2023) Internet Archive WayBack Machine. The Internet Archive. Retrieved from https://archive.org/web/

Figure 6. Timing of COVID-19 cases in Alberta following first vaccination – January 11, 2022. Reproduced by screenshot from Figure 12 on the Alberta Health website.[138]

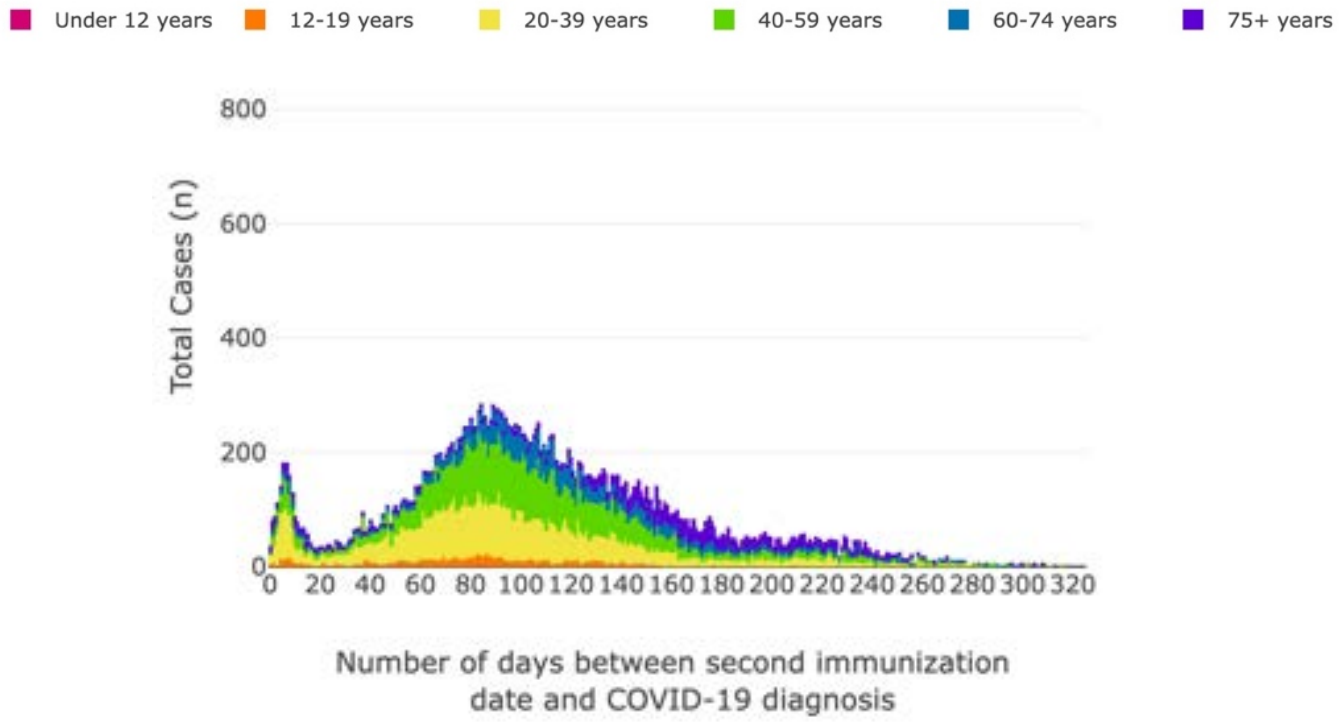


An increased risk of getting COVID-19 immediately following a second COVID-19 vaccine inoculation was also evident from the same Alberta Health website (Figure 7).[140] There was also a rise in COVID-19 cases in the first seven days. Considering that these individuals would have been vaccinated typically about 4 weeks to 6 weeks before, and should still have had peak immunity, it was surprising to see an increase in COVID-19 case counts immediately following the second shot. This likely explains why, for some people, the vaccine appeared to increase susceptibility to infection with SARS-CoV-2, which is a phenomenon also consistent with antibody-dependent enhancement (ADE). The data shown on the Alberta Health website indicated that the peak number of the COVID-19 vaccine breakthrough cases up to November 29, 2021 (just prior to the Omicron wave) occurred at around 3 months after the second shot (Figure 7). This indicated that the window of protection offered from COVID-19 by the COVID-19 vaccines for the SARS-CoV-2 Delta variant for many people was only about 3 months rather than the 6 months that was commonly stated by public health authorities. The Alberta Health website

[140] (2022) COVID-19 Alberta statistics. Interactive aggregate data on COVID-19 cases in Alberta. Government of Alberta. Retrieved for November 29, 2021 from https://web.archive.org/web/20211111180117/https://www.alberta.ca/stats/covid-19-alberta-statistics.htm#vaccine-outcomes

was one of the few such public health websites that presented such data, but it was quietly removed in January 2022.

Figure 7. Timing of COVID-19 cases in Alberta following second vaccination – November 29, 2021. Reproduced from Figure 12 on the Alberta Health website.[140] These breakthrough infections correspond to primarily Delta cases and precedes Omicron cases.



2.6.4. The Pfizer-BioNTech BNT162b2 Phase 3 Studies

The Pfizer-BioNTech BNT162b2 Phase 3 clinical studies exemplify many of the deficiencies in the general testing of the COVID-19 genetic vaccines. This vaccine was approved under Interim Order in Canada and Emergency Use Authorization in the US after just 2 months of human Phase 3 clinical data had been collected.[141] A 95.1% Relative Risk Reduction amongst the vaccinated cohort (30 µg of Spike RNA in the initial inoculation followed by a second 30 µg of Spike RNA shot 3 weeks later) relative to the unvaccinated participants was reported in the *New England Journal of Medicine (NEJM)*. The clinical trial participants were all 16 years or older, 22% were 65 years or older, but only 4.5% were 75 years

[141] Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., *et al.*; C4591001 Clinical Trial Group. (2020) Safety and efficacy of the BNT162b2 mRNA COVID-19 Vaccine. N Engl J Med. 383(27):2603–2615. doi:10.1056/NEJMoa2034577

or older. Those with more than one co-morbidity were excluded, and only 21% had a co-existing condition. A confirmed COVID-19 diagnosis was based on FDA criteria "*as the presence of at least one of the following symptoms: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, or vomiting, combined with a respiratory specimen obtained during the symptomatic period or within 4 days before or after it that was [PCR] positive for SARS-CoV-2...*"[141] There were 8 out of 21,720 vaccinated participants (0.036%) that got symptomatic COVID-19, which was also confirmed by a PCR test, 7 days to 2 months after their vaccination, compared to 162 out of 21,728 unvaccinated participants (0.7456%). This worked out to a ((0.007456-0.00036) x 100% =) 0.71% Absolute Risk Reduction of symptomatic COVID-19 and a Relative Risk Reduction of ((0.007456-0.00036)/0.007456) x 100% =) 95.2%. Following dose 1, but before dose 2, the RRR was 52.4%. In the COVID-19 vaccinated group 1 out of 8 participants (12.5%) had severe COVID-19, compared with 9 out of 162 (5.6%) in the unvaccinated group. The trial did not assess whether the COVID-19 vaccine prevented asymptomatic COVID-19 nor transmission of SARS-CoV-2. In this study, the authors did not observe an increased rate of COVID-19 in the vaccinated group compared to the unvaccinated group in the first 12 days following the first inoculation in October 2020. This contrasts with the Alberta Health data mentioned earlier that was generated from field data that was first posted in August 2021.[138] However, this may have been due to less prevalence of COVID-19 cases in the community during the Pfizer Phase 3 study than what transpired in Alberta nearly a year later.

For the 6-months stage of the same clinical Phase 3 study, Thomas *et al.* (2021), updated their clinical findings in *NEJM*, and also included data for 12- to 15-year-olds of age that were vaccinated.[133] There were 81 out of 22,166 vaccinated participants (0.365%) that got symptomatic COVID-19 confirmed by PCR 7 days to 6 months after their vaccination, compared to 873 out of 21,689 unvaccinated participants (4.025%). This worked out to a ((0.04025-0.00365) x 100% =) 3.66% ARR and a 90.7% RRR of symptomatic COVID-19. The incidence of COVID-19 apparently increased in the unvaccinated group from 81 symptomatic cases per month in the first two months of the Phase 3 study to 145.5 cases per month in the next four months of trial. However, in the double-vaccinated group, the number of symptomatic COVID-19 breakthrough cases per month increased from 4 to 20.3 in the first two months compared to the next four months. This indicated a trend toward reduced efficacy of the COVID-19 vaccine over time. Between 4 to 6 months after the second inoculation with the vaccine, the RRR with

the vaccine was reduced to 83.7%. These data indicate that for a portion of the vaccinated participants, there appeared to be an increased risk of getting COVID-19.

Some of the issues associated with the Thomas *et al.* (2021) study related to the potentially biased testing of the trial participants, since the study was unblinded to the study subjects and the researchers after 2 months into the Phase 3 trial.[142] This unblinding revealed to both the participants and the researchers who in the trial was actually inoculated and who was not with the BNT162b2 vaccine, which compromised the study and allowed the introduction of bias. The physician researchers in the study decided which participants were to be further tested by PCR to confirm COVID-19 cases. Less than 10% of the trial participants with COVID-19 symptoms were actually tested by PCR. When the suspected and confirmed cases of COVID-19 together were compared in the vaccinated (1,602/22,166 participants) and non-vaccinated (1,978/21,689 participants) populations in the 6-month Pfizer study, the RRR was actually only 19%. One has to wonder what was causing the COVID-19-like symptoms of most of the people in the vaccinated group, since the incidence of RSV and influenza in the general population had plummeted during the same period? Moreover, about 89% of the unvaccinated participants later opted to receive the COVID-19 vaccine, which effectively ended longer term evaluations of safety and efficacy with the experimental vaccines.

The 6-months Pfizer-BioNTech clinical study was performed at 153 sites world-wide, with 130 of the testing sites in the US. According to the *British Medical Journal* (*BMJ*), a former regional director Brook Jackson, who worked at one of sites that was operated by the Ventavia Research Group, alleged that "*the company falsified data, unblinded patients, employed inadequately trained vaccinators, and was slow to follow up on adverse events reported in Pfizer's pivotal phase III trial.*"[143] After repeatedly notifying Ventavia of these problems, Ms. Jackson emailed a complaint to the US FDA, and Ventavia fired her later the same day. In August 2021, after granting full approval of the Pfizer-BioNTech vaccine, the FDA reported that it had previously performed inspections at nine of the trial's 153 sites, which

[142] (2021) The Pfizer inoculations for COVID-19: More harm than good. Canadian Covid Care Alliance. https://www.canadiancovidcarealliance.org/wp-content/uploads/2021/12/The-COVID-19-Inoculations-More-Harm-Than-Good-REV-Dec-16-2021.pdf

[143] Thaker, P.D. (2021) COVID-19: Researcher blows the whistle on data integrity issues in Pfizer's vaccine trial. BMJ. 375:n2635. doi:10.1136/bmj.n2635

excluded the three Ventavia sites, but it had not undertaken any new inspections in the 8 months following the FDA's Emergency Use Authorization in December 2020.[143]

Following the release of the COVID-19 vaccines to those that were 18 years and older, Pfizer conducted an additional series of Phase 3 studies to permit the marketing of their vaccine to toddlers through to teenagers. This was based on the concept that while these age groups were at extremely low risk of severe COVID-19, they could still acquire SARS-CoV-2 infections and be highly transmissible. These were much smaller sized Phase 3 studies, and their endpoints were primarily to demonstrate that the vaccines successfully boosted anti-Spike antibody levels. Very few of the participants, even in the unvaccinated groups were actually sick with COVID-19. The number of trial participants was clearly insufficient to identify serious safety risks that may have occurred in less than one in a few thousand people.

In the first two very small *immune-bridging trials* conducted by Pfizer, fewer than 2,500 participants were enrolled. Each study was designed to establish the presence of effective neutralizing antibody concentrations in the blood of a small subset of 12- to 15-year-olds (n=190) and 5- to 11-year-olds (n=264) children compared to young adults, and provided only preliminary descriptive outcomes for clinical efficacy and safety of the Pfizer-BioNTech vaccine compared to placebo controls.[144, 145] The Phase 2/3 clinical results from testing the Pfizer-BioNTech vaccine in 1,517 children from 5- to 11-year-olds with two vaccine doses (10 µg RNA in each dose) spaced one month apart and followed for 2.3 months was compared to 751 that were treated with a placebo.[145] The mean age of the participants was 8.2 years; 20% of children had coexisting conditions (including 12% with obesity and approximately 8% with asthma), and 9% previously had SARS-CoV-2. The authors reported a RRR of 90.7% for acquiring COVID-19. However, there were only 3 presumed COVID-19 cases in total in the vaccinated group and 16 in the unvaccinated group. None of the COVID-19 cases were severe. The ARR was a mere 2% for both age groups, which were at little to no risk of developing severe COVID-19. Based on this, Health Canada authorized use of Pfizer-BioNTech COVID-19 vaccine in children 12 to 15 years of age on May

[144] Frenck, R.W., Klein, N.P., Kitchin, N., Curtman, A., Absalon, J., *et al.*; C4591001 Clinical Trial Group (2021) Safety, immunogenicity, and efficacy of the BNT162b2 COVID-19 vaccine in adolescents. N Engl J Med. 385(3):239–250. doi:10.1056/NEJMoa2107456

[145] Walter, E.B., Talaat, K.R., Sabharwal, C., Gurtman, A., Lockhart, S., *et al.*; C4591007 Clinical Trial Group (2022) Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med. 386(1):35–46. doi:10.1056/NEJMoa2116298

5, 2021, and this was followed by approval for use of this RNA vaccine (at a third of the adult dosage) for 5- to 11-year-olds on November 19, 2021.[146] Thereafter, Health Canada approved on March 17, 2022, the Moderna Spikevax COVID-19 vaccine (two doses, 50 µg RNA in each dose, four weeks apart) for 6- to 11-year-olds.[147] It should be appreciated that the amount of Spike RNA in Moderna COVID-19 vaccine for this age group of children was 67% higher than the adult dose of Spike RNA in the Pfizer-BioNTech vaccine.

On June 15, 2022, the US Food Drug Administration authorized the Pfizer-BioNTech for children 6 months or older,[148] and then similarly authorized the Moderna vaccine on July 14, 2022. In Canada, the Pfizer-BioNTech vaccine for this age group was approved on September 9, 2022, following a review by the National Advisory Committee on Immunization (NACI).[149, 150] Like the earlier Pfizer COVID-19 mRNA vaccination trials in children 5- to 11-year-olds and 12- to 15-year-olds, the studies with 2- to 4-year-olds, and 6- to 23-month-olds were also very small immuno-bridging trials, enrolling fewer than 3,000 participants in each cohort. They were "*not designed to establish the superiority of vaccination compared to naturally acquired immunity,"* but only the non-inferiority of "neutralizing" antibody concentrations in the blood of a small number of 2- to 4-year-olds (*n*=143), and 6- to 23-month-olds (*n*=82) participants compared to children that were 5- to 11-year-olds (*n*=264). Because antibody titers in the blood are not a clinically validated measure of efficacy for mucosal infections of the respiratory tract, any study claims regarding efficacy are actually speculative. Moreover, in these studies,

[146] (2021) Health Canada authorizes use of Comirnaty (the Pfizer-BioNTech COVID-19 vaccine) in children 5 to 11 years of age. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/news/2021/11/health-canada-authorizes-use-of-comirnaty-the-pfizer-biontech-covid-19-vaccine-in-children-5-to-11-years-of-age.html

[147] (2022) Health Canada authorizes use of Moderna Spikevax (50 mcg) COVID-19 vaccine in children 6 to 11 years of age. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/news/2022/03/health-canada-authorizes-use-of-the-moderna-spikevax-50-mcg-covid-19-vaccine-in-children-6-to-11-years-of-age.html

[148] (2022) Vaccines and Related Biological Products Advisory Committee June 14–15, 2022 Meeting Announcement – 06/14/2022. FDA. Retrieved from https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-june-14-15-2022-meeting-announcement

[149] (2022) National Advisory Committee on Immunization (NACI): Meetings. June 17, 2022. Public Health Agency of Canada. Retrieved from https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/meetings.html

[150] (2023) Drug and vaccine authorizations for COVID-19: List of authorized drugs, vaccines and expanded indications. Health Canada. Retrieved from https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/list-drugs.html#wb-auto-4

assessment of "neutralizing" antibodies only focused on those antibodies that block the binding of the original Wuhan strain of SARS-CoV-2 to the ACE2 protein and entry into test cells. Many of the mutations in the first Omicron variants occurred within the receptor binding domain of the Spike protein. Furthermore, over 95% of antibody responses to the SARS-CoV-2 Spike protein in both vaccinated and SARS-CoV-2-infected individuals are directed toward other regions of the Spike protein, and most of the immune protective responses are not captured by "neutralizing" antibody tests.

From 7 days to 3 months post-vaccination for those under 5 years of age, the aforementioned studies provided descriptive RRR values in symptomatic cases of COVID-19 of 82%, and 76%, respectively, for children aged 2- to 4-years-old and 6- to 23-months-old. Moreover, when outcomes were analyzed to reflect the net benefit of the vaccinations in these groups, the ARR in mild symptomatic COVID-19 was a mere 2% or lower for all groups following COVID-19 vaccination. In addition, the vaccines did not demonstrate an ability to reduce severe COVID-19 or halt transmission, rendering any claims regarding protection in the majority of children dubious. The trial was originally planned to investigate the vaccinal efficacy of two doses. Of great concern, however, were findings in the 2- to 4-year-olds cohort that showed that following the first dose, the vaccine was associated with a 199% relative risk increase in severe COVID-19 and a 149% relative risk increase in multiple COVID-19 infections compared to the placebo control subjects.[151] Astonishingly, the 76% RRR noted for 6- to 23-month-old infants was based on just three participants in this age group who tested positive for SARS-CoV-2 (1 vaccinated versus 2 placebo), and the 82% RRR based on just seven participants in the older 2–to 4-year-olds (2 vaccinated versus 5 placebo) and was only after triple vaccination of these children.

The pivotal child vaccination studies were much too short (*i.e.,* 3 months) to establish vaccinal efficacy and did not control for natural immunity. Natural immunity was only assessed by the detection of antibodies against the Nucleocapsid protein of SARS-CoV-2, which often fails to be measurable in people that have recovered from COVID-19. Moreover, the child vaccine trials were designed to test vaccines developed against the original Wuhan strain of SARS-CoV-2, which had not been in circulation for over 2 years. While this probably did not make much difference with respect to the overall immune

[151] Muñoz, F.M., Sher, L.D., Sabharwal, C., Gurtman, A., Xu, X., *et al.*; C4591007 Clinical Trial Group. (2023) Evaluation of BNT162b2 COVID-19 vaccine in children younger than 5 years of age. N Engl J Med. 2023 Feb 16;388(7):621–634. doi:10.1056/NEJMoa2211031

response to Omicron variants, this does make a difference if the serological tests narrowly rely on detection of antibodies that are "neutralizing" and just targeted the ACE2 receptor binding domain of the Spike protein.

Pregnant women were originally excluded from the earlier Pfizer-BioNTech clinical trials for their monovalent COVID-19 vaccine based on the Wuhan Spike RNA sequence. On February 18th, 2021, Pfizer-BioNTech commenced a 4,000-person Phase 2/3 study to evaluate the efficacy and safety of their vaccine on pregnant women.[152] As of December 2023, there have been no published reports from this specific trial.

2.6.5. Post-Marketing Performance of COVID-19 Vaccines

With the rollout of COVID-19 vaccines starting in December 2020, in Canada, the initial priority was to vaccinate hospital workers and those at high risk, in particular the very elderly in nursing homes, indigenous people living on reservations and those with comorbidities. A shortage of COVID-19 vaccine supply in Canada meant that most people had to wait several months after their initial vaccination to receive their second shot. This was much longer than the manufacturers' recommended 3- to 4-week interval, which was used in the Phase 3 clinical studies.

The NACI and the Canadian federal government felt that people in Indigenous communities were particularly at risk from COVID-19 and should be prioritized. This had nothing to do with any genetic differences between Indigenous and non-Indigenous people, but was because these communities had fared more poorly in past pandemics and diseases. This decision was largely political.[153] Consequently, Indigenous adults as young as 18 years old were prioritized for vaccination before non-Indigenous 70-year-old people in Canadian provinces like Ontario and British Columbia. A cynical observer might wonder why the First Nations communities would be amongst the first to receive experimental, poorly

[152] (2021) Pfizer and BioNTech commence global clinical trial to evaluate COVID-19 vaccine in pregnant women. Pfizer. Press release retrieved from https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-commence-global-clinical-trial-evaluate

[153] DeRoy-Olson, I. (2021) Why Indigenous communities are prioritized for the COVID-19 vaccine. Canadian Broadcasting Corporation Kids News. Retrieved from https://www.cbc.ca/kidsnews/post/watch-why-indigenous-communities-were-prioritized-for-the-covid-19-vaccine

tested vaccines considering the historical experimentation on these populations in North America in the past for much less altruistic reasons.

Despite the availability of COVID-19 vaccines for everyone by the summer of 2021, Canada continued to experience successive waves of COVID-19, in part from the emergence of new, more infectious variants of SARS-CoV-2. Much ado was initially expressed from health officials that it was primarily unvaccinated people who were filling the hospitals, ICU's and dying from COVID-19. Often in the late summer of 2021, provincial public health officials would state that "*since the vaccination program began in December 2020, the vast majority of hospital cases and deaths were unvaccinated*." Even US president Joseph Biden famously claimed during a town hall in Cincinnati, Ohio on July 21, 2021 that "*Ten thousand people have recently died; 9,950 of them, thereabouts, are people who hadn't been vaccinated."*[154] President Biden's comment was based on a July 1, 2021, statement by Dr. Rochelle Walensky, then the director of the US Centers for Disease Control and Prevention, that during the prior six months, 99.5% of COVID-19 deaths occurred in the unvaccinated.[155] The problem with such comments is that the vast majority of COVID-19 deaths in the previous 6 months occurred in the first couple of months of 2021 when most people were unvaccinated. One of the largest waves of COVID-19 deaths spiked in January 2021, with a smaller peak of deaths in April and May of 2021.[156] By April 3, 2021, only 13.3% of Canadians were COVID-19 vaccinated once and 1.9% vaccinated twice. By July 31, 2021, 59.2% of Canadians had been doubly vaccinated and 10.9% vaccinated only once.[157] In July 2021, with the fifth major wave of COVID-19, the number of cases and deaths slowly began to increase rather than decrease as anticipated with vaccination.

With the initial COVID-19 vaccinations applied so close to the resurgence of COVID-19 cases in the late Summer and Fall of 2021, these vaccinations were likely very effective temporarily in reducing the

[154] (2021) Joe Biden town hall in Cincinnati: Here's the full CNN transcript. The Enquirer. Retrieved from https://www.cincinnati.com/story/news/politics/2021/07/21/joe-biden-cnn-town-hall-transcript/8051311002/

[155] (2021) Press briefing by White House COVID-19 Response Team and public health officials. The White House. Retrieved from https://www.whitehouse.gov/briefing-room/press-briefings/2021/07/01/press-briefing-by-white-house-covid-19-response-team-and-public-health-officials-43/

[156] (2023) Canada COVID-19 Situation. World Health Organization. Retrieved from https://covid19.who.int/region/amro/country/ca

[157] (2023) COVID-19 vaccination: Vaccination coverage. Government of Canada Health Infobase. Retrieved from https://health-infobase.canada.ca/covid-19/vaccination-coverage/

incidence of COVID-19 hospitalization and deaths during a limited period of 3 to 6 months. However, it soon became apparent that high rates of COVID-19 vaccination in Canada, the US and elsewhere did not prevent an individual from getting COVID-19 or transmitting SARS-CoV-2 if they did become infected. Eventually, real world, in-the-field data started to reveal that these COVID-19 vaccines had limited effectiveness. At a time when vaccination should have reduced the incidence of hospitalizations and deaths from COVID-19, these actually increased in Canada and the US when compared to the pre-vaccination period in 2020.

The RNA and adenovirus COVID-19 vaccines appeared to be initially effective at inducing a strong immune response and protection from infection by SARS-CoV-2 within the first few months following an initial inoculation and a booster shot a month later. However, they clearly had waning efficacy to lower than 50% relative risk reduction by 6 months after double vaccination. This period of protection continued to decline with further boosting and started to produce negative efficacy in preventing COVID-19.

This trend was even evident in 2021. For example, one of the largest studies indicating that the effectiveness of COVID-19-injections wanes over time was conducted on more than 780,225 of the US Veteran Health Administration (VA) patients.[158] The study indicated that in a time span of around 9 months from February 1 to October 1, 2021, the ability of COVID-19 vaccines to protect from infection declined - from 86.9% to 43.3% for the Pfizer/BioNTech product, from 89.2% to 58% for the Moderna product, and from 86.4% to 13.1% for the Janssen product. For those aged 65 years and older, the ability of COVID-19 vaccines to protect from death was 70.1% for the Pfizer/BioNTech product, 75.5% for the Moderna product, and 52.2% for the Janssen product.[158] It should be appreciated that this was a passive reporting study, and included an elderly population with a high risk of death, and US veterans that have a higher rate of lifetime injury (following combat duty) and co-morbidities than the general population. The poorer performance of these vaccines in the elderly was not surprising. In the original Pfizer/BioNTech 6-month Phase 3 trial with the BNT162b2 mRNA COVID-19 vaccine, only 4% of the trial participants were 75 years of age or older, although 58% of the people at risk from death from COVID-19 were in this age group.[133]

[158] Cohn, B.A., Cirillo, P.M., Murphy, C.C., Krigbaum, N., Wallace, A.W. (2022) SARS-CoV-2 vaccine protection and deaths among US veterans during 2021. Science. 375(6578):331–336. doi:10.1126/science.abm0620

With respect to the ability of the COVID-19 vaccines to reduce the acquisition and spread of COVID-19, these vaccines have clearly failed. Early on, one study in Dane County, Wisconsin, with among the highest vaccination rates in the US at the time, indicated equally high viral loads in the vaccinated (84%) and the unvaccinated (83%) – in other words, an equal capacity of both to spread infection.[159] It is now widely accepted that COVID-19 double-vaccinated individuals can still become infected with SARS-CoV-2, develop sickness and can transmit the virus with equal viral loads as unvaccinated individuals.[160] This has been clearly expressed by Dr. Anthony Fauci, who was until the end of 2022, the Director of the US NIH National Institute for Allergy and Infectious Diseases (NIAID).[161]

One study also showed that COVID-19 vaccine boosted individuals were more likely to transmit SARS-CoV-2.[162] In this study, one-third of boosted people still carried live, culturable virus at 10 days after the beginning of the infection. This contrasted with unvaccinated people with COVID-19, of whom only 6% of the persons were still contagious at Day 10 of the same study.

British Columbia was one of the few provinces in Canada that provided breakdowns for the incidence of COVID-19 hospitalization, ICU admissions and deaths, which was regularly posted on the British Columbia Centre for Disease Control (BCCDC) website. From April to June, 2022, hospitalizations and critical care cases per 100,000 persons were at best 2-fold higher for unvaccinated as compared to double- or triple-vaccinated individuals (Figure 8).[163] Moreover, during this period, the rates of COVID-19-related deaths were fairly comparable in the vaccinated versus the unvaccinated group. This is despite the fact that deaths included all individuals with a COVID-19-positive laboratory result who had died from any cause (COVID-19 or non-COVID-19, as recorded in Vital Statistic, BC Ministry of Health,

[159] Riemersma, K.K., Haddock, L.A. 3rd, Wilson, N.A., Minor, N., Eickhoff, J., *et al.* (2022) Shedding of infectious SARS-CoV-2 despite vaccination. PLOS Pathog. 18(9):e1010876. doi:10.1371/journal.ppat.1010876

[160] Franco-Paredes, C. (2022) Transmissibility of SARS-CoV-2 among fully vaccinated individuals. Lancet Infect Dis. 22(1):16. doi:10.1016/S1473-3099(21)00768-4

[161] (2021) Dr. Fauci on COVID-19 spread: Vaccinated people who have an ... infection are capable of transmitting. Retrieved from https://www.youtube.com/watch?v=mP9iHyj1uiU

[162] Boucau, J., Marino, C., Regan, J., Uddin, R., Choudhary, M.C., *et al.* (2022) Duration of shedding of culturable virus in SARS-CoV-2 Omicron (BA.1) infection. New Engl. J. Med. 387:275-277. doi:10.1056/NEJMc2202092

[163] (2023) BCCDC COVID-19 Regional Surveillance Dashboard – Archived. BC Centre for Disease Control. Retrieved from https://public.tableau.com/app/profile/bccdc/viz/BCCDCCOVID-19RegionalSurveillanceDashboardArchived/Introduction

within 30 days of their first laboratory positive result date). In considering such data, it is important to also recognize the caveats presented earlier (Section 2.6.3). Such comparative data was no longer provided on the BCCDC website after June 23, 2022, likely because such data no longer supported the public health agency narrative. As shown in Figure 9, the data from Quebec was even worse for elderly patients that were hospitalized with a third dose of COVID-19 vaccines.[163a]

Figure 8. Age-standardized hospitalization, critical care and death rates in BC from April 17 to May 14, 2022.[163]

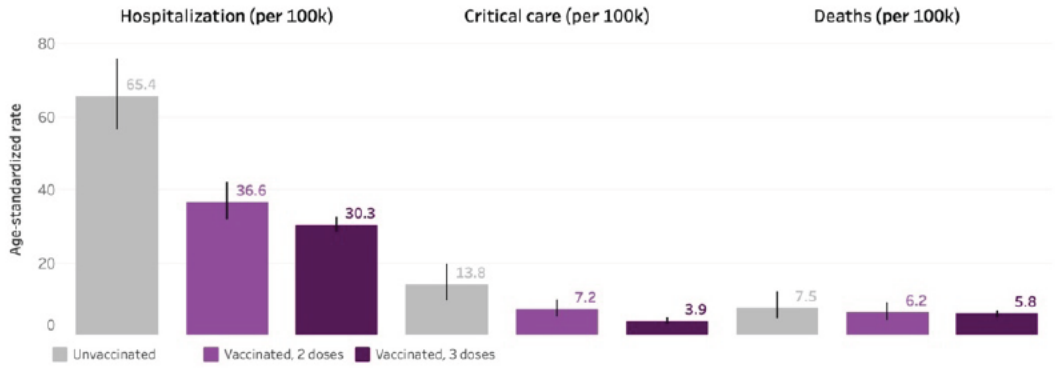
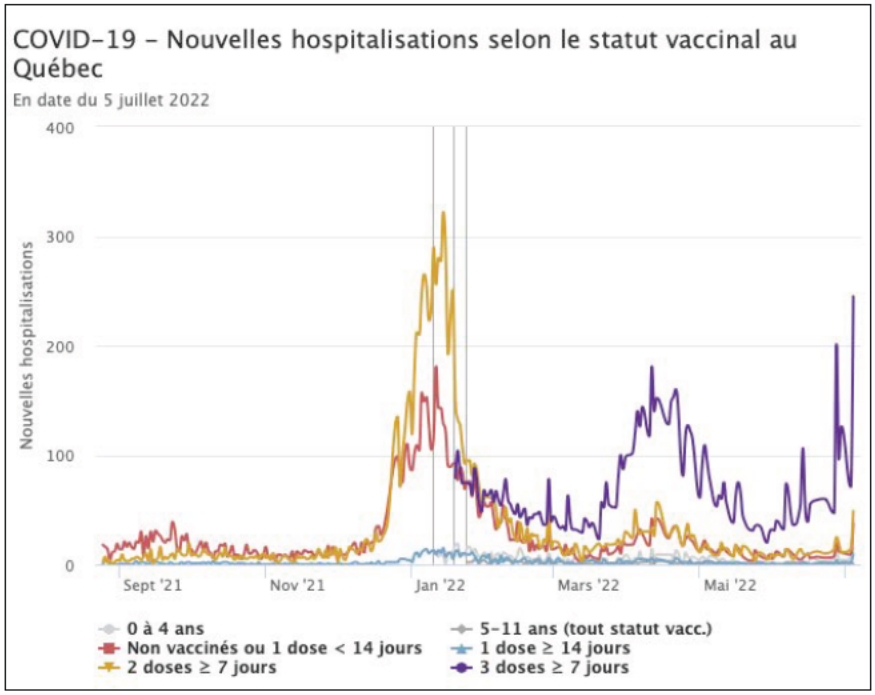


Figure 9. Quebec hospitalization data, showing a higher frequency of hospitalization in boosted patients to July 5, 2022. Retrieved from VaccinTrackerQC.[163a]



[163a] (2022) COVID-19 – Nouvelles hospitalisations selon le statut vaccinal au Quebec. July 5, 2022. Retreived from https://vaccintrackerqc.ca/cas_et_hospitalisations/#selon-le-statut-vaccinal

The phenomena of increased rates of COVID-19 cases numbers, hospitalizations and deaths in vaccinated compared to unvaccinated persons in other countries also become quite apparent in 2022 as different Omicron variants successively predominated over each other. For example, in the March 27, 2022, report of the UK Health Security Agency, using data from the Office of National Statistics, as presented in Table 13 of the report for the period of February 20 to March 13, 2022, the incidence rates of COVID-19 cases were typically 3-fold or greater for those who were at least triple vaccinated than those who were unvaccinated per 100,000 persons.[164] For those who were hospitalized or died with COVID-19, the rates between the at least triple vaccinated and unvaccinated groups for those under 50 years of age was very similar. For those over 50 years of age, there appeared to be a reduction in hospitalizations and deaths of up to 3-fold with 3 or more vaccinations, but it was likely that these individuals were just recently vaccinated and did experience some temporary protection. Interestingly, no data was provided on the COVID-19 cases numbers, hospitalizations or deaths for those who had only one or two doses of a COVID-19 vaccine in Table 13 of the same report. It can be calculated based on the data presented in the earlier Tables 10, 11 and 12 in the same report. In these tables, the numbers of COVID-19 cases, hospitalization and deaths were either higher or comparable in the population over 18 years of age who received only two vaccine doses compared to those that were not vaccinated. A footnote was added to Table 14 of the report that stated "*Comparing case rates among vaccinated and unvaccinated populations should not be used to estimate vaccine effectiveness against COVID-19 infection*."[165] However, such data was quick to be used when it appeared to support COVID-19 vaccination earlier on. The surveillance reports stopped providing this information after March 2022. Collection of such information after April 1, 2022, became limited as free COVID-19 testing was suspended by the UK government. It would seem that the epidemiology data no longer supported the UK Health Security Agency narrative of COVID-19 vaccine efficacy and was no longer presented.

[164] (2022) COVID-19 vaccine surveillance report. Week 11. UK Health Security Agency. https://assets.publishing.service.gov.uk/media/623310c88fa8f504a316aa21/Vaccine_surveillance_report_-_week_11.pdf

[165] (2023) UKHSA vaccine efficacy data stopped after new footnote added. Jikkyleaks on Twitter. Retrieved from https://twitter.com/Jikkyleaks/status/1675005411014107136

Careful analysis of studies claiming vaccine efficacy against hospitalization and death from COVID-19 have indicated that they are systemically flawed and biased.[166] Responses to FOIs requesting hospitalization rated by vaccination status data inevitably reveal disproportionately higher rates among the vaccinated. For example, Public Health Wales confirmed that in the first two weeks of October 2021, 2.5% of hospitalized patients aged 60+ were unvaccinated compared with 96% that were double vaccinated.[167] This would be during the period in which the delta variant of SARS-CoV-2 predominated, prior to prevalence of Omicron variants. Consequently, reduced immune recognition of Omicron variants does not explain why so many COVID-19 vaccinated people were hospitalized.

Large scale studies of COVID-19 vaccination in children have shown extremely poor efficacy for the RNA vaccines. In one study of 74,208 children and adolescents aged 5 to 11 years at 6,897 sites across the US, the estimated vaccine effectiveness (VE) to reduce COVID-19 incidence was only 60.1% one month after the second dose and 28.9% after two months.[168]

In another study conducted in New York State with 365,502 fully vaccinated children 5- to 11-years-old after the emergence of Omicron BA.1, VE was only 12% after 5 weeks after inoculation.[169]

2.6.6. Keeping up with "Variants of Concern"

It has been commonly suggested that inoculation with COVID-19 vaccines based on the structure of the original Wuhan strain of SARS-CoV-2 renders the antibodies that are produced much less effective against the Omicron variants. This appears to be incorrect based on several points:

a. The overall difference in amino acid structure between the Spike proteins of the Wuhan and Omicron strains is only 3% (*i.e.,* ~34 mutated amino acids out of 1273 amino acids in the whole

[166] Fenton, N.E. and Neil, M. (2023) Claims the unvaccinated were at higher risk of hospitalisation and death were based on deliberately murky record keeping. 2023. Substack. Retrieved from https://wherearethenumbers.substack.com/p/claims-the-unvaccinated-were-at-higher

[167] (2022) COVID hospitalisation rates. Public Health Wales. Retrieved from https://www.gov.wales/atisn16308

[168] Fleming-Dutra, K.E., Britton, A., Shang, N., Derado, G., Link-Gelles, R., *et al.* (2022) Association of prior BNT162b2 COVID-19 vaccination with symptomatic SARS-CoV-2 infection in children and adolescents during Omicron predominance. JAMA. 327(22):2210–2219. doi:10.1001/jama.2022.7493

[169] Dorabawila, V., Hoefer, D., Bauer, U.E., Bassett, M.T., Lutterloh, E., Rosenberg, E.S. (2022) Effectiveness of the BNT162b2 vaccine among children 5–11 and 12–17 years in New York after the emergence of the Omicron variant. medRxiv (preprint). doi:10.1101/2022.02.25.22271454

protein). Recovered COVID-19 survivors each generate antibodies against scores of different parts of the Spike protein;

b. The actual regions that most people tend to make antibodies against the Spike protein are largely distinct from where the Omicron mutations occur;

c. The vaccines that are produced with the Wuhan Spike protein RNA are still effective, at least initially for reducing Omicron infections in vaccinated people, so the antibodies that are produced must still recognize the Omicron variants;

d. RNA vaccines that are based on the Omicron Spike protein, when tested in monkeys and other animals, gave no better immune protection against COVID-19 than RNA vaccines based on the Wuhan Spike protein amino acid sequence.[170, 171, 172 , 173] Note that some studies observed a decline in "neutralizing" antibodies that specifically target the ACE2 receptor binding domain of the Spike protein.[53, 54] However, most protective antibodies can still permit the tagging of viruses and bacteria for their efficient recognition by immune cells and the complement system, which leads to their destruction; and

e. The fact that previously infected people get milder symptoms with Omicron variants and are able to more quickly recover from these variants clearly shows the capacity of the immune system of these individuals to recognize and neutralize the Omicron variants.

[170] Gagne, M., Moliva, J.I., Foulds, K.E., Andrew, S.F., Flynn, B.J., *et al.* (2022) mRNA-1273 or mRNA-Omicron boost in vaccinated macaques elicits comparable B cell expansion, neutralizing antibodies and protection against Omicron. bioRxiv (preprint). doi:10.1101/2022.02.03.479037

[171] Ying, B., Scheaffer, S.M., Whitener, B., Liang, C-Y., Dymtrenko, O., *et al.* (2022) Boosting with Omicron-matched or historical mRNA vaccines increases neutralizing antibody responses and protection against B.1.1.529 infection in mice. bioRxiv (preprint). doi:10.1101/2022.02.07.479419

[172] Hawman, D.W., Meade-White, K., Clancy, C., Archer, J., Hinkley, T., *et al.* (2022) Replicating RNA platform enables rapid response to the SARS-CoV-2 Omicron variant and elicits enhanced protection in naïve hamsters compared to ancestral vaccine. bioRxiv (preprint). doi:10.1101/2022.01.31.478520

[173] Lee, I.-J., Sun, C.-P., Wu, P.-Y., Lan, Y.-H., Wang, I.-H., *et al.* (2022) Omicron-specific mRNA vaccine induced potent neutralizing antibody against Omicron but not other SARS-CoV-2 variants. bioRxiv (preprint). doi:10.1101/2022.01.31.478406

In a large study with the Moderna mRNA-1273 COVID-19 vaccine, the VE of booster shots against Omicron variants was assessed.[174] The study included 30,809 SARS-CoV-2-positive and 92,427 SARS-CoV-2-negative individuals aged 18-years and older, tested during the January 1 to June 30, 2022 period. While three-dose VE against BA.1 infection was high and waned slowly, VE against BA.2, BA.2.12.1, BA.4, and BA.5 infection was initially moderate to high (61.0%-90.6% 14-30 days post third dose) and waned rapidly. The four-dose VE's against infection with BA.2, BA.2.12.1, and BA.4 ranged between 64.3%-75.7%, was low (30.8%) against BA.5 14-30 days post fourth dose, and was lost beyond 90-days for all subvariants. The three-dose VE's against hospitalization for BA.1, BA.2, and BA.4/BA.5 was 97.5%, 82.0%, and 72.4%, respectively; four-dose VE against hospitalization for BA.4/BA.5 was 88.5%. In analyses of three-dose VE (versus unvaccinated) against infection with Omicron subvariants by time since vaccination, the three-dose VE's against BA.1 ranged from 85.8% in the 14–30 days after the third dose to 54.9% greater than 150 days after the third dose. VE's for these two different time intervals, respectively, were 61.0% and −24.9% for BA.2, 82.7% and −26.8% for BA.2.12.1; 72.6% and −16.4% for BA.4; and 90.6% and −17.9% for BA.5. Thus, there was a clear trend to negative efficacy by 5 months after the third dose for the various Omicron variants that followed BA.1.

With the predominance of Omicron variants of SARS-CoV-2 in late 2021, there was a large number of breakthrough cases of COVID-19 in those who were double-vaccinated, which exceeded the total numbers of unvaccinated persons with COVID-19. To offset the relative loss of efficacy of the original COVID-19 vaccines with the Omicron variants, new bivalent COVID-19 vaccines were tested in clinical studies that use a combination of mRNA for the original Wuhan Spike protein and the Omicron BA.1 variant Spike protein.[175] This was despite the fact that the Wuhan SARS-CoV-2 virus and even the Omicron BA.1 variant were already supplanted by the Omicron BA.4 and BA.5 variants. On August 31, 2022, bivalent COVID-19 vaccines from Moderna and Pfizer/BioNTech that include mRNA for the Wuhan Spike protein and a variant that features the mutations in the BA.4 and BA.5 lineages of Omicron were

[174] Tseng, H.F., Ackerson, B.K., Bruxvoort, K.J., Sy, L.S., Tubert, J.E., *et al.* (2023) Effectiveness of mRNA-1273 vaccination against SARS-CoV-2 omicron subvariants BA.1, BA.2, BA.2.12.1, BA.4, and BA.5. Nat Commun. 14(1):189. doi:10.1038/s41467-023-35815-7

[175] Chalkias, S., Harper, C., Vrbicky, K., Walsh, S.R., Essink, B., *et al.* (2022) A bivalent omicron-containing booster vaccine against COVID-19. New Eng. J. Med. 387(14):1279–1291. doi:10.1056/NEJMoa2208343

approved by the FDA based only on pre-clinical studies in mice.[176] At the same time, monovalent vaccines based on the original Wuhan Spike protein were no longer authorized as booster doses for individuals 12 years or age and older. It is noteworthy that the Pfizer bivalent COVID-19 vaccine was approved based on studies with only 8 mice for their efficacy in producing "neutralizing" antibodies that blocked Omicron BA.4 and BA.5 Spike protein binding to ACE2.[177] From a safety standpoint, the Wuhan SARS-CoV-2 Spike protein is not capable of binding to mouse or rat ACE2, so evaluation of Spike protein toxicity was highly compromised in these animal models.[178] Data from no other animal model or humans was presented to the FDA by these manufactures for these particular bivalent vaccines prior to their approval.[177]

More recent studies have continued to reveal negative efficacy associated with the booster vaccines. From COVID-19 surveillance data from January to July 2023 across 33 California state prisons, primarily a male population of 96,201 individuals, the incidence rate of new COVID-19 infections among COVID-19-bivalent-vaccinated and entirely unvaccinated groups (those not having received either the bivalent or monovalent vaccine) was compared.[179] The authors noted the infection rates in the bivalent-vaccinated and entirely unvaccinated groups were 3.24% and 2.72%, respectively, with an absolute risk difference of only 0.52%. Among those aged 65 years and above, the infection rates were 6.45% and 4.5%, respectively, with an absolute risk difference of 1.95%. The bivalent-vaccinated group had a slightly but statistically significantly higher infection rate than the unvaccinated group in the statewide category and for those aged 50 years and above.[179]

One of the most devastating studies that challenged the wisdom of booster COVID-19 vaccines for reducing COVID-19 was performed on 51,017 employees of the Cleveland Clinic who were tracked for

[176] (2022) Coronavirus (COVID-19) update: FDA authorizes Moderna, Pfizer-BioNTech bivalent COVID-19 vaccines for use as booster dose. US Food and Drug Administration. Retrieved from https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-pfizer-biontech-bivalent-covid-19-vaccines-use

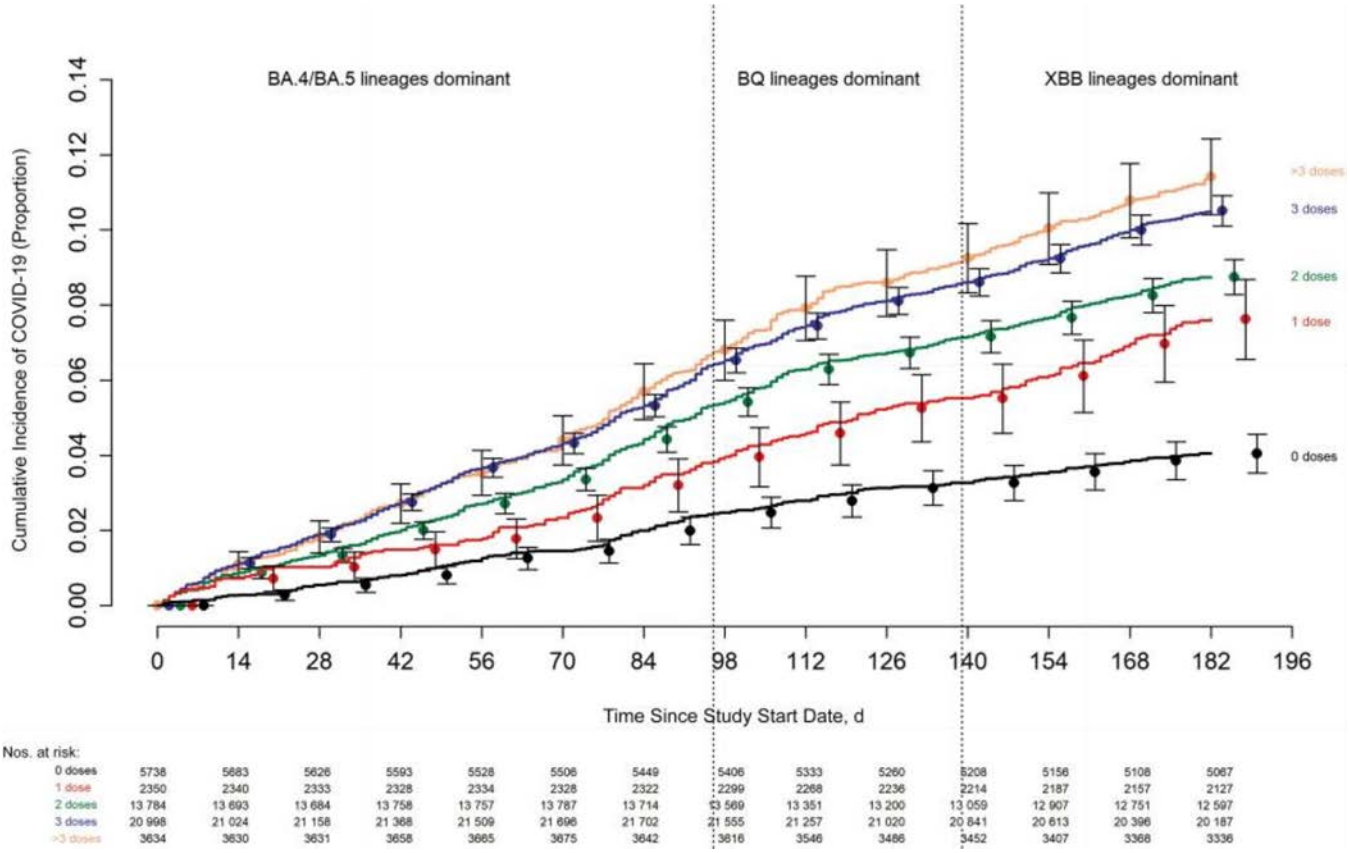
[177] Vogel, G. (2022) Omicron booster shots are coming – with lots of questions. Science. 377(6610):1029–1030. doi:10.1126/science.ade6580

[178] Rawle, D.J., Le, T.T., Dumenil, T., Yan, K., Tang, B., *et al.* (2022) ACE2-lentiviral transduction enables mouse SARS-CoV-2 infection and mapping of receptor interactions. PLOS Pathog. 17(7):e1009723. doi:10.1371/journal.ppat.1009723

[179] Ko, L., Malet, G., Chang, L.L., Nguyen, H., Mayes, R. (2023) COVID-19 infection rates in vaccinated and unvaccinated inmates: A retrospective cohort study. Cureus. 15(9):e44684. doi:10.7759/cureus.44684

VE of the bivalent COVID-19 vaccines over a 6-months period that started September 12, 2022.[180] The bivalent-vaccines were associated with a VE of 29% of COVID-19 during the BA.4/5-dominant phase, a VE of 20% in the BQ-dominant phase, and a VE of 4% during the XBB-dominant phase. What was particularly striking from the study was that the risk of getting COVID-19 increased successively with each vaccination up to four COVID-19 vaccine doses, with the lowest risk for COVID-19 by far in the unvaccinated employees (Figure 10).

Figure 10. Cumulative incidence of COVID-19 cases for Cleveland Clinic study participants stratified by the number of COVID-19 vaccine doses previously received. Day 0 was September 12, 2022, the date the bivalent vaccine was first offered to Cleveland Clinic employees. Point estimates and 95% confidence intervals are jittered along the x-axis to improve visibility. Reproduced from Figure 2 of Shreshtha *et al.* (2023).[180]



[180] Shrestha, N.K., Burke, P.C., Nowacki, A.S., Simon J.F., Hagen, A., Gordon, S.M. (2023) Effectiveness of the coronavirus disease 2019 bivalent vaccine. Open Forum Infect Dis. 10(6):ofad209. doi:10.1093/ofid/ofad209

On June 15th, 2023, the US FDA's Vaccines and Related Biological Products Advisory Committee met to discuss their recommendations for the next COVID-19 booster vaccine for Fall of 2023.[181] Presentations from Pfizer, Moderna, Novavax, the NIH and the FDA all documented that the bivalent Wuhan/BA.4/5 vaccines failed to produce neutralizing antibodies that would block the binding of the Spike protein of Omicron XBB variants to ACE2. Ultimately, the Committee recommended that these companies should focus on development of a monovalent vaccine that targeted the Spike protein of the XXB.1.5 variant. The XXB.1.5 variant was largely supplanted by newer variants such as EG.5 by the time the XXB.1.5 Spike protein-based COVID-19 vaccines were launched in September, 2023. With the focus on neutralizing antibodies against the Spike protein by industry and government agencies for assessing the effectiveness of vaccines, this undervalues the actual effectiveness of natural immunity and older COVID-19 vaccines against the earlier SARS-CoV-2 strains to prevent COVID-19 and reduce illness.

Collectively, all of these findings seriously call into question the wisdom of vaccination of youth and most working adults considering that they are already at such low risk of hospitalization and death from COVID-19, especially in view of the poor and even negative efficacy of these COVID-19 genetic vaccines, and their potential for vaccine injury in the short and long term. In fact, from a Freedom of Information request in Israel, with a population of 9.4 million, it was determined that only 356 people between ages 18 to 49 died with COVID-19 during the COVID-19 pandemic up to May 29, 2023.[182] Of the 27 people for which full data was available, none of them died from COVID-19, but instead from other comorbidities.

2.6.7. Age Demographic of COVID-19 Cases, Hospital Admissions, ICU Admissions and Deaths in Canada

Despite the risk of potentially serious symptoms and complications of COVID-19 including death, many Canadians remained completely asymptomatic following infection with SARS-CoV-2. According to Statistics Canada, by August 2022, 98% of Canadians had antibodies against the SARS-CoV-2 and 54%

[181] (2023) 182nd meeting of Vaccines and Related Biological Products Advisory Committee. June 15, 20123. US Food and Drug Administration. Retrieved from https://www.youtube.com/watch?v=gBOyPREXGh8

[182] Monk, E. (2023) Is it really true that no healthy under 50s died from COVID-19 in Israel? West Country Voices. Retrieved from https://www.westcountryvoices.com/is-it-really-true-that-no-healthy-under-50s-died-from-covid-19-in-israel/

had clear serological evidence of a natural infection with the virus.[183] Moreover, about 41% of adult Canadians and most children following infection developed immunity without any symptoms of COVID-19, *i.e*., they were asymptomatic. Clearly, those in the lower age groups are at much lower risk of hospitalization, ICU admissions and deaths than the elderly. Table 1 provides an assessment of the risks by Health Canada. The actual risks are at least an order of magnitude (*i.e.,* 10-times) lower than these estimates, because Health Canada numbers are based on less than 10% of Canadians recorded as having had COVID-19, whereas, serological testing indicates 50 to 90% of the population have antibodies that support prior infection with SARS-CoV-2. Furthermore, as much as half of recorded hospitalizations, ICU admissions and deaths were from individuals that came to hospital initially for reasons distinct from COVID-19[184, 185] Another issue is that there are 4.2-times fewer ICU admissions than recorded deaths with COVID-19 for those over age 80 years in Table 1. On top of this, the current Omicron variants of SARS-CoV-2 induce less severe clinical disease and are accompanied by lower rates of hospitalizations, ICU admissions and deaths from COVID-19 than seen with the earlier variants.[186] Overall, considering that close to 90% of around 40 million Canadians have had COVID-19 at least once, and 35,079 deaths have been attributed to this disease, its average rate of lethality is close to 1 in 1000, with it being closer to 1 in 100,000 for those from 0 to 25 years of age, and 1 in 200 for those over 65 years of age. This is a far cry from the average lethality estimates of COVID-19 that ranged from 1% to 4% from more commonly cited estimates.[187]

[183] (2023) Between April and August 2022, 98% of Canadians had antibodies against COVID-19 and 54% had antibodies from a previous infection. Statistics Canada. Retrieved from https://www150.statcan.gc.ca/n1/daily-quotidien/230327/dq230327b-eng.htm

[184] Klann, J.G., Strasser, Z.H., Hutch, M.R., Kennedy, C.J., Marwaha, J.S., *et al*.; Consortium for Clinical Characterization of COVID-19 by EHR (4CE). (2022) Distinguishing admissions specifically for COVID-19 from incidental SARS-CoV-2 admissions: National retrospective electronic health record study. J Med Internet Res. 24(5):e37931. doi:10.2196/37931

[185] Carrigg, D. (2022) Majority of new COVID-19 hospitalizations in B.C. among people admitted for other reasons. The Vancouver Sun. Retrieved from https://vancouversun.com/news/local-news/majority-of-new-covid-19-hospitalizations-among-people-admitted-for-other-reasons

[186] Lewnard, J.A., Hong, V.X., Patel, M.M., Kahn, R., Lipsitch, M. Tartof, S.Y. (2022) Clinical outcomes associated with SARS-CoV-2 Omicron (B.1.1.529) variant and BA.1/BA.1.1 or BA.2 subvariant infection in southern California. Nat Med. 28(9):1933–1943. doi:10.1038/s41591-022-01887-z

[187] (2023) Mortality Analysis. John Hopkins University of Medicine Coronavirus Resource Center. Retrieved from https://coronavirus.jhu.edu/data/mortality

Table 1. Cumulative risks of COVID-19 cases, hospitalizations, ICU admissions and deaths by age in Canada since the start of the COVID-19 pandemic to September 6, 2023.[188]

Age Group (Years)	Cases	Hospitali-zations	Hospitali-zations %	ICU Admissions	ICU Admissions %	Deaths	Deaths %
0-11	420,604	7,358	1.75	759	0.18	47	0.011
12-19	329,710	2,733	0.83	310	0.09	18	0.005
20-29	750,597	9,923	1.32	1,071	0.14	125	0.017
30-39	724,796	14,763	2.04	2,025	0.28	308	0.042
40-49	637,143	15,742	2.47	3,244	0.51	664	0.104
50-59	553,316	25,445	4.6	6,086	1.1	1,744	0.315
60-69	370,316	39,211	10.59	8,905	2.4	4,144	1.119
70-79	258,163	53,823	20.85	8,630	3.34	7,776	3.012
80+	347,257	80,501	23.18	4,860	1.4	20,253	5.832
All groups	4,391,902	249,499	5.68	35,890	0.82	35,079	0.799

2.6.8. Development of Tolerance

The apparent reduction in immune recognition following repeated large exposures to an immunogen is a classic response known as development of tolerance. It is the way in which the immune system learns to recognize self and common benign substances in the environment from new and potentially dangerous ones. Repeated booster injections over several years of large amounts of Spike mRNA, for what is essentially a protein that is 97% identical, is a recipe for immune tolerance and can account for the waning efficacy of the COVID-19 vaccines. This likely explains why highly vaccinated individuals can still suffer frequent re-infections. They have essentially damaged their natural immunity against the SARS-CoV-2 virus and potentially other coronaviruses.

With initial COVID-19 vaccinations, the primary response is the production of antibodies of the proinflammatory IgG1 and IgG3 classes, which provide immune protection against the SARS-CoV-2 virus. However, especially with more than two COVID-19 inoculations, there is a shift to the production

[188] (2023) COVID-19 epidemiology update: Summary. Health Infobase. Public Health Agency of Canada. Retrieved from https://health-infobase.canada.ca/src/data/Covidlive/epidemiological-summary-of-Covid-19-cases-in-Canada-Canada.ca.pdf

of IgG2 and IgG4 class antibodies, which confer immune tolerance.[189, 190, 191] IgG4 antibody class switching can be induced by excessive antigen concentration and prolonged exposure to an antigen, repeated vaccination, and the type of vaccine used. Elevated IgG4 levels appear to have a protective role through prevention of immune over-activation. IgG4 has a more non-inflammatory character than IgG1 and IgG3, with reduced affinity to most FcγRs and C1q (Figure 3), and much reduced potential for antibody-dependent cellular cytotoxicity (ADCC) and C1q complement-mediated killing of cells that have antigen-antibody complexes on their surfaces. IgG4 antibodies also uniquely undergoes structural changes that render them to be functionally monovalent and unable to form immune complexes. Immunosuppressive drugs been shown to have a minor inhibitory effect on the production of IgG4 antibodies after a third COVID-19 mRNA vaccine inoculation, and the production of interleukins 4 and 13 as well as tumor necrosis factor-alpha were implicated to have roles in IgG4 class switching.[192]

The development of tolerance is even more problematic when one considered that most people in B.C., more than a year into the COVID-19 pandemic already had antibodies that could recognize SARS-CoV-2 Spike and its other proteins. When 1600 participants in the Kinexus Bioinformatics COVID-19 Antibody Clinical Study, all of which had COVID-19-like symptoms and tested positive for SARS-CoV-2-directed antibodies, were asked when they first experienced these symptoms, about three-quarters of them reported having them between November 2019 and March 2020 (see Figure 11). This high rate of infection of British Columbians with SARS-CoV-2 very early in the COVID-19 pandemic was also indicated in a peer-reviewed study that was published in the flagship journal of the American Society for Clinical Investigation *JCI Insights*.[1] In this study performed in collaboration with the BC Children's Hospital Research Centre, we reported that in May of 2020, 90% of 276 healthy tested adults had antibodies that recognized the SARS-CoV-2 antibodies using the Kinexus tests as well as an

[189] Uversky, V.N., Redwan, E.M., Makis, W., Rubio-Casillas, A. (2023) IgG4 antibodies induced by repeated vaccination may generate immune tolerance to the SARS-CoV-2 spike protein. Vaccines (Basel). 11(5):991. doi:10.3390/vaccines11050991

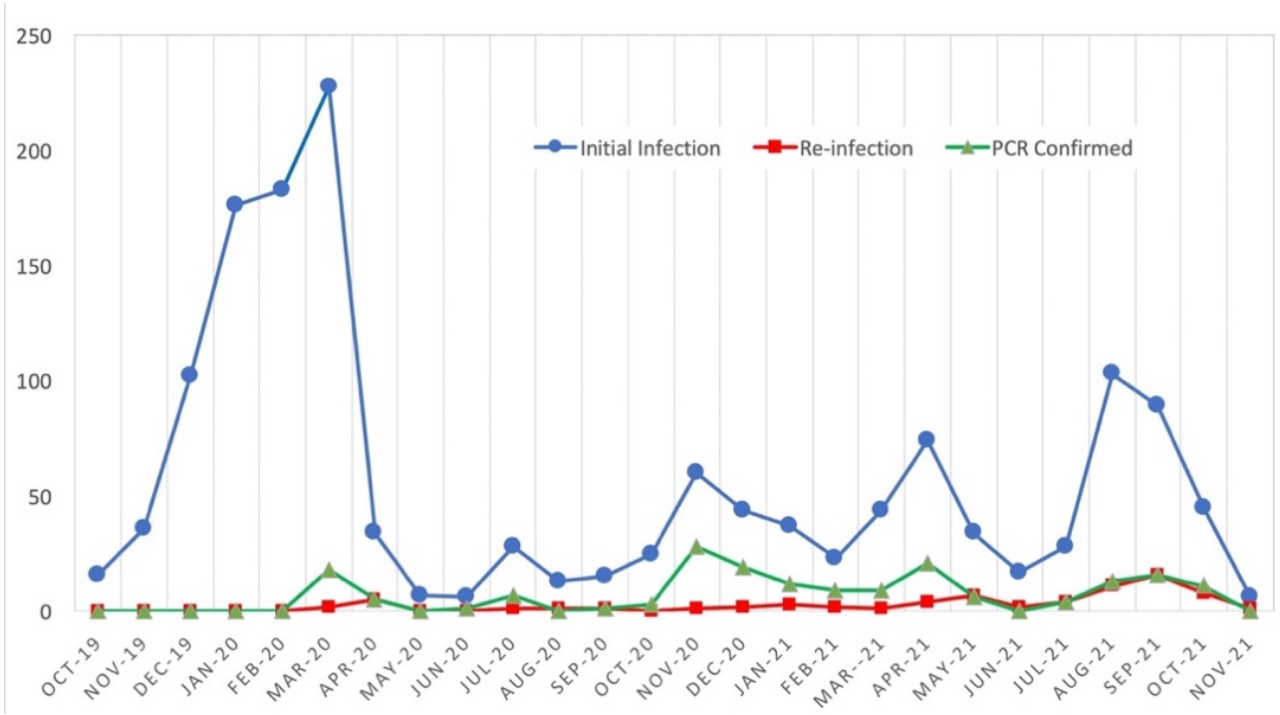
[190] Irrgang, P., Gerling, J., Kocher, K., Lapuente, D., Steininger, P., *et al.* (2023) Class switch toward noninflammatory, spike-specific IgG4 antibodies after repeated SARS-CoV-2 mRNA vaccination. Sci Immunol. 8(79):eade2798. doi:10.1126/sciimmunol.ade2798

[191] Kiszel, P., Sík, P., Miklós, J., Kajdácsi, E., Sinkovits, G., *et al.* (2023) Class switch towards spike protein-specific IgG4 antibodies after SARS-CoV-2 mRNA vaccination depends on prior infection history. Sci Rep. 13(1):13166. doi:10.1038/s41598-023

[192] Valk, A.M., Keijer, J.B.D., van Dam, K.P.J., Stalman, E.W., Wieske, L., *et al.* (2023) Suppressed IgG4 class switching in dupilumab- and TNF inhibitor-treated patients after repeated SARS-CoV-2 mRNA vaccination. medRxiv (preprint). doi:10.1101/2023.09.29.23296354

independent test developed by MesoScale Devices for SARS-CoV-2 antibodies against the Spike and Nucleocapsid proteins.[1] Interestingly, while the British Columbia and other provincial health authorities discounted natural immunity in the issuing of vaccine passports, the BC COVID Therapeutics Committee in their "Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19" stated that "*previous infection alone is equivalent to 2-dose vaccination*."[193] Thus, for most people, when they received their first dose of a COVID-19 vaccine, it was already like a booster dose for the Spike protein antibodies. The original COVID-19 vaccine clinical trials never tested for the effects of the vaccine on people who had already recovered from COVID-19, nor was the efficacy of the vaccine compared to natural immunity in Phase 3 trials.

Figure 11. Number of monthly symptomatic COVID-19 cases reports in the Kinexus SARS-CoV-2 antibody testing study from October 2019 to November 2021. The number of first cases with COVID-19 symptoms each month are shown (circles), including those that were confirmed by PCR (triangles) and apparently with a second bout of COVID-19 (squares).



[193] http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/ClinicalPracticeGuide_Therapeutics_MildModerateCOVID.pdf

The accumulating evidence has shown that the COVID-19 genetic vaccines had limited efficacy, and when used repeatedly, may actually damage the immune response towards negative efficacy. On this basis alone, the continued use of these genetic products must be called into question. In the next section, the safety of these vaccines is further investigated and found to be problematic too. This skews the benefit versus risk ratio for most people with respect to COVID-19 vaccines.

2.7. Safety Studies for COVID-19 Vaccines

Ultimately, the decision to approve a drug or vaccine for general use is based on the level of the severity of the disease, and on the safety and effectiveness of the treatment. COVID-19 was a potentially life-threatening disease for especially the elderly and those with multi-comorbidities. As presented in Section 2.5, the production of COVID-19 genetic vaccines had major issues, and in Section 2.6, these products were shown to have fleeting and even negative efficacy. In the following sections, the issue of the safety of these vaccines is given closer scrutiny. The Spike protein produced by the COVID-19 vaccines or SARS-CoV-2 is now well recognized to be pathogenic on its own.[194] Thus, high levels of Spike production in the human body with the vaccines might be expected to have negative consequences *a priori*.

2.7.1. Pre-clinical Safety Studies

With COVID-19 mRNA or DNA vaccinations, the genetic information to manufacture the Spike protein of SARS-CoV-2 is initially injected into the deltoid muscle area. From there, the lipid nanoparticle or adenovirus carriers do not remain localized, but instead disseminate throughout the body and may result in Spike production by various tissues and organs. Previous animal studies have highlighted the potential of lipid nanoparticle carriers to widely spread throughout the body, particularly as shown in earlier mice and rat studies with their accumulation in the ovaries.[195] While biodistribution data is lacking for the actual COVID-19 mRNA vaccines in animal and human studies, Pfizer did submit data to regulatory agencies in their bid for approval of their COVID-19 mRNA vaccine BNT162b2. This

[194] Parry, P.I., Lefringhausen, A., Turni, C., Neil, C.J., Cosford, R., *et al.* (2023) "Spikeopathy": COVID-19 spike protein is athogenic, from both virus and vaccine mRNA. Biomedicines11(8):2287. doi:10.3390/biomedicines11082287

[195] Schädlich, A., Hoffmann, S., Mueller, T., Caysa, H., Rose, C., *et al.* (2012) Accumulation of nanocarriers in the ovary: A neglected toxicity risk? J Control Release. 160(1):105–112. doi:10.1016/j.jconrel.2012.02.012

information first came to the attention of the public from translated documents recovered from the Japanese government regulatory bodies through the efforts of Dr. Byram Bridle of the Canadian Citizens Care Alliance.[196] The same data were later evident from Pfizer submissions to the European Medicines Agency (see page 47 of the EMA Assessment report for Comirnaty),[197] and most likely were available to the US FDA and Health Canada. These biodistribution studies (undertaken by the Canadian developer of the lipid nanoparticles Acuitas Therapeutics) performed in rats using lipid nanoparticles with a similar formulation to those used in the Pfizer/BioNTech vaccine demonstrated that they travel practically throughout the entire body, with accumulation in many tissues and organs, especially the liver, spleen, adrenals and ovaries, over the 48-hour study window, after which the experiments were terminated. These lipid nanoparticles also traversed the blood brain barrier.[196]

By not performing pharmacokinetic, and distribution studies of the encoded Spike protein, which was already known to be toxic and bioactive (off-target effects), the regulatory submissions of the mRNA vaccines were incomplete. It is also problematic that the rodent studies conducted to evaluate the toxicity of the Spike protein, when it was produced, were compromised by the fact that the Spike protein was based on the structure of Wuhan version, and the receptor binding domain of the original strain of the SARS-CoV-2 poorly interacts with the ACE2 protein in laboratory rats and mice, although later variants of SARS-CoV-2 virus developed the ability to infect these rodents.[198, 199] The Wuhan version of SARS-CoV-2 more readily infects Syrian golden hamsters, so this animal model would have been better suited for earlier testing for toxic effects of Spike protein production from the COVID-19 vaccines.[200]

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[196] (2021) SARS-CoV-2 mRNA Vaccine (BNT162, PF-07302048) 2.6.4 薬物動態試験の概要文 (translation: "Summary of pharmacokinetic study"). Retrieved from https://pandemictimeline.com/wp-content/uploads/2021/07/Pfizer-report_Japanese-government.pdf

[197] (2021) Assessment report: Cromirnaty. European Medicines Agency. Retrieved from https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf

[198] Yao, W., Ma, D., Wang, H., Tang, X., Du, C., *et al.* (2021) Effect of SARS-CoV-2 spike mutations on animal ACE2 usage and *in vitro* neutralization sensitivity. bioRxiv (preprint). 2021.01.27.428353. doi:10.1101/2021.01.27.428353

[199] Zhang, C., Cui, H., Li, E., Guo, Z., Wang, T., *et al.* (2022) The SARS-CoV-2 B.1.351 variant can transmit in rats but not in mice. Front Immunol. 13:869809. doi:10.3389/fimmu.2022.869809

[200] Rosenke, K., Meade-White, K., Letko, M., Clancy, C., Hansen, F., *et al.* (2020) Defining the Syrian hamster as a highly susceptible preclinical model for SARS-CoV-2 infection. Emerg Microbes Infect. 9(1):2673–2684. doi:10.1080/22221751.2020.1858177

It would seem from the very start that the preclinical safety studies were designed to provide data that would put the mRNA COVID-19 vaccines in a "good light." Another critical flaw was that the guidance documents used by Health Canada were only applicable to traditional vaccines, and not vaccines using gene therapy technology.

2.7.2. Clinical Safety Studies

For efficiency, the pre-clinical studies on the COVID-19 genetic vaccines were often performed in parallel with human clinical trials. As the Pfizer/BioNTech COVID-19 RNA vaccine was the most widely used of the COVID-19 vaccines in North America and Europe, this section will tend to focus on the BNT162b2 (Comirnaty) product. These initial clinical studies were all undertaken with more purified preparations of this vaccine developed with their Process 1 manufacturing method (see Section 2.5.6). The Phase 3 clinical study with BNT162b2 has been more fully described with respect to efficacy in Section 2.7.4. The initial results after 2 months were published in the *New England Journal of Medicine* (*NEJM*),[201] and this was used to justify the efficacy and safety concerns to the US FDA, Health Canada and other regulatory agencies in countries around the world to permit its conditional approval for those 18 years and older. There were 21,720 people aged 16 years of age or older in the vaccinated cohort, who received two doses of BNT162b2 a month apart, and 21,728 matched participants who were unvaccinated. In the *NEJM* publication, the authors reported that "*the safety profile of BNT162b2 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."*[201]

For the 6-months stage of the same clinical Phase 3 study, Thomas *et al.* (2021) updated their clinical findings in *NEJM*, which also included data for 12- to 15-year-olds who were vaccinated. [202] The vaccinated participants had 300% more total adverse events and 75% more severe adverse events than observed with the placebo-injected, control participants (considered unvaccinated). The authors noted, '*new adverse events attributable to BNT162b2 that were not previously identified in earlier*

[201] Polack, F.P., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., *et al.*; C4591001 Clinical Trial Group. (2020) Safety and efficacy of the BNT162b2 mRNA COVID-19 Vaccine. N Engl J Med. 383(27):2603–2615. doi:10.1056/NEJMoa2034577

[202] Thomas, S.J., Moreira, E.D. Jr, Kitchin, N., Absalon, J., Gurtman, A., *et al.*; C4591001 Clinical Trial Group. (2021) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine through 6 months. N Engl J Med. 385(19):1761–1773. doi:10.1056/NEJMoa2110345

reports included decreased appetite, lethargy, asthenia [abnormal physical weakness or lack of energy]*, malaise, night sweats, and hyperhidrosis* [excessive sweating not related to heat or exercise]." Around 5% of vaccinated recipients experienced severe adverse events from the inoculations. Moreover, there were more deaths in the vaccinated than in the unvaccinated, control group (21 versus 17 deaths; and 2 of these deaths in the vaccinated group were previously unvaccinated but opted after 2 months to get vaccinated after unblinding of the trial). The vaccine-associated deaths had higher rates of cardiovascular disease including arteriosclerosis, cardiac arrest, congestive heart failure and hypertensive heart disease.[203]

A re-analysis of the Pfizer 6-month clinical study with BNT162b2 with respect to the 38 deaths in vaccinated and unvaccinated participants was later performed by an independent group of researchers associated with the *Daily Clout*.[204] In their analysis, they noted:

> *"Surprisingly, a comparison of the number of subject deaths per week during the 33 weeks of this study found no significant difference between the number of deaths in the vaccinated versus placebo arms for the first 20 weeks of the trial, the placebo-controlled portion of the trial. After Week 20, as subjects in the Placebo were unblinded and vaccinated, deaths among this still unvaccinated cohort of this group slowed and eventually plateaued. Deaths in the BNT162b2 vaccinated subjects continued at the same rate. Our analysis revealed inconsistencies between the subject data listed in the 6-Month Interim Report and publications authored by Pfizer/BioNTech trial site administrators. Most importantly, we found evidence of an over 3.7-fold increase in number of deaths due to cardiovascular events in BNT162b2 vaccinated subjects compared to Placebo controls. This significant adverse event signal was not reported by Pfizer/BioNTech."* [204]

[203] Supplement to: Thomas, S.J., Moreira, E.D. Jr, Kitchin, N., Absalon, J., Gurtman, A., *et al.*; C4591001 Clinical Trial Group. (2021) Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine through 6 months. N Engl J Med. 385(19):1761–1773. doi:10.1056/NEJMoa2110345. Retrieved from https://www.nejm.org/doi/suppl/10.1056/NEJMoa2110345/suppl_file/nejmoa2110345_appendix.pdf

[204] Michels, C., Perrier, D., Kunadhasan, J., Clark, E., Gehrett, J., *et al.* (2023) Forensic analysis of the 38 subject deaths in the 6-Month Interim Report of the Pfizer/BioNTech BNT162b2 mRNA Vaccine Clinical Trial. (2023). Int J Vacc Theor Prac Res. 3(1):973–1008. doi:10.56098/ijvtpr.v3i1.85

Likewise, in a substack, Drs. Tore Gulbrandsen, Martin Neil and Norman Fenton described anomalous behavior of the mortality data associated with the Pfizer 6-month clinical study with BNT162b.[205] They concluded that *"the only explanation compatible with all the non-random patterns is that the records of vaccine recipients suffering adverse events and death were changed, moving them to the placebo arm after the event."*

In another secondary analysis of the 6-month, placebo-controlled, Phase 3 randomized clinical trials of the Pfizer/BioNTech and Moderna mRNA COVID-19 vaccines in adults (NCT04368728 and NCT04470427), the authors calculated an excess risk of serious adverse events (AE) with vaccination of 1 in 990, and 1 in 662 over placebo baselines, respectively.[206] These AE were defined as an adverse event that results in any of the following conditions: death; life-threatening at the time of the event; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; a congenital anomaly/birth defect; or a medically important event, based on medical judgment.

In further clinical studies with younger age BNT162b2-vaccinated participants in smaller trials, the studies were too underpowered to pick up adverse events that would occur in less than a thousand participants. However, it is noteworthy that one 13-year-old participant in the 12-15-year-olds BNT162b2 trial conducted at the Cincinnati Children's Hospital, Maddie de Garay, within 24 hours of her second dose of the vaccine experienced severe adverse reactions. As described in an FDA submission by her parents:

> *"She received her first dose on 12/30/2*[0] *and had the expected side effects which were no cause for concern. She got her second dose on 1/20/21 and less than 12 hours later she experienced severe abdominal pain, painful electric shocks on her spine and neck, swollen extremities, ice-cold hands and feet, chest pain, tachycardia, pins and needles in her feet that eventually led to the loss of feeling from her waist down. She had blood in her urine from 7 tests over 3 months, mysterious*

[205] Gulbrandsen, T., Martin, N., Fenton, N. (2023) Anomalous patterns of mortality and morbidity in Pfizer's COVID-19 vaccine trial. Substack. Retrieved from https://wherearethenumbers.substack.com/p/anomalous-patterns-of-mortality-and

[206] Fraiman, J., Erviti, J., Jones, M., Greenland, S., Whelan, P., *et al.* (2022) Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine, ISSN 0264-410X. doi:10.1016/j.vaccine.2022.08.036

rashes, peeling feet, reflux, gastroparesis, vomiting, and eventually the inability to swallow liquids or food, dizziness, passing out, convulsions, the inability to sweat, swollen lymph nodes in her armpits, urinary retention, heavy periods with clots of blood, decreased vision, tinnitus, memory loss, mixing up words, extreme fatigue, and sadly more. She spent 64 days in the hospital, had 3 hospital stays, and 9 trips to the ER. We are 9 months into this, we have no real answers."[20714]

Maddie de Garay was referred to hospital for a full assessment and a doctor diagnosed her with a "functional disorder."[208] As described by Dr. Maryanne Demasi in her substack, "*this doctor decided she had a pre-disposition to hysteria, and she was referred to a mental health facility. Professor and psychiatrist David Healy subsequently conducted a thorough review of her medical records, including an interview with her family, and found no such history of pre-existing conditions or mental illness."* While Maddie de Garay was acknowledged as a participant in a Pfizer Phase 3 study with an adverse event with BNT162b2, her condition was described in an official Pfizer report as merely abdominal pain. However, her case was not mentioned in the *NEJM* publication that published the results of this clinical study[209]

A glaring deficiency in all of the COVID-19 genetic vaccine Phase 3 trials has been the reluctance to perform biochemical tests to actively monitor potential injury from vaccination in all trial participants. For example, there were apparently no blood tests performed such as D-dimer analyses to detect for potential blood clotting, C-reactive protein for inflammation, and troponin for heart damage.

On page 27 in section 2.5.3 of Pfizer's Overview of Clinical Overview document, it states: "*Pharmacokinetic studies are not usually required for vaccines. Measurement of the plasma concentration of the vaccine over time is not feasible*."[210] At the time that Pfizer's Nonclinical Overview

[207] (2021) Docket No. FDA-2021-N-1088 for "Vaccines and Related Biological Products; Notice of Meeting." Retrieved from https://www.regulations.gov/comment/FDA-2021-N-1088-129763

[208] Demasi, M. (2021) Are adverse events in COVID-19 vaccine trials under-reported? Substack. Retrieved from https://maryannedemasi.com/publications/f/are-adverse-events-in-covid-19-vaccine-trials-under-reported

[209] Frenck R.W. Jr, Klein N.P., Kitchin N., Gurtman A., Absalon J., *et al.*; C4591001 Clinical Trial Group. (2021) Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med. 385(3):239–250. doi:10.1056/NEJMoa2107456

[210] (2021) Pfizer, Inc. BLA Submission for BNT162b2 Module 2.4. Clinical Overview. Public Health and Medical Professionals for Transparency Documents. [Online] April 30, 2021. Retrieved from https://phmpt.org/wp-content/uploads/2021/12/STN-125742_0_0Section-2.5-Clinical-Overview.pdf

was approved the definition of a vaccine was: "*A product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease.*" As this product did not meet the definition of a traditional vaccine, the pharmacokinetics of the encoded Spike protein (*i.e.,* the viral antigen) should really have been determined in an ascending dose Phase 1 clinical trial along with the appropriate biomarkers (as mentioned in the previous paragraph) associated with possible vaccine adverse effects. The other advantages for having a full pharmacokinetic profile would be to estimate the variability in levels of Spike protein production between individuals, which so far had not been established, its persistence in the circulation, and its distribution out of the circulation and into tissues, as well as the efficiency of translation from mRNA. Also, adverse effects could then be collated with the Spike protein concentration in the blood. These studies appear to have never been performed.

2.7.3 Post-marketing Safety Studies

Further concerns regarding the safety of the Pfizer/BioNTech vaccine were raised by the first release of the Pfizer's originally confidential post marketing pharmacovigilance report to the FDA.[211] On November 17, 2021, the FDA released the first batch of what was predicted to be at least 451,000 pages of documents that they were ordered by a court to provide. This was to satisfy a Freedom of Information request by a group called Public Health and Medical Professionals for Transparency, who wanted access to the data used by the FDA to approve Pfizer/BioNTech's COVID-19 inoculations. The FDA originally asked in court to have 55 years to release the documents, and then calculated it would take 75 years. It makes one wonder how the FDA was originally able to review the vaccine information within a couple of months to provide its continuing approval. With the first release that covered the period of up to February 28, 2021, there were 42,086 cases of adverse events, of which 11,361 (27%) had not recovered and 1,223 deaths recorded (Table 2).[211] In the 9 pages of the appendix of this report, there were over 1,236 different diseases that were potentially linked with the Pfizer/BioNTech COVID-

[211] (2021) 5.3.6 Cumulative analysis of post-authorization adverse event reports of PF-07302048 (BNT162B2) received through 28-FEB-2021. World-wide Safety. Pfizer. Retrieved from https://phmpt.org/wp-content/uploads/2021/11/5.3.6-postmarketing-experience.pdf

19 vaccine. As of June 18, 2022, Pfizer had records with an accumulation of 4,964,106 total adverse events across 1,485,027 total cases.[212]

Table 2. General overview: Selected characteristics of all cases received during the reporting interval. (From Table 1 of original Pfizer report.[211])

Characteristics		Relevant cases (N=42086)
Gender:	Female	29914
	Male	9182
	No Data	2990
Age range (years): 0.01 -107 years Mean = 50.9 years n = 34952	≤ 17 18-30 31-50 51-64 65-74 ≥ 75 Unknown	175[a] 4953 13886 7884 3098 5214 6876
Case outcome:	Recovered/Recovering	19582
	Recovered with sequelae	520
	Not recovered at the time of report	11361
	Fatal	1223
	Unknown	9400

a. in 46 cases reported age was <16-year-old and in 34 cases <12-year-old.

Since late 2022, Dr. Naomi Woolf and her War Room/*DailyClout* research team of over 3000 volunteers have pored through 1,875 Pfizer clinical trial documents (for ages 16 years and older) and have published regular reports on *the Daily Clout* with their findings. Some 89 reports on the Pfizer Reports have been issued on the *Daily Clout* website as of October 16, 2023.[213] Their work has revealed numerous vaccine AE and cover-ups by Pfizer to minimize the extent of these vaccine injuries. The team expects to be reviewing another 101 Pfizer adolescent (ages 12-15 years) clinical trial documents and 46 Moderna clinical trial documents throughout 2024 and 2025 (estimated to be about 4 million pages of documents).

2.7.4. Vaccine Adverse Event Reporting Databases

Several government agencies have established public reporting sites for recording adverse events related to specific drugs and vaccines post approval of these products. These websites warn that

[212] (2022) Appendix 2.2: Cumulative and interval summary tabulations of serious and non-serious adverse reactions from post-marketing data sources: BNT162B2. Page 1. Retrieved from https://lawyerlisa.substack.com/p/pfizer-data-attached-393-pages-of

[213] (2023) Pfizer reports. Daily Clout. Retrieved from https://dailyclout.io/category/pfizer-reports/

reports of injury from drugs or vaccines do not necessary infer a causal relationship, as many of the same illnesses can arise from other causes in the general population. Reports of AE and especially death from COVID-19 vaccines are typically described by public health officials '*as very rare, and when such deaths are reported, they do not necessarily mean that the vaccine caused the death*.' However, it is notable that there are more reports of severe injury and deaths from the four COVID-19 vaccines in the last three years in the US FDA Vaccine Adverse Effects Reporting System (VAERS) than in the previous 33 years for all other vaccines combined since VAERS was established in 1990.[214] As of October 27, 2023, there were 2,543,974 AE reports posted on VAERS since its inception, and 1,605,764 (63%) were related to COVID-19 vaccines. Of the total of 46,581 deaths associated with all vaccines in VAERS since its inception, 36,501 (78%) were specifically linked to COVID-19 vaccines. Of the COVID-19-related deaths, 92% occurred between December 2019 and December 2022, and only 8% in the subsequent 9 months, in parallel with the large decline in COVID-19 vaccination in 2023.

It should be appreciated that most VAERS reports are made by doctors and other health professionals, and the system is closely monitored for the quality of the reports. Table 3 shows the number of reports filed on VAERS following the release of the COVID-19 vaccines to the public around mid-December 2020.[214] Moreover, these numbers underreport the true extent of AE after injection of the COVID-19 vaccines by an underreporting factor (URF) from 10-times[215] to 41-times.[216] If the number of deaths reported in the US up to November 3, 2023 in VAERS is multiplied by the most conservative URF, this would approximate to over 180,000 deaths in the US from the COVID-19 vaccines. About half of the 1,148,691 deaths with COVID-19 in the US up to October 14, 2023 are thought to actually be from co-morbidities, in part due to Federal government offered strong financial incentives in the US to attribute

[214] (2023) VAERS COVID vaccine adverse events report. Open VAERS. Retrieved from https://www.openvaers.com/covid-data

[215] Lazarus, R., Klompas, M. (2011) Harvard Pilgrim Study – Lazarus Final Report 2011. Adverse Effect. Grant Final Report ID R18 HS 017045. Retrieved from https://www.scribd.com/document/434088983/Lazarus-Final-Report-2011

[216] Kirsch, S., Rose, J., Crawford, M. (2021) Estimating the number of COVID vaccine deaths in America. October 8, 2021 update. Trialsite News. 57. Retrieved from www.datascienceassn.org/sites/default/files/Estimating%20the%20number%20of%20COVID%20vaccine%20deaths%20in%20America%20-%20oct%208%202021.pdf

any death to COVID-19.[217] This really calls into question the benefits of lives saved by COVID-19 vaccination versus injury and deaths from the administration of COVID-19 vaccines.

Several other post-hoc passive surveillance systems also track COVID-19 vaccine injury, including the Canada Adverse Events Following Immunization Surveillance System (CAEFISS), the United Kingdom Yellow Card Scheme, the WHO VigiAccess website, and the European Medicines Agency EudraVigilance website. The data in these systems can be difficult to interpret. AE are widely underreported, and those that are filed are vetted with strict criteria.[218] Nevertheless, numerous AE have been attributed to the current COVID-19 vaccines in all of these databases. As of October 30, 2023, reported AE worldwide with COVID-19 vaccines had surpassed 5.2 million in the WHO reporting system VigiAccess.[219] Table 4 shows how vaccine injury reports with the COVID-19 genetic vaccines compare with the other most commonly applied vaccines. It is evident that the COVID-19 vaccines have 63-times more reports of vaccine AE since the release of the COVID-19 vaccines than seen for influenza vaccines during the same period, which are also widely used. This clearly shows that the COVID-19 genetic vaccines incur more adverse vaccine injuries than reported from any of the traditional vaccines in the past.

Table 3. Number of files reports in VAERS related to COVID-19 vaccinations world-wide and in the US from December 2020 to November 3, 2023. Data was recovered from Open VAERS.[214]

	Mar. 5, 2021	Dec. 31, 2021	Dec. 30, 2022	Nov. 3, 2023		Nov. 3, 2023; US only
Adverse Reports	31,079	1,016,999	1,494,382	1,615,020		997,917
Hospitalizations	3,477	113,303	188,270	212,294		88,472
Urgent Care	5,806	110,785	143,153	153,281		117,818
Deaths	1,524	21,382	33,469	36,726		18,382
Anaphylaxis	292	8,765	10,315	10,706		2,471
Bell's Palsy	367	12,765	16,572	17,575		6,294
Thrombocytopenia /Low Platelet	103	5,102	8,386	9,008		3,612
Heart Attacks	332	10,863	18,115	21,155		9,171

[217] (2023) COVID data tracker. Centers for Disease Control and Prevention. Retrieved from https://covid.cdc.gov/covid-data-tracker/#datatracker-home

[218] Di Pasquale. A., Bonanni, P., Garçon, N., Stanberry, L.R., El-Hodhod, M., Tavares Da Silva, F. (2016) Vaccine safety evaluation: Practical aspects in assessing benefits and risks. Vaccine. 34(52):6672–6680. doi:10.1016/j.vaccine.2016.10.039

[219] (2022) VigiAccess – WHO collaborating center for international drug monitoring. World Health Organization. Retrieved from http://vigiaccess.org/

Myocarditis/ Myopericarditis	NA	23,713	26,096	27,832		5,095
Severe Allergic Reaction	1,917	36,955	41,955	46,529		36,380
Miscarriages	66	3,511	4,643	5,071		2,045
Life Threatening	NA	24,344	35,788	38,959		14,834
Permanently Disabled	NA	36,758	61,764	68,819		17,647

Table 4. VigiAccess listing of vaccine adverse events (AE) associated with the most commonly used vaccines. Sourced on October 30, 2023 and search with "Comirnaty" for COVID-19 and other terms shown in the first column.[219]

Disease Targeted	Number of Total Adverse Events	Since First Year of Reporting	Number of Adverse Events since 2021	Rate Compared to Diphtheria since 2021
COVID-19	5,202,729	2021	5,202,729	32,929X
Influenza	314,501	1968	82,007	519X
Polio	136,363	1882	25,881	164X
Hepatitis B	111,791	1985	11,406	72X
BCG for TB	40,179	1973	6,675	42X
Tetanus	16,513	1968	2,316	15X
Measles	7,973	1968	2,351	15X
Diphtheria	1,965	1979	158	1X

Despite the high levels of COVID-19 vaccine injuries that have been reported with the VAERS, VigiAccess, EudraVigilance and the UK YellowCard vaccine injury reporting systems, relatively few adverse events reports are posted for the COVID-19 vaccines in Canada's CAEFISS.[220] This is likely due to the long time it takes (over 20 minutes) for a doctor or nurse to file a vaccine injury report to local public health units, the strict criteria applied to local acceptance of an injury report with significant rejection rates, and the further scrutiny subsequently applied at the level of the Public Health Agency of Canada, which manages the CAEFISS Database. Only recently have patients been able to report their own injuries. In addition to Dr. Hoffe, physicians have been reprimanded by professional colleges for filing COVID-19 vaccine injury reports, such as exemplified in disciplinary proceedings that were taken

[220] (2023) Reported side effects following COVID-19 vaccination in Canada. Public Health Canada. Retrieved from https://health-infobase.canada.ca/covid-19/vaccine-safety/

by the Ontario College of Physicians and Surgeons against Dr. Patrick Phillips.[221] Dr. Phillips submitted 6 COVID-19 vaccine injury reports to CAEFISS, and all but one were rejected, with his patients being advised to get further vaccinations for COVID-19.

About 72.5% of all AE reports to CAEFISS were from women, which is also a phenomenon observed in VAERS, YellowCard and VigiAccess.[222] This has been attributed to differences in health care seeking behavior as well as biological differences between females and males.[220]

As of September 10, 2023, there were 57,436 Canadians that reported adverse events on CAEFISS following administration of 99 million COVID-19 vaccine doses, which corresponds to about 6 out of 10,000 people that were vaccinated.[220] Of all of the reports, 11,231 were deemed to be serious. For 9,611,886 bivalent COVID-19 vaccines given to Canadians, there were 975 AE, of which 255 AE were considered serious (3 out of 100,000 vaccinations). Of 455 reports of death associated with the COVID-19 vaccines in Canada, only 4 were deemed to be causally associated with the vaccinations, although there were 166 deaths that were unclassifiable due to insufficient information.[220] It seems that when adjusted for population size, there were nearly double the number of adverse events per capita with COVID-19 vaccines reported in Americans in VAERS than Canadians in CAEFISS, and 4.5-times more deaths per capita.

Anaphylaxis was evident in about 1 report for every 100,000 COVID-19 vaccine doses administered in CAEFISS. The two safety signals for COVID-19 vaccines that were acknowledged as confirmed on CAEFISS were thrombosis (blood clotting) with thrombocytopenia syndrome (low platelet count in blood) and myocarditis/myopericarditis.

2.8. COVID-19 Vaccine Effects on Blood

2.8.1. Thrombosis and Thrombocytopenia

[221] (2023) College of Physicians and Surgeons of Ontario v. Phillips, 2023 ONPSDT 16. Tribunal File No.: 21-023. Ontario Physicians and Surgeons Discipline Tribunal. Retrieved from https://doctors.cpso.on.ca/cpso/getdocument.aspx?flash=check&pdfid=nfDo8bWUK0M%3d&id=109364&doctype=PastFinding

[222] Dutta, S., Kaur, R.J., Bhardwaj, P., Sharma, P., Ambwani, S., *et al.* (2021) Adverse events reported from the COVID-19 vaccines: A descriptive study based on the WHO database (VigiBase®). J Appl Pharm Sci. 11(08):001–009. doi:10.7324/JAPS.2021.110801

An increased risk of thrombosis was one of the earlier risks associated with COVID-19 vaccines. This concern was raised when Dr. Charles Hoffe, as a family physician in Lytton, British Columbia found that about 62% of his recently Moderna COVID-19-vaccinated patients had evidence of elevated D-dimer levels, and reported this in an open letter on April 5, 2021, to Dr. Bonnie Henry, the Chief Medical Officer in BC.[223] D-dimer is a breakdown product of blood clots, and Dr. Hoffe thought that these might be arising from microclots induced by the COVID-19 vaccines. He also noted that there had been numerous allergic reactions, including two cases of anaphylaxis, three cases of people with "ongoing and disabling" neurological deficits, and what appeared to be a vaccine-related death amongst his practice of about 900 patients of primarily Indigenous background. Elevation of D-dimer levels have since been confirmed in COVID-19 vaccinated individuals (in 9 of 20 published reports), along with thrombosis, thrombocytopenia, elevated anti-platelet factor 4 antibodies, and myocardial infarctions (heart attacks) in a systematic literature review.[224] Thus, Dr. Hoffe's initial concerns of elevated D-dimer levels have been well substantiated in the literature.

Due to issues of blood clotting and vaccine-induced immune thrombotic thrombocytopenia (VIIT) following injection with the AstraZeneca COVID-19 adenovirus vaccine Vaxzevria/COVISHIELD, the National Advisory Committee on Immunization (NACI) in Canada recommended a pause for using this vaccine in people under 55 years of age.[225] Ontario Public Health suspended offering the AstraZeneca vaccine on May 11, 2021 out of caution due to the increased risk of blood clots of 1 in 55,000 that were vaccinated,[22635] although it continued to be offered in other provinces such as British Columbia. Health Canada never approved AstraZeneca's COVID-19 vaccine for those under 18 years of age, based on

[223] Shilhavy, B. (2021) Canadian doctor defies gag order and tells the public how Moderna COVID injections killed and permanently disabled indigenous people in his community. Health Impact News. Retrieved from https://vaccineimpact.com/2021/canadian-doctor-defies-gag-order-and-tells-the-public-how-the-moderna-covid-injections-killed-and-permanently-disabled-indigenous-people-in-his-community/

[224] Mani, A., Ojha, V. (2022) Thromboembolism after COVID-19 vaccination: A systematic review of such events in 286 patients. Ann Vasc Surg. 84:12–20.e1. doi:10.1016/j.avsg.2022.05.001

[225] Cochrane, D., Tasker, P. (2021) Suspend AstraZeneca use for people under 55, vaccine committee recommends. Canada Broadcasting Corporation News. Retrieved from https://www.cbc.ca/news/politics/astrazeneca-under-55-1.5968128

[226] Draaisma, M. (2021) Ontario will no longer give AstraZeneca COVID-19 vaccine as 1st dose due to blood clot risk. Canada Broadcasting Corporation News. Retrieved from https://www.cbc.ca/news/canada/toronto/ontario-update-astrazeneca-vaccine-1.6022545

continuing increased safety concerns for this age group.[227] Ultimately, Vaxzevria/COVISHIELD along with the Jcovden COVID-19 vaccine (Ad26.COV2.S) from Janssen Inc. were withdrawn from the market in Canada.

It should be appreciated that the COVID-19 RNA vaccines have also been linked with elevated D-dimer and VITT as exemplified in cases studies of individuals that were vaccinated with either the Pfizer/BioNTech or Moderna vaccines for COVID-19.[228, 229] In a systematic review of the literature,[230] Tan *et al.* (2023) reported:

> *"Studies included in this review included 10 cohort studies and 57 case report or case series. A total of over 24,000 thrombotic events have been reported, the majority of which have been associated with adenoviral vector-based vaccine, particularly AstraZeneca (5 in 100,000 up to 6 in 1000), followed by Janssen (8–30 in 1,000,000 doses), Pfizer (6 in 1,000,000 up to 1 in 1000 doses) and Moderna (4 in 10,000,000)."* [230]

2.8.2 Post-mortem Blood Clots

With the introduction of the COVID-19 vaccines, there have been a number of morticians that have noted an increased frequency of blood clots during the embalming of cadavers, and in particular white, fibrous, calamari-like clots that are shaped like blood vessels. The Canadian Covid Citizens Alliance interviewed UK funeral director John O'Looney and US embalmer Richard Hirschman about these abnormal blood clots that they commonly found during the embalming process of the deceased.[231]

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[227] (2023) COVID-19 vaccines: Canada immunization guide. Public Health Agency of Canada. Retrieved from https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html

[228] Kaimori, R., Nishida, H., Uchida, T., Tamura, M., Kuroki, K., *et al.* (2022) Histopathologically TMA-like distribution of multiple organ thromboses following the initial dose of the BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech): An autopsy case report. Thromb J. 20(1):61. doi:10.1186/s12959-022-00418-7

[229] Bekal, S., Husari, G., Okura, M., Huang, C.A., Bukari, M.S. (2023) Thrombosis development after mRNA COVID-19 vaccine administration: A case series. Cureus15(7):e41371. doi:10.7759/cureus.41371

[230] Tan, L.J., Koh, C.P., Lai, S.K., Poh, W.C., Othman, M.S., Hussin, H. (2022) A systemic review and recommendation for an autopsy approach to death followed the COVID 19 vaccination. Forensic Sci Int. 340:111469. doi:10.1016/j.forsciint.2022.111469

[231] (2023) Morticians speak with the CCCA about abnormal blood clots in the COVID-19 vaccinated deceased. Canadian Covid Care Alliance. Rumble. Retrieved from https://rumble.com/v2au84s-morticians-discuss-abnormal-blood-clots-in-covid-19-vaccinated-patients.html

Hirschman presented images of abnormal clots retrieved from deceased individuals. Other embalmers as well as US pathologist Dr. Ryan Cole have also reported a rise in these irregular, hardened blood clots.[232, 233] Their findings have been confirmed in a survey that was prepared by Tom Haviland and Laura Kasner, which was sent to 30 state funeral director/embalmer associations and 800 funeral homes primarily in the USA to determine if they were seeing unusual blood clots in corpses.[234] From 128 respondents: 68.75% had observed large whitish "fibrous" structures/clots in the corpses embalmed. Traditional "grape jelly" clots were reported by 66.4% of the respondents, especially in 2020, 2021 and 2022. In 2022, about 68.7% of the respondents observed large whitish, "fibrous" structures/clots, with 44% of the respondents finding these in cadavers 20% or more of the time. These clots were primarily found in the neck and legs. At the Canadian NCI Hearings on COVID-19, Laura Jeffrey noted that in her 27 years of experience as a funeral director, she observed these unusual clots starting in the Spring of 2021, and had not seen these before in all of her years in the industry.[235]

In view of the frequency and large size of these abnormal blood clots, the question arises why have they not been observed in living people? Surely individuals with such occlusions would be extremely sick and easily diagnosed. It seems more likely that they are a post-mortem artefact that is generated after death by a process involving aggregation of fibrin possibly induced by the SARS-CoV-2 Spike

[232] Horwood, M. (2023) Exclusive: Embalmers speak out on unusual blood clots. The Epoch Times. Retrieved from https://www.theepochtimes.com/world/exclusive-embalmers-speak-out-on-unusual-parasite-blood-clots-5121795

[233] (2022) "Foot-long blood clots" from mRNA, says pathologist Dr. Ryan Cole w/ Dr. Kelly Victory – Ask Dr. Drew. YouTube. Retrieved from https://www.youtube.com/watch?v=2SLp6B_kkRI

[234] A Midwestern Doctor. (2023) Do the mysterious fibrous clots really exist? The Forgotten Side of Medicine Substack. Retrieved from https://www.midwesterndoctor.com/p/do-the-mysterious-fibrous-clots-really

[235] (2023) Funeral director Laura Jeffery on post-vaccine embalming. Canadian National Citizens Inquiry into COVID-19. Retrieved from https://www.youtube.com/watch?v=kYxUS9YO2rE

protein.[236, 237, 238, 239] With the termination of blood flow after death and cooling of the body temperature especially with refrigeration, the aggregation of microclots might accumulate over time and the compression of these clots as the embalming fluid is forced in and through the cadaver's circulatory system remains might account for the large size and shape of the clots observed by many morticians.

Since the spread of COVID-19 vaccine lipid nanoparticles occurs throughout the body and endothelial cells that line blood vessels are likely to have high Spike protein expression, it is feasible this might contribute to the formation of microclots that in some people could develop into more serious blood clots. More research is required to establish the frequency of the abnormal blood clots identified by several morticians, and the underlying mechanisms that produce them.

2.9.3. Menstrual Cycles and Bleeding

Soon after the COVID-19 genetic vaccines were introduced into the general population, there were many anecdotal reports that vaccinated women were experiencing prolonged menstrual cycles and heavier menstrual bleeding, even including in some post-menopausal women.[240] A Facebook group featured over 20,000 testimonials regarding abnormalities in menstrual cycles before it was deleted in an act of censorship. Since then, other organizations such as My Cycle Story have emerged to record such experiences.[241] Initially these claims were largely dismissed by health officials. However, this has

[236] Ryu, J.K., Sozmen, E.G., Dixit, K., Montano, M., Matsui, Y., *et al.* (2021) SARS-CoV-2 spike protein induces abnormal inflammatory blood clots neutralized by fibrin immunotherapy. bioRxiv (preprint). doi:10.1101/2021.10.12.464152

[237] Grobbelaar, L.M., Venter, C., Vlok, M., Ngoepe, M., Laubscher, G.J., *et al.* (2021) SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: Implications for microclot formation in COVID-19. Biosci Rep. 41(8):BSR20210611. doi:10.1042/BSR20210611

[238] Montano, M., Ryu, J.K., Sozmen, E.G., Dixit, K., Matsui, Y., *et al.* (2022) SARS-CoV-2 spike binds fibrinogen-inducing abnormal inflammatory blood clots. Topics Antiviral Medicine. 30(1 SUPPL.):9. Retrieved from https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/pt/covidwho-1880599

[239] Kerr, R., Carroll, H.A. (2023) Long COVID is primarily a spike protein induced thrombotic vasculitis. Research Square. doi:10.21203/rs.3.rs-2939263/v1

[240] Mercola, J. (2022) COVID Jabs impact both male and female fertility. Substack. Retrieved from https://takecontrol.substack.com/p/covid-vaccine-fertility-issues

[241] (2023) My Cycle Story Group. Retrieved from https://mycyclestory.com/

been investigated in several prospective studies, almost all of which support the finding of abnormal menstrual periods with COVID-19 vaccination, although to different degrees of severity.

In the Pregnancy Study Online (PRESTO) with 1,137 participants from the US and Canada, who were trying to conceive without fertility treatment, it was noted that the women "*had* [a] *1.1 day longer menstrual cycles after receiving the first dose of COVID-19 vaccine and 1.3 day longer cycles after receiving the second dose*."[242] The authors *"did not observe strong associations between COVID-19 vaccination and cycle regularity, bleed length, heaviness of bleed, or menstrual pain*." The participants were followed over 5 menstrual cycles and of the 437 that were vaccinated at least once, 93% of them received a COVID-19 RNA vaccine (60% Pfizer/BioNTech vaccine and 32.9% Moderna vaccine). Another larger US prospective study with 3,959 participants also noted a slight increase in the length of the menstrual cycle, but no change in the duration of the menses period.[243]

Another prospective study, the Nurses' Health Study 3, with 3,858 premenopausal American and Canadian female nurses that were not taking hormonal contraceptive medications, similarly found a change to longer menstrual cycles within the first 6 months after COVID-19 vaccination.[244] This was particularly evident among women who took the COVID-19 adenovirus vaccines, and whose cycles were short, long, or irregular before vaccination; by contrast SARS-CoV-2 infection did not produce any changes in menstrual cycle characteristics.

The delay in menstrual periods in recently vaccinated women was found to be reduced if they were taking hormonal contraceptive medications. In a study with 1,273 British and French women, and the study authors speculated "*that menstrual changes following vaccination may be mediated by perturbations to ovarian hormones*."[245] In this study, for participants with "progesterone-only

[242] Wesselink, A.K., Lovett, S.M., Weinberg, J., Geller, R.J., Wang, T.R., *et al.* (2023) COVID-19 vaccination and menstrual cycle characteristics: A prospective cohort study. Vaccine. 41(29):4327–4334. doi:10.1016/j.vaccine.2023.06.012

[243] Edelman, A., Boniface, E.R., Benhar, E., Han, L., Matteson, K.A., *et al.* (2022) Association between menstrual cycle length and Coronavirus Disease 2019 (COVID-19) vaccination: A U.S. Cohort. Obstet Gynecol. 139(4):481–489. doi:10.1097/AOG.0000000000004695

[244] Wang, S., Mortazavi, J., Hart, J.E., Hankins, J.A., Katuska, L.M., *et al.* (2022) A prospective study of the association between SARS-CoV-2 infection and COVID-19 vaccination with changes in usual menstrual cycle characteristics. Am J Obstet Gynecol. 227(5):739.e1-739.e11. doi:10.1016/j.ajog.2022.07.003

[245] Alvergne, A., Woon, E.V., Male, V. (2022) Effect of COVID-19 vaccination on the timing and flow of menstrual periods in two cohorts. Front Reprod Health. 4:952976. doi:10.3389/frph.2022.952976

contraception," their periods post-vaccination were significantly heavier than usual. Heavier menstrual bleed was also more evident in older women following vaccination.

Other studies have also described heavier and/or more prolonged bleeding during menses in women after COVID-19 vaccination. A Norwegian study of 3,972 women between 18 to 30 years of age found that while menstrual disturbances were common regardless of vaccination status, "*increased risks of prolonged bleeding, shorter interval between menstruations, and stronger pain during menstruation were also observed after both doses*" of COVID-19 vaccines.[246] This research group also tracked unexpected vaginal bleeding and COVID-19 vaccination in non-menstruating women both 3 months before and then after SARS-CoV-2 mRNA BNT162b2 vaccination.[247] The authors noted:

> *"Among 7,725 postmenopausal women, 7,148 perimenopausal women, and 7,052 premenopausal women, 3.3, 14.1, and 13.1% experienced unexpected vaginal bleeding during a period of 8 to 9 months, respectively. In postmenopausal women, the risk of unexpected vaginal bleeding (i.e., postmenopausal bleeding) in the 4 weeks after COVID-19 vaccination was increased two- to threefold, compared to a prevaccination period. The corresponding risk of unexpected vaginal bleeding after vaccination was increased three- to fivefold in both nonmenstruating peri- and premenopausal women."*[247]

Another study included women aged 18-50 years without known gynecologic comorbidities who regularly monitor their menstruation through electronic calendars.[248] A total of 219 women in this study met the inclusion criteria. Of these, 51 (23.3%) experienced irregular bleeding following the vaccine. Almost 40% (n = 83) of study participants reported a menstrual change following vaccination with the BNT162b2 SARS-CoV-2 mRNA vaccine.[248]

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[246] Trogstad, L., Laake, I., Robertson, A.H., Mjaaland, S., Caspersen, I.H., *et al.* (2023) Heavy bleeding and other menstrual disturbances in young women after COVID-19 vaccination. Vaccine. 41(36):5271–5282. doi:10.1016/j.vaccine.2023.06.088

[247] Blix, K., Laake, I., Juvet, L., Robertson, A.H., Caspersen, I.H., *et al.* (2023) Unexpected vaginal bleeding and COVID-19 vaccination in nonmenstruating women. *Science Advances*. 9(38):eadg1391. doi:10.1126/sciadv.adg1391

[248] Lessans, N., Rottenstreich, A., Stern, S., Saar, T.D., Porat, S., Dior, U.P. (2023) The effect of BNT162b2 SARS-CoV-2 mRNA vaccine on menstrual cycle symptoms in healthy women. Int J Gynecol Obstet. 160(1):313–318. doi:10.1002/ijgo.14356

Likewise, in a cross-sectional European study with 14,153 women, who were double COVID-19 vaccinated at least three months before, 78% of them (many of them older or smokers) reported premenstrual symptoms including "*increased fatigue (43%), abdominal bloating (37%), irritability (29%), sadness (28%), and headaches (28%)*" and the predominant changes were "*more menstrual bleeding (43%), more menstrual pain (41%), delayed menstruation (38%), fewer days of menstrual bleeding (34.5%), and shorter cycle length (32%)*."[249]

In a large US study with 39,129 participants who were followed for 3 months after receiving two doses of a COVID-19 vaccine and had not contracted COVID-19, the authors reported:[250]

> "*42% of people with regular menstrual cycles bled more heavily than usual, while 44% reported no change after being vaccinated. Among respondents who typically do not menstruate, 71% of people on long-acting reversible contraceptives, 39% of people on gender-affirming hormones, and 66% of postmenopausal people reported breakthrough bleeding. We found that increased/breakthrough bleeding was significantly associated with age, systemic vaccine side effects (fever and/or fatigue), history of pregnancy or birth, and ethnicity*."

As mentioned earlier, hormonal changes induced by the COVID-19 vaccines appear to partly underlie the menstrual changes observed with vaccination. Since the Pfizer COVID-19 vaccine lipid nanoparticles have been show to accumulate in the ovaries, it is possible that this might contribute to the abnormal menstrual cycles in some fertile women following vaccination. The hypothalamus and pituitary glands in the brain and the ovaries hormonally control the menstrual cycle, so damage to the ovaries from an inflammatory attack might contribute to this effect, as well as platelet depletion following blood clotting induced by the COVID-19 vaccines.

It is important to appreciate that a female is born with all of the oocytes that she will have in her lifetime, and once she becomes fertile after puberty, she will have approximately 400 periods in which one (and sometimes more) oocyte is converted to a fertilizable egg by the process of meiosis. The vast

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[249] Baena-García, L., Aparicio, V.A., Molina-López, A., Aranda, P., Cámara-Roca, L., Ocón-Hernández, O. (2022) Premenstrual and menstrual changes reported after COVID-19 vaccination: The EVA project. Womens Health (Lond). 18:17455057221112237. doi:10.1177/17455057221112237

[250] Lee, K.M.N., Eleanor J., Junkins, E.J., Luo, C., Fatima, U.A., *et al.* (2022) Investigating trends in those who experience menstrual bleeding changes after SARS-CoV-2 vaccination. Science Advances. 8(28):1–15. doi:10.1126/sciadv.abm7201

majority of oocytes die off without undergoing meiosis during a woman's fertile life. Menopause occurs in women when they deplete their supply of oocytes. Inflammatory damage to the ovaries can endanger the overall supply of oocytes, and could lead to an earlier onset of menopause. In working women, there is a trend to delay having children, so if the ovaries are damaged by COVID-19 vaccine injury, there could possibly be a much shorter window in which they will be able to conceive. While this is a hypothetical risk, it is serious enough to warrant caution when weighing the risks and the benefits of the COVID-19 genetic vaccines.

2.9. Female and Male Fertility

2.9.1. Birth Rates

Although menstruation changes with COVID-19 vaccination appear to be reversible, there has been a reduction in the overall birth rates in Canada and many other countries since the introduction of the COVID-19 vaccines. This decrease may be over and above a steady decline in sperm counts in men since at least the early 1970s.[251] It should be appreciated that there may be significant differences in how males and females respond to the COVID-19 mRNA vaccines, particularly based on the biodistribution studies of the lipid nanoparticles used, which become enriched in the ovaries and testes.[196]

From 2019 to 2020, the Canadian fertility rate declined by 4.1% from 1.47 children per woman in 2019 to 1.41.[252] In 2021, it slightly increased by 2.1% to 1.44 children per woman, but then dropped by 7.6% to 1.33 in 2022.[253] The highest decline in birthrate was in women 20 to 24 years with a 37.5% decline, followed by 34% in 15- to 19-year-olds, 17% in 25- to 29-year-olds, then dropping to 7.6% in 30- to 34-year-olds, and leveling off after that for 35- to 49-year-olds.[254] From 2019 to 2022 in Canada, the crude birth rate decline was 8.6%; the total fertility rate decline was 12%.

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[251] Hagai, L., Jørgensen, N., Martino-Andrade, A., Mendiola, J., Weksler-Derri, D., *et al.* (2017) Temporal trends in sperm count: A systematic review and meta-regression analysis, Hum Reprod Update. 23(6):646–659. doi:10.1093/humupd/dmx022

[252] (2022) Fewer babies born as Canada's fertility rate hit a record low in 2020. Statistics Canada. Retrieved from https://www.statcan.gc.ca/o1/en/plus/960-fewer-babies-born-canadas-fertility-rate-hits-record-low-2020

[253] (2023) Fertility indicators, provinces and territories: Interactive dashboard. Statistics Canada. Retrieved from https://www150.statcan.gc.ca/n1/pub/71-607-x/71-607-x2022003-eng.htm

[254] (2023) Crude birth rate, age-specific fertility rates and total fertility rate (live births). Statistics Canada. Retrieved from https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310041801

By contrast in the US, there has been a steady rise in the fertility rates of 0.06% to 0.11% per year from 2019 through to 2023, which is currently around 1.78 births per woman.[255] US birthrates declined by 1.6% in this period, but these data were not broken down by age.[256]

Reductions in fertility rates of women have also been noted in England and Wales, where the number of live births declined by 3.1% in 2022 compared to 2021.[257] There was a 2.0% increase in births in England and Wales from 2020 to 2021, but the number of births had previously declined by 4.2% from 2019 to 2020, and followed a downward trend since 2012. In the European Union, the total number of live births also declined by 2.4% from 2019 to 2020, was unchanged from 2020 to 2021, and then further decreased by another 4.4% from 2021 to 2022.[258]

Worldwide, the decline in fertility during the pandemic period of 2019 to 2023 in fertility has continued, but includes both countries with high mRNA vaccine uptake, as well as those with very low rates. It should be appreciated that birthrates have declined yearly by approximately 4% per annum since the 1950s in most nations.[259]

The reduction in birthrates from the beginning of the COVID-19 pandemic to the later introduction of mRNA and other COVID-19 vaccines may be due to a number of possibilities such as: the influence of COVID-19 or the COVID-19 genetic vaccines on fertility, the overall decline in male sperm levels, increased economic hardship and social impacts of the pandemic, as well as concerns about having children given the current world situation. In Canada, conscious decisions not to have children during the current uncertain period and the lack of available housing in addition to these other factors, have

[255] (2023) U.S. Fertility rate 1950–2023. Macrotrends. Retrieved from https://www.macrotrends.net/countries/USA/united-states/fertility-rate

[256] (2023) Total fertility rate of United States of America. Database Earth. Retrieved from https//database.earth/population/united-states-of-america/fertility-rate

[257] (2023) Births in England and Wales: 2022. Office for National Statistics. Retrieved from https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsummarytablesenglandandwales/2022

[258] (2023) Number of live births in the European Union (EU27) from 2009 to 2022. Statista. Retrieved from https://www.statista.com/statistics/253401/number-of-live-births-in-the-eu/

[259] (2023) World fertility rate 1950–2023. MacroTrends. Retrieved from https://www.macrotrends.net/countries/wld/world/fertility-rate

contributed to the lower birth rate during the COVID-19 crisis.[260] Thus, while it may be tempting to attribute the decline in birthrates at least in part to COVID-19 vaccines, it is premature to make this a solid conclusion.

2.9.2. Sperm Counts and Motility

Another possible factor that may have contributed to the reduction in the birth rate is a temporary reduction in the production of sperm in men following COVID-19 vaccination. Gat *et al.* (2022) reported that inoculation with two doses of the Pfizer/BioNTech BNT162b2 COVID-19 vaccine in 37 Israeli males (median age of 28 years) was associated with a 15.4% and 22.1% temporary decline, respectively, in total spermatozoa concentration in semen and in their motility 75 to 125 days after the second inoculation, which was largely recovered by 145 days later.[261] Abd *et al.* (2022) tested 60 Iraqi males (18 to 50 years of age), and found that their sperm concentrations and sperm motility were reduced by 6%, at least 90 days after a second vaccination with a COVID-19 vaccine as compared to any prior vaccination.[262]

In a meta-analysis of seven publications (which excluded the study by Gat *et al.* (2022)[261] mentioned above but included the Abd *et al.* (2020) report) where investigators examined sperm concentration and quality, the authors noted that most studies failed to observe differences in total sperm count, semen volume, sperm concentration, total sperm motility, and morphological changes with COVID-19 vaccination after two doses.[263] Gonzalez *et al.* (2021) actually reported increases in sperm counts and motility about 70 days after double vaccination in their study of 45 men (median age of 28 years).[264]

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[260] Hopper, T. (2023) First Reading: Canada's birth rate has dropped off a cliff (and it's likely because nobody can afford housing). National Post. Retrieved from https://nationalpost.com/opinion/canadas-birth-rate-has-dropped-off-a-cliff-and-its-because-nobody-can-afford-housing

[261] Gat, I., Kedem, A., Dviri, M., Umanski, A., Levi, M., *et al.* (2022) COVID-19 vaccination BNT162b2 temporarily impairs semen concentration and total motile count among semen donors. Andrology. 10:1016–1022. doi:10.1111/andr.13209

[262] Abd, Z.H., Muter, S.A., Saeed, R.A.M., Ammar, O. (2022) Effects of CCOVID-19 vaccination on different semen parameters. Basic Clin Androl. 32(1):13. doi:10.1186/s12610-022-00163-x

[263] Ma, Y.-C., Chao, C., Chi, Y., Xiang, L.-Y., Wen, J., Xi, J. (2023) The effect of COVID-19 vaccines on sperm parameters: A systematic review and meta-analysis. Asian J. Andrology. 25(4):468–473. doi:10.4103/aja2022100

[264] Gonzalez, D.C., Nassau, D.E., Khodamoradi, K., Ibrahim, E., Blachman-Braun, R., *et al.* (2021) Sperm parameters before and after COVID-19 mRNA vaccination. JAMA. 326(3):273–274. doi:10.1001/jama.2021.9976

Likewise, Barda *et al.* (2022) reported slight increases in sperm counts and total motility counts in 33 sperm donors (median age of 27 years) 72 days or later after a second dose of the Pfizer/BioNTech BNT162b2 vaccine.[265] Safrai *et al.* (2022) failed to observe any significant changes in sperm volume, counts and motility in their study of 72 men (median age of 35.7 years) about 50 days after their second dose of the BNT162b2 vaccine, but there were large differences in these parameters within each pre- and post-vaccination subgroup (as much as 16-fold for sperm motility).[266] In 106 men (older than 18 years) undergoing assisted reproduction technology, a pairwise comparison between the first (while unvaccinated) and second attempt (median of 75 days after COVID-19 vaccination) did not reveal any changes in the sperm quality or successful fertilization rates.[267] However, their sperm counts were likely to be low to begin with. Olano *et al.* (2022) also did not find any changes in sperm counts or motility in 47 males (median age of 29 years) tested 70 days after a second inoculation with BNT162b2.[268] Examination of sperm production and quality in 75 Israeli men (younger than 45 years) one to two months after a second dose of the BNT162b2 vaccine only showed one participant that had reduced sperm motility and another participant with a sperm concentration that was below the normal expected range.[269] However, in this study the sperm counts and motility of the participants were not determined prior to vaccination. In a study performed by Xia *et al.* (2022) with the Sinovac and Sinopharm recombinant Spike protein vaccines, vaccination of 105 men (median of 33 to 34 years of age) did not appear to significantly affect semen volume, and sperm count and motility.[270] The difference in time between vaccination and sperm acquisition for testing was a median of 80.6 days.

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[265] Barda, S., Laskov, I., Grisaru, D., Lehavi, O., Kleiman, S., *et al.* (2022) The impact of COVID-19 vaccine on sperm quality. Int J Gynaecol Obstet. 158(1):116–120. doi:10.1002/ijgo.14135

[266] Safrai, M., Herzberg, S., Imbar, T., Reubinoff, B., Dior, U., Ben-Meir, A. (2022) The BNT162b2 mRNA COVID-19 vaccine does not impair sperm parameters. Reprod Biomed Online. 44(4):685–688. doi:10.1016/j.rbmo.2022.01.008

[267] Reschini, M., Pagliardini, L., Boeri, L., Piazzini, F., Bandini, V., *et al.* (2022) COVID-19 vaccination does not affect reproductive health parameters in men. Front Public Health. 10:839967. doi:10.3389/fpubh.2022.839967

[268] Olana, S., Mazzilli, R., Salerno, G., Zamponi, V., Tarsitano, M.G., *et al.* (2022) 4BNT162b2 mRNA COVID-19 vaccine and semen: What do we know? Andrology. 10(6):1023–1029. doi:10.1111/andr.13199

[269] Lifshitz, D., Haas, J., Lebovitz, O., Raviv, G., Orvieto, R., Aizer, A. (2022) Does mRNA SARS-CoV-2 vaccine detrimentally affect male fertility, as reflected by semen analysis? Reprod Biomed Online. 44(1):145–149. doi:10.1016/j.rbmo.2021.09.021

[270] Xia, W., Zhao, J., Hu, Y., Fang, L., Wu, S. (2022) Investigate the effect of COVID-19 inactivated vaccine on sperm parameters and embryo quality in *in vitro* fertilization. Andrologia. 54(6):e14483. doi:10.1111/and.14483

In most of the aforementioned studies, sperm samples were typically taken about 75 days or less after the participants' second vaccination, whereas the reduction of sperm numbers and motility in the Gat *et al.* (2022)[261] study were between 75 and 125 days later. Most of the male participants in all studies were under 40 years of age, and often excluded those with low sperm counts to begin with. The vast differences in parameters from these studies in men who were vaccinated or not, make it difficult to determine if alteration in sperm concentration and mobility may be vaccine-induced.[263] At the very least, any reductions in sperm counts and motility with the COVID-19 vaccines appeared to be reversible.

It would be remiss not to mention that SARS-CoV-2 infection is strongly associated with a temporary reduction in sperm levels and motility as reviewed by Pourmasumi *et al.* (2022).[271] In many of these studies of the effects of COVID-19 on sperm concentration and quality, the COVID-19 vaccination status of the participants was not defined.

2.10. Impact of COVID-19 Vaccines on Pregnancy and Postnatal Development

2.10.1. Efficacy and Safety for Pregnant Women

This section primarily examines the evidence for the efficacy and safety of the mRNA vaccines against COVID-19 that were administered to women before or during pregnancy. To do so effectively requires consideration of the following concerns where some, often very limited, data may be available for evaluation:

a. The efficacy and safety of the mRNA vaccines in non-pregnant women in general, mostly based on the initial phase trials of the mRNA manufacturers, and some later studies in the scientific literature;
b. The impact of these vaccines on fertility;
c. The impact of these vaccines on pregnancy during the various trimesters, including any changes in rates of spontaneous abortions and miscarriages;

[271] Pourmasumi, S., Nazari, A., Ahmadi, Z., Kouni, S.N., de Gregorio, C., *et al.* (2022) The effect of Long COVID-19 infection and vaccination on male fertility: A narrative review. Vaccines (Basel). 10(12):1982. doi:10.3390/vaccines10121982

d. Health outcomes for infants born to mothers vaccinated against COVID-19; and

e. Finally, the evidence, if any, that the vaccines may induce developmental disorders, particularly of the nervous system, in some children.

Taking these in order, what does the existing literature show about efficacy or safety for women in general following vaccination with any of the COVID-19 mRNA vaccines? The efficacy of any intervention in health is typically assessed by the use of a double-blind, randomized clinical trial (RCT), as described in previous sections. This level of evaluation was never done for pregnant or potentially future pregnant women before the deployment and recommendation of the COVID-19 vaccines to the entire population. In fact, pregnant women were excluded from the initial Phase 3 studies. Remarkably, this omission did not stop medical authorities in various countries from recommending COVID-19 vaccination for women before, or during any trimester of pregnancy on the assumption, never tested, that infection with COVID-19 *might* be more serious for the mother and potentially harmful to the fetus. The same authorities then opted to measure effectiveness (real world data), in place of efficacy. Note that efficacy can only be determined prospectively in the context of an randomized control trial (RCT). To do so, often unblinded data was frequently used (mostly from registries), often retrospectively, using different definitions of what a COVID-19 case was (typically positive PCR testing exclusively), from symptomatic COVID-19 diagnoses, to hospitalizations based on PCR tests, *etc*. More importantly, studies determining effectiveness, almost never investigated adverse events in the same populations, so a risk/benefit analysis in the pregnant population is non-existent when it should be the basis of any rational consideration of whether COVID-19 vaccination during pregnancy is indeed "safe and effective."

After more than three and a half years since the COVID-19 crisis started, there has been more than enough time to undertake a double blind RCT in pregnant women with a large enough sample to be able to extrapolate results to the general pregnant population. However, the latest results from Pfizer, published in the US Clinical Trials.gov website,[272] regarding the Phase 2-3 placebo-controlled,

[272] (2023) History of changes for study: NCT04754594. To evaluate the safety, tolerability, and immunogenicity of BNT162b2 against COVID-19 in healthy pregnant women of 18 years of age and older. Clinical Trial.gov Archive. Retrieved from https://classic.clinicaltrials.gov/ct2/history/NCT04754594?V_21=View#StudyPageTop

randomized, observer-blind trial in pregnant women, had managed to recruit only 174 women in each group (*i.e.,* total of 348 women) which is statistically insufficient to detect all potential poor outcomes, and makes extrapolation to the full population of pregnant women impossible. Comparatively, the retrospective design studies with statistical corrections that allegedly equalize the differences across groups (*e.g.,* the study of Fell *et al*. (2022)[273] have managed to compare 43,099 vaccinated women versus 42,063 non-vaccinated women. So, the question that needs to be answered is why are there no larger RCTs under way given how important the issue is?

It should also be noted that the cited Pfizer study did not administer the vaccine before week 24 or 27 of gestational age, so there is little to no data related to miscarriages (defined as pregnancy before 20 weeks), which has been one (or the main) point of debate regarding administering mRNA vaccines to pregnant women.[210] Indeed, Table 6 of the Pfizer report may deliberately blend data across trimesters giving the impression that vaccinated and non-vaccinated have the same level of miscarriages when Pfizer's own data may support the opposite. The above concerns render the pregnancy data far less than evidence-based. Sadly, the data for fertility, lactation and postpartum adverse events are even less acceptable. In conclusion, the data presented in support of COVID-19 vaccination during pregnancy fails to make a successful case that the vaccines are safe or effective.

Almost all the studies supposedly designed to evaluate the safety of mother and baby were determined retrospectively in case control studies, using registry data, which did not match groups of vaccinated and unvaccinated pregnant women, that is women with similar characteristics (*i.e*., demographic, ethnic, socioeconomic characteristics, substance consumption profile, comorbidities, *etc*.). Such matching is essential since these different characteristics (regardless of the vaccination status of the mother) may be responsible for differences in the outcome of the pregnancy and the overall health of the mother and the baby. Instead of attempting to match the groups, many researchers opted for complicated statistical corrections which tended to make the different characteristics across groups disappear, leading to a conclusion that the vaccinations were not responsible for any differences in outcomes. However, some of the most striking differences between the vaccinated versus the

[273] Fell, D.B., Dimanlig-Cruz, S., Regan, A.K., Håberg, S.E., Gravel, C.A., *et al.* (2022) Risk of preterm birth, small for gestational age at birth, and stillbirth after COVID-19 vaccination during pregnancy: Population based retrospective cohort study. BMJ. 378:e071416. doi:10.1136/bmj-2022-071416

unvaccinated for COVID-19 were not separately considered. These variables, such as cigarette use, consumption of other substances, and socioeconomic income or poverty index, known to negatively impact pregnancy were higher in the unvaccinated group.[273]

An important question to consider in relation to such data is how good are the statistical methods to erase differences between unvaccinated mothers who consumed cigarettes or other drugs, and lived in more impoverished conditions (which generally entail worse overall health status and nutritional status) versus vaccinated mothers who did not consume any substances and who benefited from a better socioeconomic status (which generally means better overall health baseline status)? Can one be certain that a lower number of adverse events in vaccinated pregnant women means that the vaccination is not associated with poorer outcomes (*i.e*., harms), or could it be that the harms in the healthier vaccinated population becomes like that of unvaccinated mothers dealing with worse overall health conditions, cigarette consumption and/or other substance use issues, all of which are known to produce poorer outcomes during pregnancy? This is a key question to resolve.

The initial Phase 3 trials for mRNA vaccines, specifically those by Pfizer, did not separate the male and female participants such that women of reproductive age were not separately assessed. Additionally, any women who might be pregnant were excluded from the trials. Moderna's initial trials also assessed the efficacy and safety data for both sexes, without considering a separate analysis in woman of reproductive age.

Based on these evaluations of male and female efficacy and safety data, few sex-based conclusions about the impact of mRNA vaccines can be used as baseline values. Further, such data cannot really be used as a comparator to women during the various trimesters of pregnancy.

In place of this, is a 2021 report by Pfizer/BioNtech on BNT162B2 entitled "Cumulative Analysis of Post-Authorization Adverse Event Reports of PF-07302048 (BNT162B2) Received Through 28-FEB-2021."[211] This analysis covered through to the end of February 2021. It evaluated 42,086 vaccine recipients, of whom 29,214 were female and 9,182 were male. A further 2,990 patients were listed as "No data", which may simply mean that the sex of some participants was not recorded, as odd as that conclusion might be. The data were gathered from reports in 26 countries in which the trials were held.

In regard to safety as measured by adverse events in pregnant women, Tables 5 and 6 of the document are revealing. In Table 5, the report discusses "Vaccine-Associated Enhanced Disease" (VAED) or Vaccine-Associated Enhanced Respiratory Disease (VAERD). It lists 138 cases including 317 "potentially relevant events." The authors write:

> *"Conclusion: VAED may present as severe or unusual clinical manifestations of COVID-19. Overall, there were 37 subjects with suspected COVID-19 and 101 subjects with confirmed COVID-19 following one or both doses of the vaccine; 75 of the 101 cases were severe, resulting in hospitalization, disability, life-threatening consequences or death. None of the 75 cases could be definitively considered as VAED/VAERD. In this review of subjects with COVID-19 following vaccination, based on the current evidence, VAED/VAERD remains a theoretical risk for the vaccine. Surveillance will continue."* [211]

Whether these cases might represent antibody-dependent enhancement (ADE) was not clear, nor was it apparently evident to Pfizer, assuming the company even acknowledged that ADE exists.

Table 6 in the Pfizer report listed 413 adverse event cases, of which 84 were listed as "serious" and 329 as "non-serious." How these descriptions were determined is not specified. Of these overall adverse events, in the presumably serious cases, 23 showed spontaneous abortions, premature death with neonatal death (2) and spontaneous abortion with intrauterine death (2) (for a total of 27). The adverse events during pregnancy listed as "non-serious" included those in the first trimester (15), second trimester (7) and third trimester (2).[211]

In the next paragraph of the report, it listed 124 "mother cases", with 49 cases characterized as non-serious and 75 cases as serious.[211] Why the numbers varied was not clear. In this paragraph, spontaneous abortions included 25 of the cases. Taking the latter number and not being certain in which trimester the 25 spontaneous abortions occurred (although the first trimester would be most likely) would give a rate of 29.98 % for "serious cases" (which one would have to conclude these cases were) or 7.6% of those deemed "non-serious." In comparison, US data for pregnancy in general shows the percentage of the first trimester spontaneous abortions were highly dependent on the mother's

age, with 15% occurring in those under 35 years, 20-35% in the 35-45 age range, and 50% in the over 45 age group.[274]

A clearer answer to the question of the potentially negative impacts of COVID-19 vaccines on pregnancy would be to look at stillbirth data, which is the death of fetuses over 20 weeks of gestational age. In the richer countries with advanced medical care, stillbirths are quite uncommon so it would be extremely concerning if the numbers of stillbirths in women taking the COVID-19 vaccines just before or during the pregnancy were higher. However, the Pfizer study did not appear to clearly distinguish spontaneous abortions from stillbirths. Some insights into this issue can be found in the last paragraph of page 12 in the report in the section on "Pregnancy cases." Of the 270 adverse effects reported, 4 were described as "serious foetus/baby cases" of which 2 were "premature baby" and 1 death. Two of these are described as occurring in the first trimester.

Taking the numbers of spontaneous abortions in this report as accurate, the Pfizer mRNA vaccines would seem to have almost doubled the number of such cases for under 35-year-olds, coming in at about the same in the 35- to 45-year-old group, and showing lower numbers than in the over 45 years and up age group. It should be stressed however, that the overall numbers in the Pfizer data were small and will thus not have the same accuracy and statistical power to make valid conclusions or extrapolation of the data to the general pregnant population.

During the same time period as when the Pfizer report came out, a number of studies appeared in the peer-reviewed literature as referenced below. The main issues for these studies include concerns about study design, exclusion criteria, the use of PCR testing at too high thermal cycle numbers, and the fundamental differences between the use of relative risk reduction and safety versus absolute risk reduction (see Section 2.6.2) and safety values.

An article by Morgan *et al.* (2022) also demonstrated other study design issues, namely that non-vaccinated women were younger, belonged to the Hispanic or the African-American community, had a higher BMI (body mass index) and a positive smoking status.[275] The authors attempted to deal with

[274] Villines, D. (2021) What are the average miscarriage rates by week? Medical News Today. Retrieved from https://www.medicalnewstoday/com/articles/322634#miscarriage

[275] Morgan, J.A., Biggio, J.R., Jr., Martin, J.K, Mussarat N., Chawla, H.K., *et al.* (2022) Maternal outcomes after Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in vaccinated compared with

these issues by statistical correction. Additionally, Remdesivir had been taken by 20 women in the unvaccinated group compared to none in the vaccinated group, a variable that was not corrected for.[275, 276, 277, 278, 279] Remdesivir itself can have profound side-effects.

In terms of effectiveness, the relative rate reported by these studies ranged from 71% to 88%; the absolute rate was between 0.1% to 5.6%. Effectiveness was also assessed in relation to specific severe forms of COVID-19, such as cases requiring hospitalization, with a relative risk reduction of 71.4%, but an absolute risk reduction of only 0.1%.[276] In one retrospective observational study, researchers from Tel Aviv and the US carefully matched 15,060 pregnant women in Israel according to age, gestational age, residential area, population subgroup, parity, and influenza immunization status, into vaccinated/unvaccinated pairs.[278] Their findings indicated that vaccination with BNT162b2 in pregnant women lowered the risk of SARS-CoV-2 infection, with a relative efficacy rate of 78%, but an absolute difference of only 1.31%. In both the vaccinated and non-vaccinated women that were infected with SARS-CoV-2, about 16% were asymptomatic. Of 88 pregnant women who were symptomatic for COVID-19 in the vaccinated group, 10 were hospitalized (11.4%), whereas 23 of the 149 non-vaccinated pregnant women were hospitalized (15.4%). Therefore, there appeared to be little difference with respect to the severity of COVID-19 once it was acquired in either vaccinated or nonvaccinated women. The authors noted that *"there were no notable differences between the vaccinated and unvaccinated groups regarding preeclampsia, intrauterine growth restriction, infant birth weight, abortions, stillbirth, maternal death, or pulmonary embolism*." While 68/7,530 (0.9%) of the vaccinated women experienced vaccine-related adverse events, none of these were considered severe.[278]

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unvaccinated pregnant patients. Obstet Gynecol. 2022 Jan 1;139(1):107–109. doi:10.1097/AOG.0000000000004621

[276] Dagan, N., Biron-Shental, T., Makov-Assif, M., Key, C., Kohane, I.S., *et al.* (2021) Effectiveness of the BNT162b2 mRNA COVID-19 vaccine in pregnancy. Nat Med. 27(10):1693–1695. doi:10.1038/s41591-021-01490-8

[277] Butt, A.A., Chemaitelly, H., Al Khal, A., Coyle, P.V., Saleh, H., *et al.* (2021) SARS-CoV-2 vaccine effectiveness in preventing confirmed infection in pregnant women. J Clin Invest. 131(23):e153662. doi:10.1172/JCI153662

[278] Goldshtein, I., Nevo, D., Steinberg, D.M., Rotem, R.S., Gorfine, M., *et al.* (2021) Association between BNT162b2 vaccination and incidence of SARS-CoV-2 infection in pregnant women. JAMA. 326(8):728-735. doi:10.1001/jama.2021.11035

[279] Kadour-Peero, E., Sagi-Dain, L., Sagi, S. (2021) Early exploration of COVID-19 vaccination safety and effectiveness during pregnancy: Interim descriptive data from a prospective observational study. Vaccine. 39(44):6535–6538. doi:10.1016/j.vaccine.2021.09.043

Bookstein Peretz *et al*. (2021) compared 390 pregnant Israeli women who were vaccinated with 260 non-pregnant women who were also vaccinated between January and February of 2021, and concluded that there were no significant differences in reported side-effects of Pfizer-BioNTech vaccinations after two doses associated with pregnancy.[280] However, in this retrospective study, the pregnant women had 21% lower serum SARS-CoV-2 IgG levels compared to non-pregnant, vaccinated women ($p < 0.001$)). This study had no comparable cohort of unvaccinated pregnant women with which to compare, and it did not evaluate whether vaccination reduced the incident of COVID-19.

In several studies, most of the pregnant women who were admitted to hospital that were positive for SARS-CoV-2 had no symptoms of COVID-19 at presentation. This amounted to 87.9% of 33 PCR-positive obstetrics patients at the New York–Presbyterian Allen Hospital and Columbia University Irving Medical Center,[281] 52.2% of 23 PCR-positive pregnant patients at an Indonesian hospital,[282] and in a meta-analysis of five studies, between 45% to 100% of 131 PCR-positive obstetric patients presenting to hospitals, of which 49% to 68% remained asymptomatic for COVID-19 during their hospital stay.[283]

Cumulatively, a summary of the existing data on vaccine effectiveness in vaccinated versus unvaccinated women during pregnancy shows major flaws in study design and interpretation, much like that which attended the Phase 3 trials discussed earlier. First, claims made that the COVID-19 genetic vaccines may be effective in pregnant women to prevent infection with SARS-CoV-2 are speculative, especially given the absolute efficacy numbers. Also, because a woman's immune system is distinctly different during pregnancy than in non-pregnant states, any statements about how well the COVID-19 mRNA vaccines work in pregnant women based on studies that excluded these women as in the original Phase trial data are largely conjecture. Also, of note, a key problem in most studies

[280] Bookstein Peretz, S., Regev, N., Novick, L., Nachshol, M., Goffer, E., *et al.* (2021) Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine. Ultrasound Obstet Gynecol. 58(3):450–456. doi:10.1002/uog.23729

[281] Sutton, D., Fuchs, K., D'Alton, M., Goffman, D. (2020) Universal screening for SARS-CoV-2 in women admitted for delivery. N Engl J Med. 382(22):2163–2164. doi:10.1056/NEJMc2009316

[282] Wardhana, M.P., Maniora, A., Maniora, M.C., Aryananda, R.A., Gumilar, K.E., *et al.* (2021) *Lesson from Indonesia: COVID-19 testing strategy in obstetric emergency cases at low-resource health care setting.* Pakistan J Med Health Sci. 15(2):508–513. ISSN 1996-7195

[283] Yanes-Lane, M., Winters, N., Fregonese, F., Bastos, M., Perlman-Arrow, S., *et al*. (2020) Proportion of asymptomatic infection among COVID-19 positive persons and their transmission potential: A systematic review and meta-analysis. PLOS One. 15(11):e0241536. doi:10.1371/journal.pone.0241536

has been the short reporting time post vaccination and the small sample sizes. In some cases, they are simply based on surveys that are filled retrospectively by study participants, as exemplified in the Canadian COVERED study by McClymont *et al.* (2023).[284]

In the COVERED study with 4,528 respondents,[284] 99% were either vaccinated before, during and/or after their pregnancy. Less than a percent remained unvaccinated. About 80% of the participants were white and only 3.4% had a maximum of a high school education or less. The extent of natural immunity in all of the study respondents from previous SARS-CoV-2 infections prior to pregnancy was not considered, although this would be difficult to ascertain without serological testing since about 41% of adults are asymptomatic for COVID-19 following infection with this virus.[285] About 27.4% of the vaccinated study participants tested positive for an active SARS-CoV-2 infection after vaccination. While none of these infected individuals experienced more than mild symptoms of COVID-19, the study was silent about the severity of COVID-19 cases in the unvaccinated group. However, the authors did note that the side-effects of COVID-19 vaccination (redness, pain or swelling at the site of injection (in over 65% of vaccinated participants), tiredness, headache, muscle pain, chills, fever and nausea) in the pregnant women were more commonly observed than evident in non-pregnant COVID-19 vaccinated women, and these were generally more pronounced after the second dose of a COVID-19 vaccine. Only 23.6% of the vaccinated group received one or two doses of a COVID-19 vaccine in the first trimester, which would be the most dangerous to the developing fetus as Spike levels would be at their peak soon after vaccination. Since the study was underpowered in the number of participants, rarer adverse effects of the COVID-19 vaccinations would be harder to identify. Receiving a vaccination in the latter half of the second trimester (weeks 13 through 27 of pregnancy) or in the third trimester (weeks 28 to 40) would not cause a spontaneous abortion (which by definition occurs before the 20th week of pregnancy). Even so, the higher rate of spontaneous abortions in the vaccinated group (18/2,868) as compared with the unvaccinated group (4/1,660) (*i.e.,* 0.63% vs 0.24%) was dismissed on the basis that the survey was retrospective and the number of respondents between the two groups was unequal,

[284] McClymont, E., Atkinson, A., Albert, A., Av-Gay, G., Andrade, J., *et al.*; COVERED Team. (2023) Reactogenicity, pregnancy outcomes, and SARS-CoV-2 infection following COVID-19 vaccination during pregnancy in Canada: A national prospective cohort study. Vaccine. S0264-410X(23)01215-X. doi:10.1016/j.vaccine.2023.10.032

[285] (2023) Between April and August 2022, 98% of Canadians had antibodies against COVID-19 and 54% had antibodies from a previous infection. Statistics Canada. Retrieved from https://www150.statcan.gc.ca/n1/daily-quotidien/230327/dq230327b-eng.htm

even though the rates were adjusted for this by percentage. It was also evident that there were 5 stillbirths and 3 neonatal deaths in the COVID-19 vaccinated group and none in the unvaccinated group. While not statistically significant, there were seizures in 9 babies born to vaccinated mothers (0.32%) compared to 4 babies with unvaccinated mothers (0.24%).[284]

To draw a meaningful conclusion regarding the effects of vaccines on pregnancy, the outcomes should be recorded from vaccination until birth. Moreover, a snapshot of 7-day post-vaccination (as recorded in certain studies, such as that of Sadarangani *et al.* (2022),[286] seems meaningless when the health authorities themselves consider people who received one dose of the vaccine less than 14 days prior as unvaccinated, and people with two doses were only considered fully vaccinated more than seven days post-second dose. So, as per the definition of health authorities, when counting hospitalized vaccinated patients, these vaccinated-pregnant women would have fallen in the category of unvaccinated for the one-dose recipients (unvaccinated and one dose less than 14 days), and of one-dose patients (one dose greater than 14 days) for the two-dose recipients. They would have never counted in the fully vaccinated hospitalized patients. Immune-mediated mechanisms (such as autoimmunity or molecular mimicry) typically takes longer to manifest, as opposed to local reactions, general systemic reactions (like fever or malaise) and allergies.

Among other concerns is the lack of animal or Phase 1/2 studies in humans that addressed teratogenic/toxic effects of individual components of these vaccines, for example, lipids used in the nanoparticles and the Spike protein and its potential truncated versions. Another issue is the low numbers of participants in the clinical trials, particularly in the first trimester when most miscarriages typically occur. In these studies, where there were claims of no increased risk of miscarriage, these statements were based on comparison to historic cohorts, where the frequency of miscarriages varies widely between 8 and 20%.

[286] Sadarangani, M., Soe, P., Shulha, H.P., Valiquette, L., Vanderkooi, O.G., *et al.* (2022) Safety of COVID-19 vaccines in pregnancy: A Canadian National Vaccine Safety (CANVAS) network cohort study. Lancet Infect Dis. 22(11):1553–1564. doi:10.1016/S1473-3099(22)00426-1

Finally, the data for adults using a non-vaccine immune population may be clinically irrelevant since at the time of the trial most people already had some level of immunity – either acquired naturally or vaccine-induced.

Despite of all of the aforementioned caveats, it is still important to collectively review the data that is available with respect to the maternal and neonatal outcomes of COVID-19 vaccination during pregnancy. Amongst the best available is a meta-analysis of 37 published studies that together tracked maternal, neonatal and immunological outcomes in 141,107 pregnant women (36.8% vaccinated) performed by Marchand *et al.* (2023).[287] I was originally one of the peer-reviewers for the journal that eventually published this meta-analysis. The extent of SARS-CoV-2 infections in the vaccinated women was 13.1% and in the non-vaccinated women was 19.1%. Such a difference can easily be accounted for by extra testing in non-vaccinated women who were pregnant from strong encouragement from their biased health care providers. The meta-analysis revealed that vaccination for COVID-19 was associated with what was described as a reduced risk of premature delivery (Odds Ratio of 0.71; $p<0.00001$) by a day or so, and slightly increased risk for a Cesarean section delivery (Odds Ratio of 1.20; $p=0.007$) as compared to non-vaccinated pregnant women. (Odds Ratios provide a measure of the association of an exposure with an outcome. If the Odds Ratio is close to 1, there is no association. A positive number supports a positive relationship, where a negative number supports an inverse relationship.) The authors described the delivery of the babies as occasionally slightly more premature in the non-vaccinated mothers. However, presumably the non-vaccinated mothers should be considered as the expected normal controls, especially since 80.9% of them were apparently not infected with the SARS-CoV-2 virus during their pregnancies. Thus, it is more appropriate to suggest that the vaccinated women may have a slight risk of a delay in their deliveries. Although not quite statistically significant in their analysis, there also appeared to be a small trend towards increased gestational diabetes in the vaccinated pregnant women (Odds Ratio of 1.28 based on two studies; 10.6% vs 8.96%) and postpartum hemorrhage (Odds Ratio of 1.68 based on 3 studies; 3.9% versus 3.4%; $p=0.08$).[286]

[287] Marchand, G., Masoud, A.T., Grover, S., King, A., Brazil, G., *et al.* (2023) Maternal and neonatal outcomes of COVID-19 vaccination during pregnancy, a systematic review and meta-analysis. NPJ Vaccines. 8(1):103. doi:10.1038/s41541-023-00698-8

A recent retrospective cohort of 6,057 women by Dick *et al.* (2023) also found a slightly higher rate of gestational diabetes (47% increase; 12.2% versus 8.3%; p=0.02) amongst vaccinated pregnant women, and in triple-vaccinated women as compared to non-vaccinated mothers slightly more Cesarean deliveries (12% increase; 18.6% versus 16.6%, p=0.52), as well as higher rates of postpartum hemorrhage (195% increase; 9.5% versus 3.21%; p<0.001).[288] Another meta-analysis of the literature by Pratama *et al.* (2023) based on 13 observational studies with COVID-19 mRNA vaccines with 48,039 pregnant women failed to detect any differences between vaccinated and non-vaccinated women with respect to maternal, delivery and neonatal outcomes.[289]

2.10.2. Breast Feeding

In regard to lactation, there are limited studies, of which the work of Kachikis *et al.* (2022), may be the most representative.[290] One of the possible adverse effects reported by 355 of 10,278 (3.5%) lactating women included a decrease in their breast milk supply. However, all signs and symptoms were recorded during the first 24 hours post-vaccination and from a pre-determined list of options. When asked about other signs and symptoms post-vaccination, the participants were instructed to record them only if they thought they were related to vaccination, which makes the data collection subjective to the participants' own biases.

In the Pfizer analysis,[210] the authors considered 133 reports of breast feeding in vaccinated mothers, where 116 were taken to be normal and 17 cases included adverse events with 3 that were considered as "serious" and 14 "as non-serious." The symptoms in the infants included: pyrexia (fever), rash, irritability, vomiting, diarrhea, insomnia, poor feeding, lethargy, abdominal discomfort, allergy to vaccine, increased appetite, anxiety, crying, poor sleep quality, belching (eructation) agitation, pain and hives (uticaria).

[288] Dick, A., Rosenbloom, J.I., Karavani, G., Gutman-Ido, E., Lessans, N., Chill, H.H. (2022) Safety of third SARS-CoV-2 vaccine (booster dose) during pregnancy. Am J Obstet Gynecol MFM. 4(4):100637. doi:10.1016/j.ajogmf.2022.100637

[289] Pratama, N.R., Wafa, I.A., Budi, D.S., Putra, M., Wardhana, M.P., Wungu, C.D.K. (2022) mRNA COVID-19 vaccines in pregnancy: A systematic review. PLOS One. 17(2):e0261350. doi:10.1371/journal.pone.0261350

[290] Kachikis, A., Englund, J.A., Covelli, I., Frank, Y., Haghighi, C., *et al.* (2022) Analysis of vaccine reactions after COVID-19 vaccine booster doses among pregnant and lactating individuals. JAMA Netw Open. 5(9):e2230495. doi:10.1001/jamanetworkopen.2022.30495

Fu *et al.* (2022) conducted a meta-analysis of 23 studies that examined the immune response in pregnant and lactating individuals to COVID-19 vaccination.[291] They noted that these individuals experienced vaccine-related reactions at a similar rate to the general population. With respect to whether the levels of IgA anti-Spike protein in breast milk was higher following vaccination against COVID-19 or if it was higher in lactating mothers who had previously been infected with SARS-CoV-2, the authors noted that the findings in the literature were conflicting.

In addition to the previously mentioned problems with the published studies on vaccination of pregnant women in general and with breast feeding specifically, other issues included small sample sizes and lack of control groups, as well as short duration follow up of 4.6 to 17 weeks.[292] A small sample size was also used by Blakeway *et al.* (2023),[293] none of whom were vaccinated during the first trimester with 85.7% vaccinated in the third trimester, thus limiting the ability to monitor stillbirths. Additionally, many of the reporting authors had conflicts of interest with relationships with COVID-19 vaccine companies.

2.10.3. Impacts of mRNA Vaccines on Early Infant Health

Much of the literature about this age range is based on the official reports from health agencies such as NIH, CDC, Health Canada and others. These simply repeat the mantra that the mRNA vaccines are "safe and effective" without critical analysis. However, in the Pfizer report,[210] part of the list in Table 6 may provide some insight, primarily into what was not analyzed. In a section entitled "Use in Paediatric Individuals <12 years of Age", it listed 34 cases ranging from 2 months of age to 9-year-olds. The following adverse effects are reported: vaccination site pain (3), upper abdominal pain (2), COVID-19 (2), facial paralysis (2), lymphadenopathy (disorder of the lymph nodes) (2), malaise (2), pruritus (itchy

[291] Fu, W., Sivajohan, B., McClymont, E., Albert, A., Elwood, C., *et al.* (2022) Systematic review of the safety, immunogenicity, and effectiveness of COVID-19 vaccines in pregnant and lactating individuals and their infants. Int J Gynaecol Obstet. 156(3):406–417. doi:10.1002/ijgo.14008

[292] Trostle, M.E., Limaye, M.A., Avtushka, V., Lighter, J.L., Penfield, C.A., Roman, A.S. (2021) COVID-19 vaccination in pregnancy: Early experience from a single institution. Am J Obstet Gynecol MFM. 3(6):100464. doi:10.1016/j.ajogmf.2021.100464

[293] Blakeway, H., Prasad, S., Kalafat, E., Heath, P.T., Ladhani, S.N., *et al.* (2022) COVID-19 vaccination during pregnancy: Coverage and safety. Am J Obstet Gynecol. 226(2):236.e1-236.e14. doi:10.1016/j.ajog.2021.08.007

skin) and swelling (2). From this, the authors concluded that there was no significant difference compared to "the non-paediatric population."

2.10.4. Impacts of mRNA Vaccines on Neurological Development in Children

Finally, the question about whether children born to women vaccinated against COVID-19 have more developmental delays is a question that cannot yet be answered, and especially for neural development. For example, autism spectrum disorder (ASD) remains a neurological disorder of unknown etiology. While claims have been made that ASD levels have risen in lock step to the increase in pediatric vaccines that are recommended for children, clearly, correlation, even if suggestive, does not equal causation. Other environmental insults have also been proposed and there are indications that ASD has a genetic component, although one that likely involves at most selected nucleotide sequences, often in non-coding regions of DNA. (For references to these and other points, see Shaw, *Dispatches from the Vaccine Wars*, 2021.[294]) Regardless, while ASD may be diagnosed as early as 18 months of age, it is not usually diagnosed prior to a mean age of 5.5 years of age.[295]

This fact alone would preclude an early answer to the question of mRNA vaccines in pregnancy and neural outcomes in postnatal life. In addition, such a study would be highly complicated by the numerous other prenatal and postnatal events to which children might be exposed.

2.10.5. Concluding Remarks on Vaccine Safety in Pregnant Mothers and Their Babies

FDA's February 28, 2021, review of Pfizer's early pharmacovigilance safety database clearly showed that mRNA product (BNT162b2) injections may cause harm to mothers, pregnancy, lactation, and breastfeeding infants. This review makes clear that this database cannot be used to calculate incidence rates or test hypotheses, but that it should be used to detect potential indicators of harm or safety signals. This raises the question of how much harm is acceptable before halting use of these products. Despite a deficiency of safety data, these products continue to be declared as "safe" in pregnancy.

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[294] Shaw, C.A. (2021) Dispatches from the Vaccine Wars: Fighting for human freedom during the Great Reset. New York: Skyhorse Publishers

[295] Van T'Hof, M., Tisseur, C., Berckelear-Onnes, I., Van Nieuwenhozen, A., Daniels, A.M., *et al.* (2020) Age at autism spectrum disorder diagnosis: A systematic review and meta-analysis from 2012 to 2019. Sage Journals. Autism. 25(4):862–873. doi:10.1177/1362361320971107

Studies used to support these claims are generally of poor quality, consisting mainly of observational studies and voluntary registries. As such, they are only able to speculate that associations seen between suspected injuries and the mRNA product are not due to the COVID-19 mRNA products. The primary limitation of most of these studies is that they focus on short-term harms to the mother or only highly observable immediate harms such as miscarriage, stillbirth, preterm birth, or infant size at birth. None of the studies monitored the health of the mother and child carefully enough – or long enough – to detect subtle but significant changes to maternal or infant bodily systems, including but not limited to, the reproductive, immune, or cardiovascular system. Additionally, these studies have significant statistical issues that further bring their findings into question. They lacked any reliable denominators, standardization, stratification of significant variables, adequate tracking and follow-up of participants, and they incorrectly interpreted what data is available. Recently meta-analyses of these same observational trials have been published and have failed to establish safety risks for these COVID-19 mRNA products in pregnant women. These analyses suffer from the same limitations as the observational trials and are no substitute for the robust and long-term RCT data that is required to prove product safety.

2.11. Myocarditis and Myopericarditis

2.11.1. Nature of Myocarditis and Incidence Pre-COVID-19

Myocarditis, also known as inflammatory cardiomyopathy, is a disease that results from infiltration of heart muscle with immune cells that attack, damage and may kill cardiomyocytes. These are the contractile cells of the middle layer of the heart that permit it to beat and pump blood through the circulation. If the cardiomyocytes are killed, they are replaced by non-contractile scar tissue, and the surviving heart cells have to expand in size to maintain circulation and blood pressure, which results in enlargement of the heart. **Myocarditis is the principal cause of about 20% of sudden cardiac death in people under 40 years of age**.[296] It can occur within an hour of symptoms, such as dizziness, chest pain, sudden loss of consciousness, lack of pulse and no breathing. Continuing symptoms include feeling fatigued, short of breath, chest pains and palpitations (sensation of heart racing). While the symptoms of myocarditis subside gradually, the actual physical damage to the heart may become permanent,

[296] Drory, Y., Turetz, Y., Hiss, Y., Lev, B., Fisman, E.Z., *et al.* (1991) Sudden unexpected death in persons less than 40 years of age. Am J Cardiol. 68(13):1388–1392. doi:10.1016/0002-9149(91)90251-f

although full recovery is usually observed. Myopericarditis has a similar pathology to myocarditis, and involves damage to the pericardium muscle tissue that envelopes and protects the heart. It tends to be less severe than myocarditis. Both myocarditis and myopericarditis can be triggered by a wide range of factors such as kidney failure, cancer, drugs, toxins and many viruses, including SARS-CoV-2.[297] It can also be induced by COVID-19 vaccines.

Historically, the outcomes from myocarditis are usually favorable. However, since the damage from myocarditis can be irreversible and may be cumulative, it is inappropriate to suggest that a person can have a mild case of myocarditis based on symptoms. The acute observable effects may be experienced as mild, and apparently asymptomatic in most cases, but it may induce more serious heart issues in the longer term. The scarring that may result with myocarditis can cause life-threatening arrhythmia of the heart. While the long-term outcomes of COVID-19 vaccine-induced myocarditis are yet unknown, viral induced myocarditis causes death in about 20% of those afflicted within 6 years.[298] The lethality of myocarditis is also highlighted in *The Journal of Clinical Medicine* article: "Occurrence, Trends, Management and Outcomes of Patients Hospitalized with Clinically Suspected Myocarditis—Ten-Year Perspectives from the MYO-PL Nationwide Database*." [299]* which concluded that:

> *"Myocarditis has been shown in post-mortem studies to be a major cause (up to 42% of cases) of sudden and unexpected death in children and young adults. In contrast, a recently published study on autopsies reported that 6% of 14,294 sudden deaths were assigned as being caused by myocarditis. In patients with biopsy-proven myocarditis in long-term observation (the median follow up of 4.7 years), all-cause mortality was 19.2%, while sudden death occurred in 9.9% of cases."* [299]

Another older report noted that:

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[297] Castiello, T., Georgiopoulos, G., Finocchiaro, G., Claudia, M., Gianatti, A., *et al*. (2022) COVID-19 and myocarditis: A systematic review and overview of current challenges. Heart Fail Rev. 27(1):251–261. doi:10.1007/s10741-021-10087-9

[298] Kang, M. (2022) Viral myocarditis. An J. Viral Myocarditis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK459259/

[299] Ozierański, K., Tymińska, A., Kruk, M., Koń, B., Skwarek, A., *et al.* (2021) Occurrence, trends, management and outcomes of patients hospitalized with clinically suspected myocarditis – ten-year perspectives from the MYO-PL nationwide Database. J Clin Med. 10(20):4672. doi:10.3390/jcm10204672

"The Myocarditis Treatment Trial reported mortality rates for biopsy-verified myocarditis of 20% and 56% at 1 year and 4.3 years, respectively. These outcomes are similar to the Mayo Clinic's observational data of 5-year survival rates that approximate 50%. Survival with giant cell myocarditis is substantially lower, with <20% of patients surviving 5 years." [300]

The global incidence of myocarditis and deaths from this disease steadily climbed over 30 years between 1990 and 2019 by 62% and 65%, respectively, although the age-standardized death rate (ASDR) (about 16 per 100,000) was stable during this period.[301][110] The age-standardized incidence rate (ASIR) in North America during this period for all ages and sexes was 18.2 per 100,000, and this serves as a useful bench mark for consideration of the expected background rates of myocarditis during the COVID-19 pandemic. World-wide in 2019, men were on average 35% more likely than women to get myocarditis. The risk of myocarditis increases with age; in 2019, 77.76% of cases were in those 65 years and older, 12.26% in 40- to 64-year-olds, and 9.98% in those under 40 years of age. The ASDR from myocarditis is less than 1 in 100,000 for those under 70 years of age. In the 15 to 24 years-old bracket, the ASIR were 12.3 in males and 7.3 in females per 100,000, and the ASDR were 0.13 in males and 0.07 in females per 100,000.[301] Due to the rarity of myocarditis in children and young adults, it is much easier to observe unusual incidence of this disease in these populations, including from COVID-19 and COVID-19 vaccines.

Another study by Nasreen *et al.* (2022) examined the historical rates in Ontario between 2015 and 2022 of myocarditis and myopericarditis along with a range of other diseases that have been linked to COVID-19 vaccine adverse events.[302] They noted:

"The average annual population was 14 million across all age groups with 51% female. The pre-pandemic mean annual rates per 100,000 population during 2015-2019 were 191 for acute

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[300] Magnani, J., Dec, G. (2006) Myocarditis: Current trends in diagnosis and treatment. Circulation. 113(6):876–890. doi:10.1161/CIRCULATIONAHA.105.584532

[301] Wang, T.-W.-Y., Lui, R.-B., Huang, C.-Y., Li, H.-Y., Zhang, Z.-X., *et al.* (2023) Global, regional, and national burdens of myocarditis, 1990–2019: Systematic analysis from GBD 2019. BMC Public Health. 23(1):714. doi:10.1186/s12889-023-15539-5

[302] Nasreen, S., Calzavara, A., Buchan, S.A., Thampi, N., Johnson, C., *et al.* (2022) Canadian Immunization Research Network (CIRN) Provincial Collaborative Network (PCN) Ontario investigators. Background incidence rates of adverse events of special interest related to COVID-19 vaccines in Ontario, Canada, 2015 to 2020, to inform COVID-19 vaccine safety surveillance. Vaccine. 40(24):3305–3312. doi:10.1016/j.vaccine.2022.04.065

myocardial infarction, 43.9 for idiopathic thrombocytopenia, 28.8 for anaphylaxis, 27.8 for Bell's palsy, 25.0 for febrile convulsions, 22.8 for acute disseminated encephalomyelitis, 11.3 for myocarditis/pericarditis, 8.7 for pericarditis, 2.9 for myocarditis, 2.0 for Kawasaki disease, 1.9 for Guillain-Barré syndrome, and 1.7 for transverse myelitis. Females had higher rates of acute disseminated encephalomyelitis, transverse myelitis and anaphylaxis while males had higher rates of myocarditis, pericarditis, and Guillain-Barré syndrome. Bell's palsy, acute disseminated encephalomyelitis, and Guillain-Barré syndrome increased with age. The mean rates of myocarditis and/or pericarditis increased with age up to 79 years; males had higher rates than females: from 12 to 59 years for myocarditis and ≥12 years for pericarditis." [302]

2.11.2. Myocarditis from COVID-19

Early on in the COVID-19 pandemic, health officials widely proclaimed that a person who got COVID-19 was much more likely to get myocarditis than from a COVID-19 vaccine. For example, as part of a resource guide produced by the Office of the Chief Medical Officer for Ontario, which was presented in information sessions to doctors, nurses and pharmacists to encourage COVID-19 vaccination of children 5 to 11 years of age, in slide number 41, it is indicated that for those under 16 years of age, the risk of hospitalized myocarditis is "*133 per 100k COVID-19 infections or 1 in almost every 750 infections*."[303] The citation provided in the slide was Boehmer *et al.* (2021),[304] which was based on the number of US children under 16 years of age that showed up in hospitals and clinics, between March 2020 and January 2021, with COVID-19. This was not the total number of children who were actually infected with SARS-CoV-2, which should include those that were asymptomatic or mildly sick, and would be about a 100-fold higher (see Table 1). The total number of children tracked in this age group was 3,735,660, of which only 1.7% were reported to be infected with SARS-CoV-2. The number of children under 16 years of age presenting at hospitals with myocarditis was 132 with COVID-19 and 86 without COVID-19. The incidence of myocarditis in all ages groups was only 42.3% higher in 2020 than

[303] Office of the Chief Medical Officer for Ontario. (2021) COVID-19 vaccination in children aged 5–11. Ontario Ministry of Health. Retrieved from https://www.ontariofamilyphysicians.ca/tools-resources/covid-19-resources/covid-19-vaccines/covid-19-vaccination-children-2021-11-26-session-slides.pdf

[304] Boehmer, T.K., Kompaniyets, L., Lavery, A.M., Hsu, J., Ko, J.Y., *et al.* (2021) Association between COVID-19 and myocarditis using hospital-based administrative data – United States, March 2020–January 2021. MMWR Morb Mortal Wkly Rep. 70(35):1228–1232. doi:10.15585/mmwr.mm7035e5

in pre-pandemic 2019. When all age groups were considered in aggregate, there were 2,116 cases presenting at hospitals with symptomatic myocarditis with COVID-19 and 2,953 cases without COVID-19. Only about 4% of the total number of people tracked in this study (*i.e.,* 36,005,294) had been diagnosed with COVID-19, but the actual number was likely substantially higher as only about 5.7% of known COVID-19 cases were likely hospitalized (Table 1).

Interestingly, when Nasreen *et al.* (2022)[302] examined the prevalence rates of various diseases using the mean of incidence values from 2015 to 2019 and compared them with 2000, the first year of the pandemic in Ontario, there were no increases in the total incidence of myocarditis and pericarditis, and actually slight decreases of 15% and 2.5%, respectively. They also noted that the rates of **Guillain-Barré syndrome also decreased by 28%, and acute myocardial infarctions (heart attacks) by 11%.** The authors ascribed the reduced myocarditis due to the effectiveness of lockdown measures and less influenza in 2020.

Another study by Singer *et al.* (2021) has been used to support the contention that the risk of myocarditis is substantially higher from COVID-19 than from COVID-19 vaccines for those under 20 years of age. [305] The authors used proprietary data for over 60 million people tracked by 48 US health care organizations in aggregate to examine the general population of 12- to 19- year-olds who were pre-screened to have had COVID-19. There were only 6 out of 6,846 reported COVID-19 cases (0.09%) for 12- to 17-year-old males tracked from April 2020 to March 2021 who had symptomatic myocarditis, which is about a 1 in 1,141 rate. Apart from being a very low number of symptomatic myocarditis cases, it is clear that the total number of male teenagers in this age group in the database likely exceeded 1.5 million, which would indicate an infection rate of with SARS-CoV-2 of only around 0.45%, which is highly unlikely, and even the authors considered that about 9.2% of the 12- to 17-year-olds were infected by this point. This and other dubious assumptions led the authors to suggest an adjusted rate for symptomatic myocarditis of 45 per 100,000 for males, and 21.3 per 100,000 females following SARS-CoV-2 infection. Since about 99.5% of people with symptomatic myocarditis are typically admitted to a hospital, it is likely that total symptomatic myocarditis cases were captured in the study, but the number of SARS-CoV-2 infections was likely underestimated by more than an order of magnitude.

[305] Singer, M.E., Taub, I.B., Kaelber, D.C. (2021) Risk of myocarditis from COVID-19 infection in people under age 20: A population-based analysis. medRxiv (preprint). doi:10.1101/2021.07.23.21260998

Yet another multicenter, retrospective study by Kamath *et al.* (2023) of the Hospital Corporation of America enterprise-wide database identified 8,162 patients 18 years and older with SARS-CoV-2 infections from January 1, 2020, to May 14, 2020.[306] They reported that 929 (11.38%) of these patients met their diagnostic criteria for myocarditis, which was elevated blood troponin T (a marker of heart damage) and brain natriuretic peptide as proxies (as observed in other studies of COVID-19-induced myocarditis[307]). About 48% of the patients had European ethnicity, 26.3% has African ancestry and the rest were from other races, and most of them had pre-existing medical conditions, including over a quarter with previous heart disease. Of the COVID-19 patients with acute myocarditis, 37.9% required respiratory support via ventilation during their hospital stay and 29.8% died, compared to only 9% of COVID-19 patients without acute myocarditis that required ventilation and 5.8% that experienced in-hospital mortality.[306] These findings were similar to another earlier study that was performed with 187 patients with myocarditis in Wuhan, China from January 23, 2020, to February 23, 2020.[308] These studies indicate that COVID-19 can have very serious consequences for hospitalized patients with pre-existing conditions, but these rates of myocarditis with COVID-19 should not be taken as applicable to young, healthy individuals that become infected with SARS-CoV-2, the majority of which are symptom-free.

There have been very few studies that have accessed the incidence of myocarditis amongst otherwise healthy young adults who get COVID-19. For high performance athletes under 24 years who had COVID-19, the occurrence of clinical symptomatic myocarditis was estimated in one study to be about 1 in 177. This number was based on full testing with cardiac magnetic resonance imaging (MRI) of 1,597 COVID-19-recovered athletes (60.4% males) from 13 US universities from March 1, 2020, through December 15, 2020, for myocarditis. Only 9 participants were symptomatic for myocarditis, and

[306] Kamath, S., Gomah, M.T., Stepman, G., DiMartino, P., Adetula, I. (2023) COVID-19-associated acute myocarditis: Risk factors, clinical outcomes, and implications for early detection and management. Cureus. 15(9):e44617. doi:10.7759/cureus.44617

[307] Pirzada, A., Mokhtar, A.T., Moeller, A.D. (2020) COVID-19 and myocarditis: What do we know so far? CJC Open. 2(4):278–285. doi:10.1016/j.cjco.2020.05.005

[308] Guo, T., Fan, Y., Chen, M., Wu, X., Zhang, L., *et al.* (2020) Cardiovascular implications of fatal outcomes of patients with Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 5(7):811–818. doi:10.1001/jamacardio.2020.1017

another 28 were subclinical and asymptomatic (27 of the 38 were males).[309] Data on age and race were not collected. The higher rates of COVID-19-associated myocarditis with this particular select group of athletes likely reflects the extreme physical exertions that come with practice from training and competition. It appeared that there were 3-times more asymptomatic myocarditis, but underlying heart damage was still evident based on cardiac MRI. It is reasonable that high performance athletes are much more likely to develop symptomatic myocarditis than the general public, as the intense exercise can precipitate symptomatic myocarditis. It is important to note that 2,461 athletes in this study were identified as COVID-19 cases based on PCR testing for SARS-CoV-2, but many asymptomatic individuals may not have been tested. Some 9000 athletes would have been training in the 13 universities at the time. A higher proportion of the athletes in the study were likely infected by the virus by the end of 2020, higher than 27%. Thus, the risks of SARS-CoV-2-induced myocarditis were likely lower than represented. However, these studies demonstrate that most people with asymptomatic myocarditis from SARS-CoV-2 infection are unaware of the damage to their hearts from the underlying inflammation. This would also be true with asymptomatic myocarditis and myopericarditis from COVID-19 vaccines.

A significant advantage of these early studies is that COVID-19 vaccines were not yet available, so the impacts of vaccination on the rates of myocarditis and myopericarditis are not a confounding issue. However, previous exposure to SARS-CoV-2 might have a significant impact on COVID-19 vaccine-induced rates of myocarditis and myopericarditis. Furthermore, the Wuhan SARS-CoV-2 virus was more virulent than later variants that predominated, so this may have also reduced the risks of myocarditis and myopericarditis as the COVID-19 pandemic progressed, at least for the un-vaccinated. The previous infection and development of natural immunity, followed by COVID-19 vaccination that became mandatory in 2021 in most of these colleges may have caused even higher rates of myocarditis and myopericarditis in college athletes, but this has not been formally tested as in the 13 US universities study.

[309] Daniels, C.J., Rajpal, S., Greenshields, J.T., *et al.* (2021) Prevalence of clinical and subclinical myocarditis in competitive athletes with recent SARS-CoV-2 infection: Results from the Big Ten COVID-19 Cardiac Registry. JAMA Cardiol. 6(9):1078–1087. doi:10.1001/jamacardio.2021.2065

Based on PCR testing alone, by April 26, 2023, over 104 million Americans had been infected with SARS-CoV-2.[310] Studies of serological testing for SARS-CoV-2 anti-nucleocapsid antibodies in Canada up to the same time indicate that at least 75% of Canadians had been infected with SARS-CoV-2,[311] and this is probably true for Americans as well. If the risks of myocarditis and myopericarditis from SARS-CoV-2 viral infections were as high as suggested in these earlier studies, then a very much higher rate of these diseases would have been evident in North America and world-wide, which apparently has not transpired. One might suggest that this was circumvented due to the wide-spread adoption of COVID-19 vaccines. However, as will be evident in the next subsection, the COVID-19 vaccines have been linked to increased rates of myocarditis. So, for at least healthy men under 30 years of age, there is a greater risk of myocarditis and myopericarditis from these vaccines than from a SARS-CoV-2 infection.

2.11.3. Myocarditis and Myopericarditis from COVID-19 Vaccines

In the Phase 3 clinical studies with COVID-19 vaccines, the risks of myocarditis and pericarditis following inoculation were not readily apparent. Tracking for COVID-19 vaccine-induced adverse events in the VAERS after the dissemination of these vaccines soon flagged this as a problem (Figure 12).[312] A very comprehensive, early Israeli study by Barda *et al.* (2021) compared pathology from COVID-19 vaccine injury to that produced with COVID-19 from SARS-CoV-2 infection.[313] However, this study, which covered the first five months of the start of the vaccination program in Israel, reflected only up to a second dose of the Pfizer/BioNTech vaccine, and provided comparisons with the risks of COVID-19 injury associated with the Wuhan and earlier variants of COVID-19 that were more severe than from the Omicron variant. The most problematic aspect of this study, despite its comprehensive approach, is that it did not provide a breakdown of the risks by age group or gender. In this study, it was suggested

[310] Silk, B.J., Scobie, H.M., Duck, W.M., Palmer, T., Ahmad, F.B., *et al.* (2023) COVID-19 surveillance after expiration of the Public Health Emergency Declaration – United States, May 11, 2023. MMWR Morb Mortal Wkly Rep. 72(19):523–528. doi:10.15585/mmwr.mm7219e1

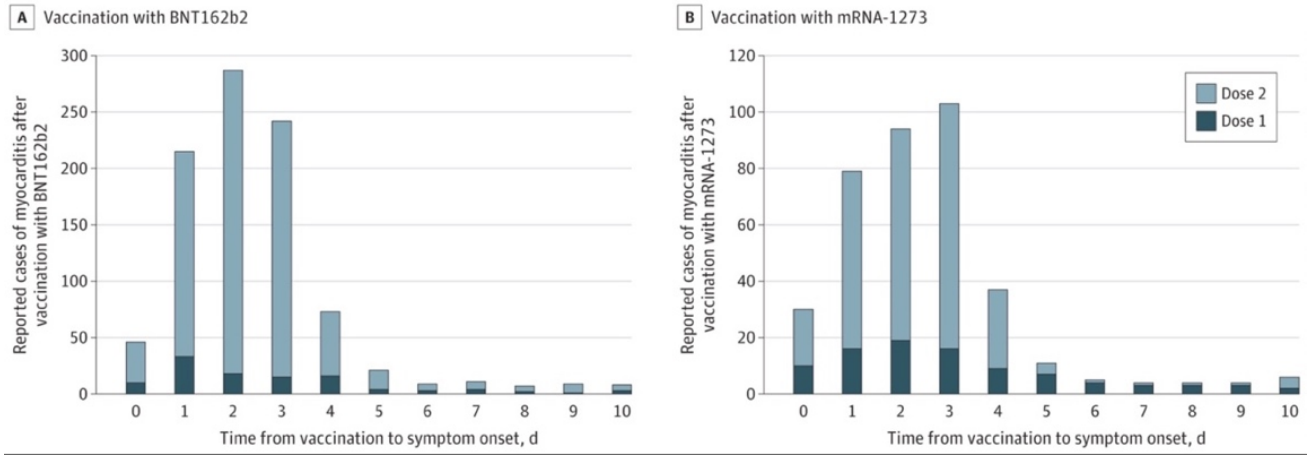
[311] Murphy, T.J., Swail, H., Jain, J., Anderson, M., Awadalla, P., *et al.* (2023) The evolution of SARS-CoV-2 seroprevalence in Canada: A time-series study, 2020–2023. CMAJ. 195(31):E1030-E1037. doi:10.1503/cmaj.230949

[312] Oster, E.O., Shay, D.K., Su, J.R. *et al.* (2022) Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. JAMA. 327(4):331-340. https://jamanetwork.com/journals/jama/fullarticle/2788346)

[313] Barda, N., Dagan, N., Ben-Shlomo, Y., Kepten, E., Waxman, J., *et al.* (2021) Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. N Engl J Med. 385(12):1078–1090. doi:10.1056/NEJMoa2110475

that there was an overall risk of about 1 in 45,000 in getting symptomatic myocarditis from the Pfizer/BioNTech vaccine for those over 18 years of age, but this was still about 3.24-times higher than in the unvaccinated when all ages groups were aggregated.

Figure 12. Daily US VAERS myocarditis cases reported for COVID-19 vaccines. Reproduced from Figure 2 of Oster *et al.* (2022).[312]



Montag and Kampf (2022) following analysis of German hospitalized cases of myocarditis or pericarditis noted that "*In 2019 and 2020, there were no or only very few cases (<4) of myocarditis or pericarditis described as adverse events after any type of vaccination*."[314] Of these, none of them required intensive-care treatment. In 2020, there were 32 hospitalized COVID-19 patients that had myocarditis or myopericarditis and 15 of them needed intensive-care treatment. However, in 2021, the number of hospitalized myocarditis or pericarditis cases among juveniles (10– to 17-year-olds) more than doubled from 270 (2019) and 196 (2020) to 506 (2021). In total, only 11 cases (2.2%) were associated with SARS-CoV-2 infection, whereas 160 cases (31.6%) were associated with a COVID-19 vaccine or vaccination in general, and 32 of these cases required intensive-care treatment. Similar results were also described for young adults of 18- to 29-years of age.[314]

[314] Montag, K., Kampf, G. (2022) Hospitalised myocarditis and pericarditis cases in Germany indicate a higher post-vaccination risk for young people mainly after COVID-19 vaccination. J Clin Med. 11(20):6073. doi:10.3390/jcm11206073

In a meta-analysis of 22 published studies following administration of 405 million doses of COVID-19 vaccines, Li *et al.* (2022) concluded that "*there was no statistically significant difference in the overall incidence of myocarditis or pericarditis between those with COVID-19 vaccination and those without. It was also found that the risk of myocarditis was higher with mRNA-based vaccines as compared to non-mRNA vaccines as well as the second vaccination dose posing a higher risk for myocarditis than the first-time doses*."[315] The authors also noted that in seven studies of adolescents aged 12- to 19-years-old that 111 of 1,008,753 (1 in 9088, or 11 in 100,000) vaccinated youth developed symptomatic myocarditis or myopericarditis, with females in this age group being about 13.9-fold less likely to be afflicted with these diseases.

It is now well recognized that the incidence of symptomatic myocarditis in males who are from 12- to 29-years of age with the second shot of the BNT162b2 vaccine ranges from 1 in 5,000 to 1 in 15,000 depending on the study (Table 5). For Moderna's mRNA-1273, with this demographic, the risk of myocarditis is even higher, at around 1 in 4,400.[316] Similar risks are observed with symptomatic myopericarditis in male adolescents and young adults. When the risks of either symptomatic myocarditis or myopericarditis are considered together, the chances of acquiring one of these diseases becomes even greater, as high at 1 in 704 with BNT162b2 and 1 in 264 for 16- to 24-years-old males following a second dose in one Nordic study.[317] By contrast, in these same studies, there were no recorded female cases with symptomatic myocarditis or myopericarditis (*i.e.*, no measurable risk). However, in most studies with 12- to 39-year-olds, the risks of these diseases in young females can be calculated from Table 5 to be about 6.2-fold lower on average than in their male counterparts. The reasons for the predominance in myocarditis and myopericarditis in men is not known, but may relate to sex hormone differences in the immune response and myocarditis, and possibly the under diagnosis of cardiac disease in women.

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[315] Li, M., Wang, X., Feng, J., Feng, Z., Li, W., Ya, B. (2022) Myocarditis or pericarditis following the COVID-19 vaccination in adolescents: A systematic review. Vaccines (Basel). 10(8):1316. doi:10.3390/vaccines10081316

[316] Klein, N.P. (2021) Myocarditis analyses in the Vaccine Safety Datalink: Rapid cycle analyses and "head-to-head" product comparisons. ACIP meeting COVID-19 Vaccines. Retrieved from https://stacks.cdc.gov/view/cdc/110921

[317] Karlstad, Ø., Hovi, P., Husby, A., Härkänen, T., Selmer, R.M., *et al.* (2022) SARS-CoV-2 vaccination and myocarditis in a Nordic cohort study of 23 million residents. JAMA Cardiol. 7(6):600–612. doi:10.1001/jamacardio.2022.0583

The incidence of myocarditis and myopericarditis following a third dose of BNT162b2 continued to be high in males under 30 years of age according to the data presented from a study conducted in British Columbia by *Naveed et al.* (2020), and was further increased for older men in the 30- to 49-years- old age bracket.[318] For example, with the booster dose of BNT162b2 in men between 40- and 49- years of age, the incidence of symptomatic myocarditis was 1 in 3922. For males under under 69 years of age, there was also trend toward increased myopericarditis with the third dose of BNT162b2, and in the 12- to 17-years-old males, the risk of myopericarditis increased to 1 in 4,024 compared to 1 in 6,281 with the second dose. These increases in the rates of myocarditis and myopericarditis were not evident with the mRNA-1273 booster, and were lower than seen following the second dose. This may have been in part because fewer people took a third shot of this mRNA vaccine after the stronger adverse effects experienced with earlier inoculations discouraged them. In an examination of the Permanente Northwest Health Plan with male and female members aged 18- to 39-years in the US, Sharff *et al.* (2022) recorded 4 males and 2 females with symptomatic myopericarditis.[319] In the case of the males in the study, the incidence of symptomatic myopericarditis with the BNT162b2 booster worked out to 1 in 6,800.

Table 5. Rates of COVID-19 vaccine induced myocarditis and myopericarditis in people under 40 years after a second dose of the same COVID-19 vaccine.

Vaccine	Disease	Incidence per 100,000	Incidence/ Vaccinated Study Participants	Demo-graphic	Country	Study Period	Reference
Pfizer/ BioNTech - BNT162b2	Myocarditis	6.73	9/133,633	Males, 12-17 years	Canada, BC	December 15, 2020 to March 10, 2022	Naveed *et al.* (2022) [318]
		1.53	2/130,628	Females, 12-17 years			
Moderna - mRNA-1273	Myocarditis	22,97	25/108,820	Males, 18-29 years	Canada, BC	December 15, 2020 to March 10, 2022	Naveed *et al.* (2022) [318]
		2	2/99,895	Females, 18-29 years			
Pfizer/ BioNTech	Myopericarditis	9	12/133,633	Males, 12-17 years	Canada, BC	December 15, 2020 to	Naveed *et al.* (2022) [318]

[318] Naveed, Z., Li, J., Spencer, M., Wilton, J., Naus, M., García, H.A.V., *et al.* (2022) Observed versus expected rates of myocarditis after SARS-CoV-2 vaccination: A population-based cohort study. CMAJ. 94(45):E1529-E1536. doi:10.1503/cmaj.220676

[319] Sharff, K.A., Dancoes, D.M., Longueil, J.L., Lewis, P.F., Johnson, E.S. (2022) Myopericarditis after COVID-19 booster dose vaccination. Am J Cardiol. 172:165–166. doi:10.1016/j.amjcard.2022.02.039

- BNT162b2		3.1	4/130,628	Females, 12-17 years		March 10, 2022	
Moderna - mRNA-1273	Myopericarditis	32.2	35/108,820	Males, 18-29 years	Canada, BC	December 15, 2020 to March 10, 2022	Naveed *et al.* (2022) [127]
		5	5/99,895	Females, 18-29 years			
Vaccine	**Disease**	**Incidence per 100,000**	**Incidence/ Vaccinated Study Participants**	**Demo-graphic**	**Country**	**Study Period**	**Reference**
Pfizer/ BioNTech - BNT162b2	Myocarditis	5.24	6/114,450*	Males, 20-51 years (median 25)	United States Military	January to April, 2021	Montgomery *et al.* (2021) [320]
		0	0/28,350*	Females, 20-51 years (median 25)			
Moderna - mRNA-1273	Myocarditis	4.35	14/321,550*	Males, 20-51 years (median 25)	United States Military	January to April, 2021	Montgomery *et al.* (2021) [320]
		0	0/79,650*	Females, 20-51 years (median 25)			
Pfizer/ BioNTech - BNT162b2	Myocarditis and myopericarditis	19.31	44/?	Mixed, 12-39 years	United States	December 2020 to October 9, 2021	Klein (2021) [316]
Moderna - mRNA-1273	Myocarditis and myopericarditis	37.51	22/?	Mixed, 18-39 years	United States	December 2020 to October 9, 2021	Klein (2021) [316]
Pfizer/ BioNTech - BNT162b2	Myocarditis and myopericarditis	11.65	56/480,407	Males, 18-25 years	United States	December 18, 2020, to December 25, 2021	Wong *et al.* (2022) [321]
		3.49	20/572,330	Females, 18-25 years			
Moderna - mRNA-1273	Myocarditis and myopericarditis	14.20	34/239,420	Males, 18-25 years	United States	December 18, 2020, to December 25, 2021	Wong *et al.* (2022) [321]
		2.84	8/282,057	Females, 18-25 years			
Pfizer/ BioNTech		1.70	60/3,535,806	Males, 13-39 years	England	December 1 2020, to	Patone *et al.* (2022) [322]

[320] Montgomery, J, Ryan, M., Engler, R., Hoffman, D., McClenathan, B., *et al.* (2021) Myocarditis following immunization with mRNA COVID-19 vaccines in members of the US Military. JAMA Cardiol. 6(10):1202–1206. doi:10.1001/jamacardio.2021.2833

[321] Wong, H.L., Hu, M., Zhou, C.K., Lloyd, P.C., Amend, K.L., *et al.* (2022) Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: A cohort study in claims databases. Lancet. 399(10342):2191–2199. doi:10.1016/S0140-6736(22)00791-7

[322] Patone, M., Mei, X.W., Handunnetthi, L., Dixon, S., Zaccardi, F., *et al.* (2022) Risk of myocarditis after sequential doses of COVID-19 vaccine and SARS-CoV-2 infection by age and sex. Circulation. 146(10):743–754. doi:10.1161/CIRCULATIONAHA.122.059970

- BNT162b2	Myocarditis and myopericarditis	0.22	9/4,131,123	Females, 13-39 years		December 15, 2021	
Moderna - mRNA-1273	Myocarditis and myopericarditis	102.60	36/35,074	Males, 13-39 years	England	December 1 2020, to December 15, 2021	Patone *et al.* (2022) [322]
		0	0/328,311	Females, 13-39 years			
Vaccine	**Disease**	**Incidence per 100,000**	**Incidence/ Vaccinated Study Participants**	**Demo-graphic**	**Country**	**Study Period**	**Reference**
AstraZeneca - ChAdOx1	Myocarditis and pericarditis	2.21	21/949,865	Males, 13-39 years	England	December 1 2020, to December 15, 2021	Patone *et al.* (2022) [322]
		0	0/1,437,517	Females, 13-39 years			
Pfizer/ BioNTech - BNT162b2	Myocarditis and myopericarditis	9.42	48/509,590	Mixed, 12-39 years	Denmark	October 1, 2020 to October 5, 2021	Husby *et al.* (2021) [323]
Moderna - mRNA-1273	Myocarditis and myopericarditis	28.21	21/74,441	Mixed, 12-39 years	Denmark	October 1, 2020 to October 5, 2021	Husby *et al.* (2021) [323]
Pfizer/ BioNTech - BNT162b2	Myopericarditis	9.74	13/133,477	Males, 12-17 years	Denmark	May 15 to September 15, 2021	Nygaard *et al.* (2022) [324]
		1.56	2/127,857	Females, 12-17 years			
Pfizer/ BioNTech - BNT162b2	Myocarditis and myopericarditis	142	59/?	Males, 16-24 years	Denmark, Finland, Norway, Sweden	December 27, 2020 to October 5, 2021	Karlstad *et al.* (2022) [317]
		0	0/?	Females, 16-24 years			
Moderna - mRNA-1273	Myocarditis and myopericarditis	379	22/?	Males, 16-24 years	Denmark, Finland, Norway, Sweden	December 27, 2020 to October 5, 2021	Karlstad *et al.* (2022) [317]
		0	0/?	Females, 16-24 years			
Pfizer/ BioNTech - BNT162b2	Myocarditis	8.68	8/92,200	Males, 16-29 years	Israel	June 2 to November 30, 2021	Witberg *et al.* (2022) [325]
		1.08	1/90,405	Females, 16-29 years			
Pfizer/ BioNTech		13.23	58/438,511	Males, 16-24 years	Israel		

[323] Husby, A., Hansen, J.V., Fosbøl, E., Thiesson, E.M., Madsen, M., *et al.* (2021) SARS-CoV-2 vaccination and myocarditis or myopericarditis: Population based cohort study. BMJ. 375:e068665. doi:10.1136/bmj-2021-068665

[324] Nygaard, U., Holm, M., Bohnstedt, C., Chai, Q., Schmidt, L.S., *et al.* (2022) Population-based incidence of myopericarditis after COVID-19 vaccination in Danish adolescents. Pediatr Infect Dis J. 1(1):e25-e28. doi:10.1097/INF.0000000000003389

[325] Witberg, G., Magen, O., Hoss, S., Talmor-Barkan, Y., Richter, I., *et al.* (2022) Myocarditis after BNT162b2 vaccination in Israeli adolescents. N Engl J Med. 387(19):1816–1817. doi:10.1056/NEJMc2207270

- BNT162b2	Myocarditis and myopericarditis	1.85	8/431,666	Females, 16-24 years		December 20, 2020 to May, 2021	Mevorach *et al.* (2021) [326]
Vaccine	**Disease**	**Incidence per 100,000**	**Incidence/ Vaccinated Study Participants**	**Demo-graphic**	**Country**	**Study Period**	**Reference**
Pfizer/ BioNTech - BNT162b2	Myocarditis	20.94	38/181,392	Males, 12-17 years	Hong Kong	March 10 to October 18, 2021	Li *et al.* (2022) [327]
		2.82	5/177,405	Females, 12-17 years			
Pfizer/ BioNTech - BNT162b2	Myocarditis and myopericarditis	4.3	19/442,025	Mixed, 16-18 years	South Korea	July 19 to October 2021	June Choe *et al.* (2022) [328]

*Exact numbers of military personnel vaccinated with the Moderna and Pfizer/BioNTech vaccines were not provided. However, it was reported that the US Army initially procured 5.9 million doses from Moderna and 2.1 million doses from Pfizer.[329] This ratio was applied to the total numbers of males (436,000) and females (108,000) that were vaccinated to calculate the myocarditis rates.

A small study by Levi *et al.* (2023) with 324 healthcare workers (59% female, median age of 52 years) in Israel with a fourth dose of BNT162b2 was undertaken to evaluate whether there was an increased risk of myocarditis with further vaccine boosting.[329a] The authors reported that two of the participants had acute vaccine-related myocardial injury, a female who had mild symptoms and the other a male who was asymptomatic. Despite high cardiac troponin levels in their blood, myocarditis was ruled out in both cases. About 41% of the participants had some sort of vaccine-adverse reaction, most commonly injection-site local pain, muscle aches and pains, and fatigue. A particularly interesting

[326] Mevorach, D., Anis, E., Cedar, N., Bromberg, M., Haas, E.J., *et al.* (2021) Myocarditis after BNT162b2 mRNA vaccine against COVID-19 in Israel. N Engl J Med. 385(23):2140–2149. doi:10.1056/NEJMoa2109730

[327] Li, X., Lai, F.T.T., Chua, G.T., Kwan, M.Y.W., Lau, Y.L., *et al.* (2022) Myocarditis following COVID-19 BNT162b2 vaccination among adolescents in Hong Kong. JAMA Pediatr. 2022 Jun 1;176(6):612–614. doi:10.1001/jamapediatrics.2022.0101

[328] June Choe, Y., Yi, S., Hwang, I., Kim, J., Park, Y.J., *et al.* (2022) Safety and effectiveness of BNT162b2 mRNA COVID-19 vaccine in adolescents. Vaccine. 40(5):691–694. doi:10.1016/j.vaccine.2021.12.044

[329] Cronk, T.M. (2020) Pfizer, Moderna produce COVID-19 vaccine. U.S. Department of Defence. Retrieved from https://www.defense.gov/News/News-Stories/Article/Article/2453288/pfizer-moderna-produce-covid-19-vaccine/

[329a] Levi, N., Moravsky, G., Weitsman, T., Amsalem, I., Bar-Sheshet Itach, S., *et al.* (2023) A prospective study on myocardial injury after BNT162b2 mRNA COVID-19 fourth dose vaccination in healthy persons. Eur J Heart Fail. 25(2):313–318. doi:10.1002/ejhf.2687

observation in this study was the elevated levels of troponin in 6.5% of the subjects just prior to receiving their fourth vaccine dose, which might be evidence of prior heart damage.

As discussed in the previous subsection, the risk of myocarditis from a SARS-CoV-2 infection by age is much higher in elderly people who are known to also have more severe COVID-19 than in younger people. Consequently, the risk to benefit ratio with COVID-19 vaccination versus SARS-CoV-2 infection when it comes to myocarditis and myopericarditis is very different when based on age, sex and pre-existing morbidities. Yet, almost categorically in these aforementioned studies, the authors still advocated that everyone should be vaccinated against COVID-19 due to higher risks associated with a SARS-CoV-2 infection.

268. As seen with SARS-CoV-2-induced myocarditis, it should be appreciated that risks of undiagnosed asymptomatic myocarditis or myopericarditis would be expected to be much higher in adolescent and younger males, especially since they would normally have a long life before them. The prevalence of asymptomatic myocarditis or myopericarditis was never assessed in any of the clinical studies with COVID-19 vaccines, and not quantified in any of the aforementioned studies. However, it was carefully investigated by Mansanguan *et al.* (2022) in a study of 301 teenagers of 13 to 18 years of age in Thailand following their receipt of a second dose of the Pfizer/BioNtech BNT162b2 vaccine.[329b] **Cardiovascular effects were found in 29.24% of the teenagers, ranging from tachycardia, palpitation, and myopericarditis. Of the 201 males, four had evidence of asymptomatic myocarditis, one had myopericarditis, and two had pericarditis for a rate of 1 in 29**. This involved active monitoring of heart abnormalities, including presence of heart proteins such as troponin in the blood, cardiac MRI, electrocardiogram measurements and physical examinations.

In light of the relatively high frequency of risk for myocarditis and myopericarditis among younger males following COVID-19 vaccination, the question arises whether or not this is serious and potentially lethal. Kracalik *et al.* (2022) analyzed 519 US individuals (88% male) aged 12- to 19- years-old (median

[329b] Mansanguan, S., Charunwatthana, P., Piyaphanee, W., Dechkhajorn, W., Poolcharoen, A., Mansanguan, C. (2022) Cardiovascular manifestation of the BNT162b2 mRNA COVID-19 vaccine in adolescents. Trop. Med. Infect. Dis. 7(8):196. doi:10.3390/tropicalmed7080196

was 17 years) three months after the onset of COVID-19 vaccine-induced myocarditis.[330] They noted that while most patients showed marked improvements in cardiac diagnostic markers (*e.g.,* troponin) and testing (echocardiograms, electrocardiograms, exercise stress), 54% still showed abnormalities by cardiac MRI.

Barmada *et al.* (2023) found that 80% of those with vaccine-induced symptomatic myocarditis in their US study still had lasting effects on their hearts as revealed by MRI scans over 6 months after diagnosis.[331] Patone *et al*. reported in their analysis of 2,861 hospitalized English patients that got symptomatic myocarditis following COVID-19 vaccination, 345 (12%) died within 28 days of hospital admission with myocarditis or with myocarditis as the cause of death recorded in the death certificate.[322] Cho *et al.* (2023) in their study of 480 Koreans that got COVID-19 vaccine-induced symptomatic myocarditis observed 21 had died (4.4%) after a year.[332] Within a week of their COVID-19 mRNA vaccination, eight of these individuals, six males and two females all under 45 years of age, died from sudden cardiac death. These rates of death are consistent with the rates of death observed with viral-induced myocarditis.[298]

In a meta-analysis of 14 publications that described the autopsy results of 28 people who died mostly within a week following their COVID-19 vaccination, Hulscher *et al.* (2023) noted that 26 of them involved exclusively the cardiovascular system.[333] The authors established that all of these 28 deaths were causally linked to COVID-19 vaccination by independent adjudication and stated:

> ***"****The temporal relationship, internal and external consistency seen among cases in this review with known COVID-19 vaccine-induced myocarditis, its pathobiological mechanisms and related*

[330] Kracalik, I., Oster, M.E., Broder, K.R., Cortese, M.M., Glover, M., *et al.* (2022) Myocarditis outcomes after mRNA COVID-19 vaccination investigators and the CDC COVID-19 Response Team. Outcomes at least 90 days since onset of myocarditis after mRNA COVID-19 vaccination in adolescents and young adults in the USA: A follow-up surveillance study. Lancet Child Adolesc Health. 6(11):788–798. doi:10.1016/S2352-4642(22)00244-9

[331] Barmada, A., Klein, J., Ramaswamy, A., Brodsky, N.N., Jaycox, J.R., *et al.* (2023) Cytokinopathy with aberrant cytotoxic lymphocytes and profibrotic myeloid response in SARS-CoV-2 mRNA vaccine-associated myocarditis. Sci Immunol. 8(83):eadh3455. doi:10.1126/sciimmunol.adh3455

[332] Cho, J.Y., Kim, K.H., Lee, N., Cho, S.H., Kim, S.Y., *et al.* (2023) COVID-19 vaccination-related myocarditis: A Korean nationwide study. Eur Heart J. 44(24):2234–2243. doi:10.1093/eurheartj/ehad339

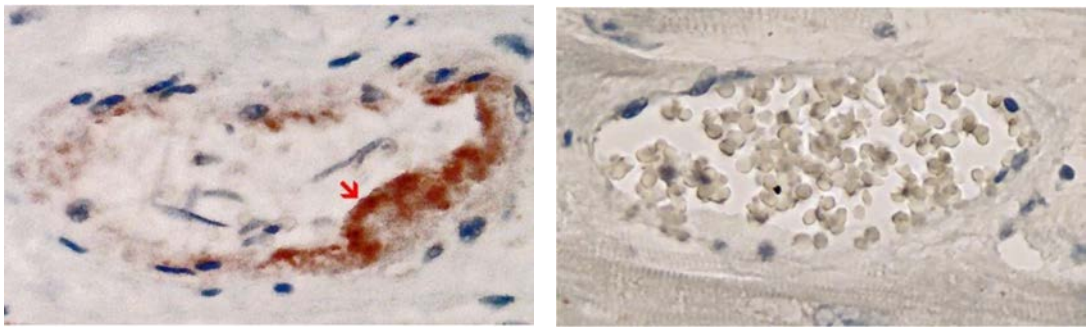
[333] Hulscher, N., Hodkinson, R., Makis, W., McCullough, P. (2023) Autopsy proven fatal COVID-19 vaccine-induced myocarditis. *Preprints.* 2023071198. doi:10.20944/preprints202307.1198.v1

excess death, complemented with autopsy confirmation, independent adjudication, and application of the Bradford Hill criteria to the overall epidemiology of vaccine myocarditis, suggests there is a high likelihood of a causal link between COVID-19 vaccines and death from suspected myocarditis in cases where sudden, unexpected death has occurred in a vaccinated person." [333]

2.12. Mechanism of COVID-19 Vaccine-Induced Pathology from Autopsy

The mechanism by which COVID-19 genetic vaccines induce myocarditis has been revealed from careful autopsy studies. This became first apparent in the scientific literature from immunohistochemistry studies performed by German pathologist Dr. Michael Mörz on a deceased male, 76-years-old Parkinson's patient who died within 3 weeks of receiving his third inoculation with the BNT162b2 mRNA.[334] Using specific antibodies to detect either the Spike or Nucleocapsid proteins in tissue slices, only the Spike protein was detected within the foci of inflammation in both the brain and the heart, particularly in the endothelial cells of small blood vessels (Figure 13). No Nucleocapsid protein could be detected at these sites, which ruled out an actual SARS-CoV-2 infection to account for the Spike protein detection. From inspection of the foci of Spike protein detected in the brain and heart slices, it was evident that the Spike protein had been locally produced, almost certainly from the spread of the lipid nanoparticles in the COVID-19 vaccine.

Figure 13. Immunohistochemistry of Spike (left panel with anti-Spike antibody) and Nucleocapsid protein (right panel with anti-Nucleocapsid antibody) expression in the heart left ventricle in a 76-year-old patient with Parkinson's disease that died 3 weeks after his third COVID-19 vaccination. The lack of brown stain indicates that Nucleocapsid protein from the SARS-CoV-2 virus was not in the heart tissue. The prevalence of blue-stained, mononuclear immune cells in image on the left was also associated with prominent endothelial swelling from the inflammation. Retrieved from Mörz (2022).[334]



[334] Mörz, M. (2022) Case report: Multifocal necrotizing encephalitis and myocarditis after BNT162b2 mRNA vaccination against COVID-19. Vaccines (Basel). 10(10):1651. doi:10.3390/vaccines10101651

Even more extensive analyses of 75 people in the Reutlingen area that had died following COVID-19 vaccinations were performed by another German pathologist Professor Arne Burkhardt and his international team of nine other pathologists, coroners, biologists and chemists. These deceased individuals (40 men and 35 women with a median age at death of 65.7 years) had died one day to ten months after their last COVID-19 vaccination, most commonly with the BNT162b2 vaccine. The cause of death for 68 of them was previously ruled as "natural" or "uncertain" by pathologists or coroners at the time of death (only 7 were possibly linked to COVID-19 vaccination), and 19 of these cases were examples of unexpected Sudden Adult Death Syndrome. Dr. Burkhardt's team subsequently determined that 77% of these deaths (21 beyond reasonable doubt and 37 probable) were caused by their COVID-19 vaccination. The CCCA Scientific and Medical Advisory Committee was privileged to review many of Professor Burkhardt's findings with him, and a video copy of his presentation is posted on the CCCA website.[335] In the immunohistochemistry images of the various tissues retrieved from the deceased individuals that Dr. Burkardt's team analyzed, it was apparent that the Spike protein was widely and highly expressed in many of the tissue samples, whereas the Nucleocapsid protein was absent, ruling out active SARS-CoV-2 infections. Furthermore, in these images it was clear that there was infiltration of immune cells and clear tissue pathology. This included, as observed by Dr. Matthew Mörz with the deceased Parkinson's patient, Spike protein expression, immune cell presence and cellular damage in the heart muscle. These findings are in line with the expected inflammatory responses that would arise from the expression of Spike protein on the surface of cells. Significantly, the detection of Spike protein was evident in the deceased who died even 10 months after their last vaccination, and the Spike protein production was concentrated in the tissue images at the sites of destruction. This means that the detected Spike protein was not simply produced at the site of injection in the muscle and released from the muscle cells into the circulation, but rather the lipid nanoparticles or adenoviruses in the vaccines traveled throughout the body and produced the Spike protein locally.

With respect to the type of immune cells that could be responsible for the inflammatory attack on Spike-producing cells in the heart with myocarditis and myopericarditis, the work of Barmada *et al.* (2023) provides some insight.[331] These investigators ruled out the production of cross-reactive

[335] Burkhardt, A. (2023) The underlying pathology of spike protein biodistribution in people that died post COVID-19 vaccination. Canadian Covid Care Alliance. Retrieved from https://www.canadiancovidcarealliance.org/all/professor-arne-burkhardt-video/

antibodies that recognized normal cardiac proteins or expansion of the T- and B-lymphocytes. They also noted that there was not an overproduction of Spike-recognizing antibodies especially in these patients compared to other people vaccinated for COVID-19. However, there were many immune changes, including more production of interleukins (*e.g.,* IL-1β, IL-1RA (actually a receptor for IL-1) and IL-15) and chemokines (*e.g.,* CCL4, CXCL1 and CXCL10), and activation of cytotoxic T-lymphocytes and natural killer (NK) cells, and inflammatory monocytes. These responses are consistent with the Spike protein-induced changes illustrated in Figure 3, which result in damage and potentially death to Spike protein-producing cells by immune cell attack and the activation of the complement-cascade. Other causes may include the dsRNA contamination which act as an intrinsic adjuvant and may induce uncontrolled immune-inflammatory reactions. Vaccine lipid nanoparticles have been proposed to preferentially transfect macrophages and dendritic cells residing in peripheral tissue such as myocardium, and may induce autoimmunity.[336] Initiatives to reduce dsRNA contamination in the vaccines have been noted by Moderna who have designed a T7 RNA polymerase that produces very little dsRNA.[337]

In view of the potential mechanisms of how myocarditis and myopericarditis can come about from COVID-19 genetic vaccines, there is no compelling reason to believe that these adverse effects at the cellular and tissue level are not also produced at high levels in many females and the elderly. The symptoms of vaccine-induced myocarditis and myopericarditis may be simply more manifested in young males, due to their tendency to be much more physically active, which could exacerbate the condition.

2.13. Increased Sudden Cardiac Arrest in Athletes

Prior to the COVID-19 pandemic, the incidences of sudden cardiac arrest (SCA) and sudden cardiac death (SCD) were relatively low in students and professional athletes under 30 years of age. Peterson *et al*. (2023) collected data in this regard from the US National Center for Catastrophic Sports Injury Research, the University of Washington Medicine Center for Sports Cardiology, searches of student-

[336] Milano, G., Gal, J., Creisson, A., Chamorey, E. (2021) Myocarditis and COVID-19 mRNA vaccines: A mechanistic hypothesis involving dsRNA. Future Virol. 10.2217/fvl-2021-0280. doi:10.2217/fvl-2021-0280

[337] Dousis, A., Ravichandran, K., Hobert, E.M., Moore, M.J., Rabideau, A.E. (2023) An engineered T7 RNA polymerase that produces mRNA free of immunostimulatory byproducts. Nat Biotechnol. 41(4):560–568. doi:10.1038/s41587-022-01525-6

athlete deaths on the National Collegiate Athletic Association's Resolutions List, the National Federation of State High School Associations, and the Parent Heart Watch.[338] From July 2014 through to June 2018, the authors identified 331 cases, of which 173 were fatal. The majority of these cases occurred in males (83.7%), high school athletes (61.6%), and during exercise (74%), with cardiomyopathies accounting for nearly half (47%) of the cases with college and professional athletes. Ice-hockey (1 in 23,550) followed by basketball (1 in 39,811) and then football (1 in 82,587) had the highest incidence rates of SCD for males. From their data, it can be calculated that there was an average of 43 SCD per year in the US student athletes.

An earlier study by Bille *et al.* (2006) on SCD in sport in the scientific literature for athletes under 35 years of age noted that between 1966 to 2004, there were 1,101 reported cases.[339] Of these about 50% had congenital anatomical heart disease and cardiomyopathies. The expected rate of SCD in young athletes averaged to about 29 per year.

And yet in recent times, there has been a surge in the number of news and social media reports of collapses and sudden deaths of athletes world-wide since the availability of COVID-19 vaccines. The most comprehensive list of athletes that have lost consciousness or died since January 2021 is available on the social media website www.goodsciencing.com.[340] Most of these reports arise out of US news sources. While the authors of the website are anonymous, they provide direct url links to news sources for most of the 2,024 athletes identified by name up to September 30, 2023, who have collapsed or died (69.4%), and who were confirmed or highly suspected to have been vaccinated against COVID-19. This list includes those over 40 years of age, but none apparently with reported congenital heart abnormalities. For the entries where the age of the person was provided (1,894), 1,293 (68%) were under 40 years of age and of these 625 (48%) had died. Some of the deaths were also identified as from

[338] Peterson, D.F., Kucera, K., Thomas, L.C., Maleszewski, J., Siebert, D., *et al.* (2021) Aetiology and incidence of sudden cardiac arrest and death in young competitive athletes in the USA: A 4-year prospective study. Br J Sports Med. 55(21):1196–1203. doi:10.1136/bjsports-2020-102666

[339] Bille, K., Figueiras, D., Schamasch, P., Kappenberger, L., Brenner, J.I., *et al.* (2006) Sudden cardiac death in athletes: The Lausanne Recommendations. Eur J Cardiovasc Prev Rehabil. 13(6):859–875. doi:10.1097/01.hjr.0000238397.50341

[340] (2023) 2024 athlete cardiac arrests or serious issues, 1417 of them dead, since COVID injection. Real Science. Retrieved from https://goodsciencing.com/covid/athletes-suffer-cardiac-arrest-die-after-covid-shot/

comorbidities such as cancer. From the 1,417 deaths over the 2.75-years period, this corresponds to a rate of 515 deaths per year on average since the introduction of COVID-19 vaccine.

Binkhorst and Goldstein (2023) analyzed the incidence of SCA and SCD in US athletes under 40 years of age from January 2021 to December 2022, using highly filtered data from the www.goodsciencing.com website.[341] They recognized that COVID-19 vaccination status of those that experienced SCA or SDA was unverified, and so they tried to apply the strict criteria indicated in the study by Peterson *et al.* (2021).[338] They noted that the deaths primarily occurred at rest (32.5%) (some died in their sleep) or under unknown circumstances (38.6%). Binkhorst and Goldstein concluded that the "*SCD rate among young US athletes in 2021-2022 was comparable to pre-pandemic estimates*." And, that there was at that time, "*no evidence to substantiate a link between (mRNA) COVID-19 vaccination and SCD in (young) athletes*." Most the www.goodsciencing.com website data were omitted from this analysis, because there was insufficient information about COVID-19 vaccination status of the affected people in most of the news reports. However, it is significant that during the time period of the COVID-19 vaccinations, there was a strong correlation between the rates of COVID-19 vaccination and the frequency of news reports of SDA and SCD. As vaccine uptake declined in 2023, so did the number of news reports in the www.goodsciencing.com website for the same period. It is also important to recognize that there was a strong push for COVID-19 vaccination of athletes in universities and professional sports, so it is highly likely that the vast majority of the cases captured in the www.goodsciencing.com website were vaccinated individuals. What is needed is the participation of the sporting organizations that supported the Peterson *et al*. (2023) study to provide equivalent data for their athletes after the release of COVID-19 vaccines.

2.14. Neurological Disorders Linked to COVID-19 Vaccines

A wide range of neurological disorders that affect the central or peripheral nervous systems (CNS, PNS) have also been linked to COVID-19 vaccination. This has been reviewed extensively in the recent

[341] Binkhorst, M., Goldstein, D.J. (2023) Athlete deaths during the COVID-19 vaccination campaign: Contextualization of online information. medRxiv (preprint). doi:10.1101/2023.02.13.232855851

scientific literature.[342, 343] In particular, headache, intracerebral hemorrhage, venous sinus thrombosis (VST), Guillain–Barré syndrome (GBS), and facial palsy (*e.g.,* Bell's Palsy) are the most commonly described adverse events. As pointed out by Finsterer (2023), other neurological conditions that appear to be induced by COVID-19 vaccines in the CNS include cerebro-vascular disorders (in addition to VST and intracerebral bleeding, ischemic stroke, subarachnoid bleeding, reversible, cerebral vasoconstriction syndrome, vasculitis, pituitary apoplexy, Susac syndrome), inflammatory diseases (encephalitis, meningitis, demyelinating disorders, transverse myelitis), epilepsy, and a number of other rarely reported CNS conditions. PNS disorders related to SARS-CoV-2 vaccines include neuropathy of cranial nerves, mono-/polyradiculitis (*e.g.,* GBS), Parsonage–Turner syndrome (plexitis), small fiber neuropathy, myasthenia, myositis/dermatomyositis, rhabdomyolysis, and a number of other conditions. CNS diseases can also indirectly arise from adverse effects of COVID-19 vaccines in extra-neural tissues such as myocarditis or vaccine-induce immune thrombotic thromocytopenia (VITT). VITT is a condition characterized by acute blood clots, and then a deficiency of platelets, which can lead to easy or excessive bruising and internal bleeding.

Headache has been reported in about 30 to 51% of COVID-19 vaccinees with neurological disorders. [342, 344] It was also amongst the most common side-effects of COVID-19 vaccines in Phase 3 clinical studies.

In the Italian NEURO-COVAX study conducted by Salsone *et al*. (2023), the investigators aimed to evaluate the neurological complications after the first and/or second dose of different COVID-19 vaccines and identify factors potentially associated with these adverse effects.[345] Adults aged 18 years and older in Novegro (Milan, Lombardy) who received two vaccine doses of Pfizer/BioNTech's BNT162b2 (15,368 participants), Moderna's mRNA-1273 (2,077 participants) and AstraZeneca's

[342] Alonso Castillo, R., Martínez Castrillo, J.C. (2022) Neurological manifestations associated with COVID-19 vaccine. Neurologia (Engl Ed). 23:S2173–5808(22)00141-9. doi:10.1016/j.nrleng.2022.09.007

[343] Finsterer, J. (2023) Neurological adverse reactions to SARS-CoV-2 vaccines. Clin Psychopharmacol Neurosci. 21(2):222–239. doi:10.9758/cpn.2023.21.2.222

[344] Undugodage, C., Dissanayake, U., Kumara, H., Samarasekera, B., Yapa, L., *et al.* (2021) Reactogenicity to ChAdOx1 nCoV-19 vaccine in health care workers: A multicenter observational study in Sri Lanka. Ceylon Med J. 66:177–184. doi:10.4038/cmj.v66i4.9508

[345] Salsone, M., Signorelli, C., Oldani, A., Alberti, V.F., Castronovo, *et al.* (2023) NEURO-COVAX: An Italian population-based study of neurological complications after COVID-19 vaccinations. Vaccines. (Basel) 11(10):1621. doi:10.3390/vaccines11101621

ChAdOx1nCov-19 vaccine (1,651 participants) described any neurological complications from their vaccination between July 7 and 16, 2021. Approximately 31.2% of the participants developed post-vaccination neurological complications, particularly with ChAdOx1nCov-19, and about 40% of these symptomatic individuals had comorbidities in their clinical histories. ChAdOx1nCov-19 was associated with increased risks of headaches, tremors, muscle spasms and insomnia. For Moderna's mRNA-1273 vaccine, there were increased risks of paresthesia (burning or prickling sensation on skin), vertigo (dizziness associated with sensation of motion or spinning), diplopia (double vision), and sleepiness. However, in the period that ranged from March to August 2021, none of the participants were hospitalized and/or died of severe complications related to COVID-19 vaccinations.

Of recent concern is the apparent increased risk of seizures/convulsions after BNT162b2 to 2- to 4-year-olds) and mRNA-1273 to 2- to 5-year olds from an analysis by Hu *et al.* (2023) of COVID-19 vaccine administered to 4,102,106 US children aged 6 months to 17-years-old.[346] In this report in which the corresponding author is from the FDA, 21 pre-specified outcomes were tracked from administrative claims data provided by Optumn Carelon Research, and CVS Health as well as pharmacy claims and data from participating local and state Immunization Information Systems. There were 65 observed COVID-19-vaccine-related seizures/convulsions cases amongst 752,415 doses (8.64 in 100,000 risk) given to aged 2- to 4/5-year-olds across a 7-day risk window following vaccination. Seizures/convulsions were also observed in 6-months to one-year-olds with an incidence of 5.32 in 100,000 doses, and in 5/6- to 17-year-olds with an incidence of 3.14 in 100,000 doses. In the same analysis, myocarditis/myopericarditis in ages 12- to 17-years-old was the other outcome that met the statistical threshold for a warning signal with 107 cases out of 3,083,412 doses with BNT192b2 for a 3.47 in 100,000 risk. The risk of Bell's Palsy for those aged 5/6- to 17-years-old was 1.97 in 100,000 based on 115 cases in 5,837,942 doses.

In the next subsections, the discussion focuses on GBS and Bell's Palsy, as these are neuropathies that have been more commonly associated with COVID-19 vaccine adverse effects in previous studies. However, it is important to appreciate that the full spectrum of neurological side-effects of these

[346] Hu, M., Shoaibi, A., Feng, Y., Lloyd, P.C., Wong, H.L., *et al.* (2023) Safety of monovalent BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and NVX-CoV2373 (Novavax) COVID-19 vaccines in US children aged 6 months to 17 years. medRxiv (preprint). doi:10.1101/2023.10.13.23296903

vaccines is broad, ranging in severity from initially asymptomatic to mild to severe, and outcomes that range from full recovery to death. A wide range of hypotheses have been proposed to account for these side-effects, including effects of the Spike protein directly on cellular targets such as Angiotensin 2 and Neuropilin, to the inflammatory responses that the vaccines evoke from their components (*e.g.,* pegylated lipids in the lipid nanoparticles) as they spread through the circulation, or Spike protein on the surface of cells that take up the lipid nanoparticles or adenoviruses used for delivery of Spike mRNA.

2.14.1. Guillain-Barré Disease

Guillain-Barré syndrome (GBS) is a neurological disorder in which one's immune system attacks the myelin coating of long axons, primarily of peripheral nerves. Incidence is approximately 1-2 in 100,000 people, and lower in children.[347, 348] While GBS can occur at any age, the incidence rate markedly increases after 50 years of age, by about 20% for each additional decade.[349]

GBS typically causes weakness and tingling in the arms and legs that can spread throughout the body. The typical presentation is bilateral. GBS can lead to paralysis and death by respiratory failure. The cause of GBS is unknown,[350] but is typically triggered by an infection with a wide range of bacteria and viruses or even by surgery.[351] A more controversial risk factor is that of vaccination, which may trigger an autoimmune response by a process known as molecular mimicry.[352] In 1976, those that were

[347] Mayo Clinic Staff. (2023) Guillain-Barré syndrome. Mayo Clinic. Retrieved from https://www.mayoclinic.org/diseases-conditions/guillain-barre-syndrome/symptoms-causes/syc-20362793

[348] Yale Medicine. (2023) Guillain-Barré syndrome. Retrieved from https://www.yalemedicine.org/conditions/guillain-barre-syndrome

[349] Sejvar, J.J., Baughman, A.L., Wise, M., Morgan, O.W. (2011) Population incidence of Guillain-Barré syndrome: A systematic review and meta-analysis. Neuroepidemiology. 36(2):123–133. doi:10.1159/000324710

[350] Cafasso, J., Reed-Guy, L. (2021) Guillain-Barré syndrome (GBS). Healthline. Retrieved from https://www.healthline.com/health/guillain-barre-syndrome

[351] (2023) Guillain-Barré syndrome. Wikipedia. Retrieved from https://en.wikipedia.org/wiki/Guillain%E2%80%93Barr%C3%A9_syndrome

[352] Ang, C.W., Jacobs, B.C., Laman, J.D. (2004) The Guillain–Barré syndrome: A true case of molecular mimicry. Trends Immunol. 25(2):61–66. https://www.sciencedirect.com/science/article/abs/pii/S1471490603003855

inoculated with the Swine Flu vaccine had an increased risk of about 1-2 per 100,000 doses for developing GBS.[353][164]

Diagnosis with GBS is usually based on the signs and symptoms with tests such as nerve conduction studies and examination of the cerebrospinal fluid. There are several GBS subtypes known to exist.[351]

Treatment for GBS includes supportive care, intravenous immunoglobulin, plasmapheresis, the latter replacing the patient's blood through transfusion to remove anti-myelin antibodies. Recovery from GBS may take years; some 30% of patients may retain some longer-term weakness.[347,351]

From a meta-analysis of 18 studies published in 2020 investigating GBS incidence in 136,746 hospitalized and non-hospitalized COVID-19 patients, Palaiodimou *et al.* (2021) estimated an incidence of 15 GBS cases per 100,000 COVID-19 cases.[354] Considering that a relatively low percentage of the population was expected to have been infected with SARS-CoV-2 in 2020, this indicates that the overall incidence of GBS would unlikely change appreciably during the first year of the COVID-19 pandemic. Keddie *et al.* (2021) observed a slight decrease in GBS cases in UK hospitals during the early stages of the COVID-19 pandemic between March and May of 2020.[345]

Ogunjimi *et al.* (2023) in their meta-analysis of 71 publications regarding GBS with COVID-19 vaccination established a rate of 0.8 cases per 100,000 doses, with a higher prevalence in males (59.4%) and in people between 40 and 60 years of age.[346] They found the onset of GBS typically occurred within two weeks of vaccination. The highest rates of GBS were associated with the AstraZeneca vaccine (56% of cases), which was 1.4- to 10-fold higher than expected depending on the studies analyzed. About

[353] Babazadeh, A., Mohseni Afshar, Z., Javanian, M., Mohammadnia-Afrouzi, M., Karkhah, A., *et al.* (2019) Influenza vaccination and Guillain-Barré Syndrome: Reality or fear. J Transl Int Med. 7(4):137–142. doi:10.2478/jtim-2019-0028

[354] Palaiodimou, L., Stefanou, M.I., Katsanos, A.H., Fragkou, P.C., Papadopoulou, M., *et al.* (2021) Prevalence, clinical characteristics and outcomes of Guillain-Barré syndrome spectrum associated with COVID-19: A systematic review and meta-analysis. Eur J Neurol. 28(10):3517–3529. doi:10.1111/ene.14860

[345] Keddie, S., Pakpoor, J., Mousele, C., Pipis, M., Machado, P.M., *et al.* (2021) Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. Brain. 144(2):682–693. doi:10.1093/brain/awaa433

[346] Ogunjimi, O.B., Tsalamandris, G., Paladini, A., Varrassi, G., Zis, P. (2023) Guillain-Barré Syndrome induced by vaccination against COVID-19: A systematic review and meta-analysis. Cureus. 15(4):e37578

20% of the GBS cases were associated with the Pfizer/BioNTech COVID-19 vaccine and 5% with the Moderna product.

An outstanding question is whether prior infection with SARS-CoV-2 and subsequent COVID-19 vaccination may increase the rate of incidence of GBS. Zheng *et al.* (2023) tried to answer this question, but obtained inconclusive results, and this is worthy of further investigation.[347]

2.14.2. Bell's Palsy

Bell's palsy (BP) is a condition in which damage to the facial nerve (cranial nerve (CN)7) causes weakness in the muscles on one side of the face, leading that side of the face to droop. It can occur at any age.

Symptoms include lopsided smiles and an impact on eye closure on the affected side of the face. It can result from various forms of inflammation that may affect CN7. It is listed as one of the outcomes of pregnancy and from various infections causing inflammation. The face droop feature of BP is often temporary, but may be longer lasting, sometimes for life.[348]

The incidence of Bell's palsy prior to COVID-19 was 15-50 per 100,000 people.[349] Tamaki *et al.* (2021) from an analysis of data from 41 health organizations collected in 2020, identified 284 BP patients from 348,088 COVID-19 patients for an incidence rate of 81.6 BP cases per 100,000 COVID-19 cases.[350] About 46.1% of these BP patients had a previous history of Bell's palsy. Considering that most people in 2020 were not COVID-19 vaccinated, the rate of BP in the general population was not appreciably different with SARS-CoV-2.

[347] Zheng, X., Fang, Y., Song, Y., Liu, S., Li, K., *et al.* (2023) Is there a causal nexus between COVID-19 vaccination and Guillan-Barre syndrome? Eur J Med Res. 28(1):98. doi:10.1186/s40001-023-01055-0

[348] Mayo Clinic Staff. (2022) Bell's palsy. Mayo Clinic. Retrieved from https://www.mayoclinic.org/diseases-conditions/bells-palsy/symptoms-causes/syc-20370028

[349] Tiemstra, J.D., Khathate, N. (2007) Bell's palsy: Diagnosis and management. Am Fam Physician. 76(7): 997–1002.

[350] Tamaki, A., Cabrera, C.J., Li, S., Rabbani, C., Thuener, J.E., *et al.* (2021) Incidence of Bell's palsy in patients with COVID-19. JAMA Otolaryngol Head Neck Surg. 147(8):767–768. doi:10.1001/jamaoto.2021.1266

In another meta-analysis, Rafati *et al.* (2023) picked 17 published studies to calculate the rate of BP in COVID-19 vaccine recipients and following SARS-CoV-2 infection.[351] By pooling data from four randomized Phase 3 studies with COVID-19 vaccines, it can be calculated that there was a 221% increase in BP incidence with vaccination compared to placebo controls, with a rate of 19.3 cases of BP per 100,000 participants in the COVID-19 vaccinated, and 6.0 cases of BP per 100,000 unvaccinated participants. The authors claimed that no significant increase was evident when the data from observational studies were also considered, which included a study by Klein *et al.* (2021) that provided an incident rate that was 20.1 BP cases per 100,000 unvaccinated participants, but only 4.58 BP cases per 100,000 vaccinated participants.[352] Apart from having an opposite trend from most of the other studies cited, this data accounted for 88% of the people tracked in all the studies combined. However, by excluding the data from Klein *et al.* (2021) and aggregating the remaining data from the 12 studies presented, it can be calculated that there was a 13% decrease in BP incidence with vaccination compared to the unvaccinated, with a rate of 9.0 BP cases per 100,000 participants in the COVID-19 vaccinated, and 10.3 BP cases per 100,000 unvaccinated participants. An important caveat for consideration in this type of comparison is the time sampling period for quantifying COVID-19 vaccine-induced cases of BP, which are usually within a few weeks of receipt of the vaccine, whereas in the unvaccinated population, this is based on the duration of the study, which may be over a year. This is why the findings from controlled random clinical studies are much more insightful. The authors did not detect any differences between the rates of BP between the Pfizer/BioNTech and AstraZeneca vaccines.

In the meta-analysis of 86 articles on neurological disorders associated with COVID-19 vaccination by Castillo and Castrillo (2022), they calculated that 4,936 of 13,809 (35.7%) of these patients experienced BP, and it was more prevalent in women (60%) than men.[342]

Collectively, these studies indicate that incidence levels for Bell's palsy likely were not appreciably increased by SARS-CoV-2 infection and may not be by the COVID-19 vaccines. However, the diverse

[351] Rafati, A., Pasebani, Y., Jameie, M., Yang, Y., Ilkhani, S., *et al.* (2023) Association of SARS-CoV-2 vaccination or infection with Bell's Palsy: A systematic review and meta-analysis. JAMA Otolarygology Head Neck Surg. 149(6):493–504. doi:10.1001/jamaoto.2023.0160

[352] Klein, N.P., Lewis, N., Goddard, K., Fireman, B., Zerbo, O., *et al.* (2021) Surveillance for adverse events after COVID-19 mRNA vaccination. JAMA. 326(14):1390–1399. doi:10.1001/jama.2021.15072

findings across the quoted studies justify further investigations as to the relationships between BP, COVID-19, and its vaccines.

2.15. Excess Deaths and All-Cause Mortality Statistics

Since the introduction of the COVID-19 genetic vaccines, there has been at least an 8-fold surge in news reports of collapses and unexpected deaths in otherwise young healthy people, pilots, musicians and athletes.[340,353] Sudden Adult Death Syndrome of "unknown" cause became amongst the top category of deaths in Alberta in 2021 since the rollout of the COVID-19 vaccines.[354] It is hard to ignore the rise of these unusual deaths with the timing of the launch of the COVID-19 genetic vaccines. The question is whether there has in fact been an increase in the total numbers of deaths since the advent of COVID-19 and with the introduction of the COVID-19 vaccines. This is best revealed by examining the available data on excess all-cause mortality.

With respect to deaths with COVID-19, the average age of a person that died of COVID-19 in Canada was about 84 years compared to about 82 years for all-cause mortality. There was no major increase in all-cause mortality in the first year of the COVID-19 pandemic, when the virus was more virulent, and there were no specific medications for its treatment or vaccination for its prevention. The total number of deaths from all causes in 2019 in Canada was 285,270, and 307,205 in 2020.[355] Infectious diseases accounted for only 8.6% of these deaths in 2019 and 12.6% of deaths in 2020 in Canada. By comparison, in 2020, cancer, and heart and stoke disease accounted for 27.0% and 23.2% of all deaths, respectively. The total number of deaths with COVID-19 in 2020, which was 16,151 (of which about half was due to a co-morbidity), accounted for 5.25% of the total number of deaths. Accidents and suicides killed more people in Canada in 2020 than COVID-19. Figure 14, show measurements of all-

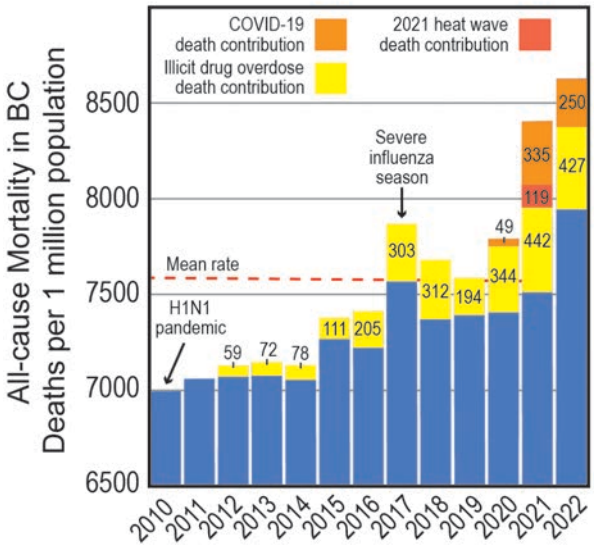
[353] Makis, W. (2023) Collapsed suddenly – 21 videos of collapses on stage and live on air: Greek South African rapper Costa Titch, age 27, collapsed & died; TV reporters collapsing or having strokes live on air. Substack. https://makismd.substack.com/p/18-videos-of-collapses-on-stage-and?utm_source=substack&utm_medium=email#play

[354] Donato, N.D. (2022) Deaths with unknown causes now Alberta's top killer: Province. Calgary CTV News. Retrieved from https://calgary.ctvnews.ca/deaths-with-unknown-causes-now-alberta-s-top-killer-province-1.5975536

[355] (2023) Statistics Canada. Table 13-10-0394-01 Leading causes of death, total population, by age group. doi:10.25318/1310039401-eng Retrieved from https://www150.statcan.gc.ca/n1/en/catalogue/13100394

cause mortality increases in British Columbia. Most of the excess all-cause mortality in 2022 in BC cannot be attributed to COVID-19.

Figure 14. British Columbia annual all-cause and COVID-19 mortality rates from October 1 to September 31 and illicit drug deaths rates from January 1 to December 31.[356]



It is also important to understand that there were fewer deaths from other infectious diseases such as influenza and RSV during the first two and a half years of the COVID-19 pandemic, and about half of the deaths ascribed to COVID-19 were in people that died with COVID-19, but actually may have been due to their co-morbidities. Rancourt *et al.* (2023) have concluded that there was no increase in all-cause mortality in the US in 2020, especially when compared to 2017.[357] Although there was virtually no increase in overall excess all-cause mortality in the 2020, the first year of the COVID-19 pandemic in Canada and elsewhere, it has increased significantly in 2021 and 2022, since the introduction of the

[356] Sourced data from https://bccdc.shinyapps.io/Mortality_Context_ShinyApp/ sourced February 24, 2023; https://www2.gov.bc.ca/gov/content/lifeevents/death/coroners-service/statistical-reports sourced February 24, 2023

[357] Rancourt, D. (2023) 2020-06-02: All-cause mortality during COVID-19 – No plague and a likely signature of mass homicide by government response. Ontario Civil Liberties Association. Retrieved from https://denisrancourt.ca/entries.php?id=9&name=2020_06_02_all_cause_mortality_during_covid_19_no_plague_and_a_likely_signature_of_mass_homicide_by_government_response

COVID-19 vaccines.[358,, 359, 360] In a recent study of all-cause mortality in 31 European countries, this was positively correlated with increased COVID-19 vaccination. [361] A one percent increase in COVID-19 vaccine uptake in 2021 between the countries was associated with a statistically significant monthly increase in mortality in the first nine months of 2022 by 0.105%.

The United Kingdom is one of the few jurisdictions where all-cause and COVID-19 linked mortality has been correlated with COVID-19 vaccination status, age and sex, and this data is available for public scrutiny.[362] Graphic representation of some of the findings provided by the UK Office for National Statistics for England are shown in Figure 15. The data indicate that with the emergence of Omicron variants, there has been no real benefit of single or double COVID-19 vaccination for preventing COVID-19 deaths compared to not being vaccinated against SARS-CoV-2. There is evidence that triple vaccination might have reduced COVID-19 deaths prior to September 2022, but not significantly afterwards. This might be due to a temporary protection afforded by the booster vaccination in vulnerable groups and that many who were particularly susceptible to dying from COVID-19 may have already succumbed by the time a third vaccine dose was available. However, with all-cause mortality, especially with the first dose of the COVID-19 vaccines early in the vaccination program, and the second dose subsequently after September 2021, the inoculations are associated with higher rates of death. After May 2022, there is little support that even a third shot of COVID-19 vaccines provided any significant benefit in reducing all-cause mortality. Interpretation of the data in Figure 15 is complicated,

[358] Rancourt, D.G. (2022) Probable causal association between India's extraordinary April–July 2021 excess-mortality event and the vaccine rollout. Correlation Research in the Public Interest. Retrieved from https://correlation-canada.org/report-probable-causal-association-between-indias-extraordinary-april-july-2021-excess-mortality-event-and-the-vaccine-rollout/

[359] Rancourt, D.G., Baudin, M., Mercier, J. (2022) Probable causal association between Australia's new regime of high all-cause mortality and its COVID-19 vaccine rollout. Correlation Research in the Public Interest. Retrieved from https://correlation-canada.org/report-probable-causal-association-between-australias-newregime-of-high-all-cause-mortality-and-its-covid-19-vaccine-rollout/

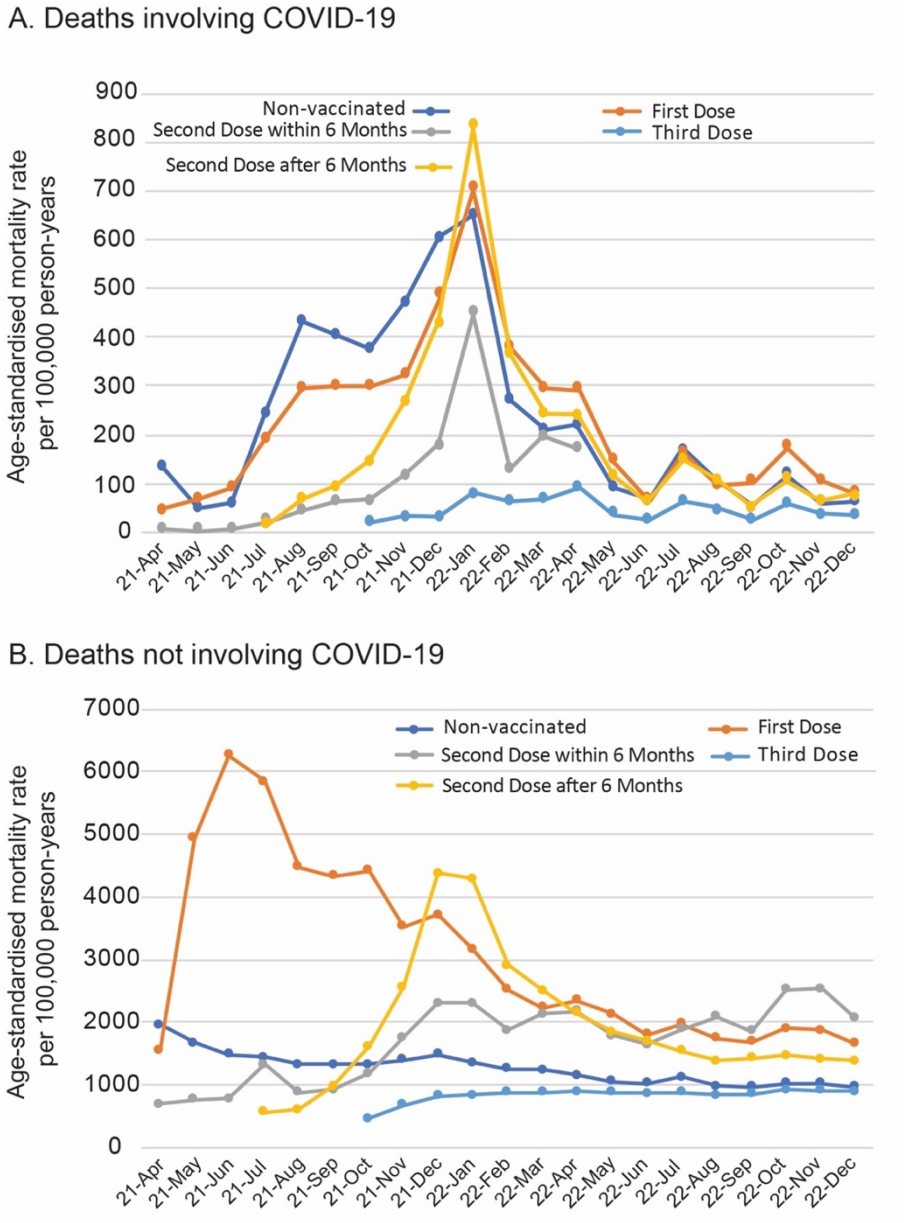
[360] Rancourt, D.G., Baudin, M., Hickey, J., Mercier, J. (2023) Age-stratified COVID-19 vaccine-dose fatality rate for Israel and Australia. Correlation Research in the Public Interest. Retrieved from https://correlation-canada.org/report-age-stratified-covid-19-vaccine-dose-fatality-rate-for-israel-and-australia/

[361] Aarstad, J., Kvitastein, O.A. (2023) Is there a link between the 2021 COVID-19 vaccine uptake in Europe and 2022 excess all-cause mortality? Asian Pacific J Health Sci. 10(1):25–31. doi.10.21276/apjhs.2023.10.1.6

[362] (2023) Deaths by vaccination status, England. Deaths occurring between 1 April 2021 and 31 December 2022 edition. UK Office for National Statistics. Retrieved from https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsbyvaccinationstatusengland

since the virulence of the SARS-CoV-2 was steadily reduced with the evolution of new variants and the extent of natural immunity in the UK population also increased. However, it is evident by comparison of the top and bottom panels of Figure 15 that COVID-19 associated deaths only accounted for a small portion of the excess deaths in England.

Figure 15. England monthly all-cause and COVID-19 mortality rates from April 1, 2021 to December 31, 2022 as a function of COVID-19 vaccine status.[362]



While such a temporal link in these increased deaths with COVID-19 vaccination exists, it does not necessarily have to be a causal. However, in considering the proposed mechanisms of action of the

COVID-19 genetic vaccines, their inadequate testing prior to wide-spread dissemination, and the unacceptably high risks for these vaccines for adverse reactions, it is not surprising that they do correlate.

2.16. The Changing Response of Public Health Abroad to COVID-19 Vaccination

While most Canadian public health authorities still zealously embrace COVID-19 vaccines, public health authorities in Quebec[363] and many other countries are much less enthusiastic. In fact, the COVID-19 adenovirus vaccines and Medicago, while initially approved by Health Canada, have all since been discontinued by the Fall of 2023.

In view of the mounting and disturbing data about the limited efficacy and serious safety issues associated with the COVID-19 genetic vaccines, health regulatory agencies around the world have begun to discourage or ban the use of these vaccines, especially in younger people. Denmark was the first nation in Europe to invoke this step by halting vaccination invitations on May 14, 2022.[364] By autumn 2022, Denmark recommended vaccination only to those over 50 years old and some vulnerable populations.[365]

Many European countries as well as Australia and some US states such as Florida have stopped recommending vaccinations for COVID-19 to anyone under 40, 50 or 60 years of age and especially children. Even in 2021, France and Scandinavian countries did not recommend the Moderna vaccine for people under 30 years of age.[366, 367] The United Kingdom Joint Committee on Vaccination and

[363] Rigs, A. (2023) COVID-19: Quebec drops recommendation that all should get booster vaccine. Montreal Gazette. Retrieved from https://montrealgazette.com/news/local-news/quebec-covid-vaccine-recommendation-hybrid-immunity

[364] Ellyatt, H. (2022) Denmark becomes the first country to halt its COVID vaccination program. CNBC News. Retrieved from https://www.cnbc.com/2022/04/28/denmark-the-first-country-to-halt-its-covid-vaccination-program.html

[365] Goldenberg, J. (2022) Denmark halts COVID vaccinations for low-risk people under 50. The Suburban. Retrieved from https:/www.thesuburban.com/news/city_news/denmark-halts-covid-vaccinations-for-low-risk-people-under-50/article_1e0264ec-dea3-59e0-bf3e-db59eee4378d.html

[366] (2021) France advices against Moderna for under-30s over rare heart risk. France 24. Retrieved from https://www.france24.com/en/live-news/20211109-france-advises-against-moderna-for-under-30s-over-rare-heart-risk

[367] Lehto, E. (2021) Finland joins Sweden and Denmark in limiting Moderna's COVID-19 vaccine. Retrieved from https://www.reuters.com/world/europe/finland-pauses-use-moderna-covid-19-vaccine-young-men2021-10-07/

Immunisation (JCVI) no longer recommends vaccination of healthy individuals under 50 years of age in the UK except for those in clinical risk groups or those attending to such individuals.[368] The Federal Office of Public Health in Switzerland also no longer recommends COVID-19 vaccination for healthy people in all age groups, and will not pay for COVID-19 vaccination for anyone, unless medically indicated by a physician for a patient with a clear risk-benefit analysis.[369] The Australian government has advised that as of February 2023 a booster dose is **not recommended** for children and adolescents up to 18 years who do not have any risk factors for severe COVID-19, and only for those 18-64 years of age who have undergone a risk-benefit analysis with their healthcare provider.[370] The German Federation of Hospitals (DKG) had called for the mandatory vaccination obligation of healthcare personnel to be revoked after the German Ministry of Health admitted that 1 in 5,000 COVID-19 vaccination shots led to serious side-effects.[371]

In April 2023, the European Medicine Agency and the European Parliament finally recognized that at least 11,448 deaths in the EU occurred following COVID-19 vaccination, and that there were 50,648 deaths attributed to these vaccines in the EudraVigilance database as of April 10, 2023.[372] It would appear that health regulatory agencies in Europe and elsewhere have come to realize the clear and present dangers of the COVID-19 genetic vaccines.

It seems that the populations of Canada and the US have also finally come to recognize the efficacy and safety issues of the COVID-19 vaccines, despite the heavy messaging from public health officials to

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[368] (2023) JCVI statement on the COVID-19 vaccination programme for 2023: 8 November 2022. Updated 27 January 2023. UK Department of Health and Social Care. Retrieved from https://www.gov.uk/government/publications/covid-19-vaccination-programme-for-2023-jcvi-interim-advice-8-november-2022/jcvi-statement-on-the-covid-19-vaccination-programme-for-2023-8-november-2022

[369] (2023) COVID-19: Vaccination. Federal Office of Public Health FOPH. Retrieved from https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/impfen.html#21889874

[370] (2023) COVID-19. Australian Immunisation Handbook. Australian Government Department of Health and Aged Care. Retrieved from https://www.health.gov.au/our-work/covid-19-vaccines/advice-for-providers/clinical-guidance/clinical-recommendations

[371] Mek, A. (2022) German Hospital Federation demands withdrawal of vaccination mandate after massive side effects revealed. RAIR Foundation USA. Retrieved from https://rairfoundation.com/german-hospital-federation-demands-withdrawal-of-vaccination-mandate-after-massive-side-effects-revealed/

[372] Joro, V. (2023) European Parliament: How many deaths have been caused by “COVID vaccines”? Question for written answer E-001201/2023. Retrieved from https://www.europarl.europa.eu/doceo/document/E-9-2023-001201_EN.html

the contrary. For example, only about 16% of those 6 months or older in Ontario within the past year had received a COVID-19 vaccination by September 14, 2023.[373] Canada-wide, only about 3.4% of Canadian chose to be vaccinated between March 10 and September 10, 2023.[374] In the US, only about 5.4% of children and 14.8% of adults 18 years and older received the updated XBB1.5 COVID-19 vaccines by November 17, 2023, whereas 35.1% of children and 36.3% of adults opted to be vaccinated against influenza.[375]

Canadians and public health officials in other countries have figured out that COVID-19 vaccines at this stage causes more harm than good. Surely it is time for our respected news outlets in Canada to finally learn this too.

Respectfully submitted by

Steven Pelech, Ph.D.
Professor,
Department of Medicine,
University of British Columbia

President and Chief Scientific Officer,
Kinexus Bioinformatics Corporation

Vice-President, and Co-Chair,
Scientific and Medical Advisory Committee,
Canadian Citizens Care Alliance

[373] (2023) COVID-19 vaccine uptake in Ontario: December 14, 2020 to November 5, 2023. Public Health Ontario. Retrieved from https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-vaccine-uptake-ontario-epi-summary.pdf?la=en

[374] Merkowsky, C.M. (2023) Only 3% of Canadians have taken most recent COVID booster: gov't data. LifeSite. Retrieved from https://www.lifesitenews.com/news/only-3-of-canadians-have-taken-most-recent-covid-booster-govt-data/

[375] (2023) Respiratory viruses. Vaccination trends – Adults. Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/respiratory-viruses/data-research/dashboard/vaccination-trends-adults.html