2021 HOUSE HUMAN SERVICES

HB 1320

2021 HOUSE STANDING COMMITTEE MINUTES

Human Services Committee
Pioneer Room, State Capitol

HB 1320
1/19/2021

Relating to immunizations required for entry to school or day care

Chairman Weisz opened the hearing at 3:18 p.m.

Representatives	Attendance
Representative Robin Weisz	P
Representative Karen M. Rohr	P
Representative Mike Beltz	P
Representative Chuck Damschen	P
Representative Bill Devlin	P
Representative Gretchen Dobervich	P
Representative Clayton Fegley	P
Representative Dwight Kiefert	P
Representative Todd Porter	P
Representative Matthew Ruby	P
Representative Mary Schneider	P
Representative Kathy Skroch	P
Representative Bill Tveit	P
Representative Greg Westlind	P

Discussion Topics:

- Immunization information system
- Vaccination mandate
- Immunization data exchange

Rep. Jeff Hoverson, District 3 (3:19) introduced the bill, testified in favor, and submitted testimony #1777.

Kolette Kramer (3:31) testified in favor.

Alexis Wangler, Co-Founder & President Health Freedom North Dakota (3:39) testified in favor and submitted testimony #1453.

Tara Dukart, Hazen North Dakota (3:43) testified in favor and submitted testimony #1595.

Dr. Ted Fogarty MD, Bismarck North Dakota (3:46) testified in favor and submitted testimony #1625.

Steve Nagel, Owner/DC 18 Health Solutions (4:01) testified in favor and submitted testimony #1645, #1646, #1647, #1648.

Thea Lee (4:03) testified in favor.

Matt Gardner, Greater North Dakota Chamber (4:04) testified in opposition.

Amy DeKok, North Dakota School Board Association Legal Council (4:05) testified in opposition.

Tracie Newman, Sanford Health/Fargo Public School Board (4:13) testified in opposition and submitted testimony #1212.

Molly Howell, Immunization Director North Dakota Department of Health (4:18) testified in opposition and submitted testimony #1329.

Additional written testimony: #1069, #1175, #1214, #1224, #1279, #1388, #1400, #1405, #1425, #1429, #1464, #1473, #1508, #1518, #1524, # 1531, #1532, #1542, #1544, #1546, #1598, #1609, #1615, #1616, #1619, #1628, #1636, #1683,

Chairman Weisz adjourned at 4:27 p.m.

Tamara Krause, Committee Clerk

What You NEED TO KNOW About COVID-19 Vaccines

COVID-19 vaccine makers cannot be sued for injuries or deaths caused by their product.[1] Victims may file a claim with the federal Countermeasures Injury Compensatic Program (CICP), but as yet, there is no Table of Covered Injuries for COVID-19 vaccines. Outcomes for past claims for other products fail to inspire confidence – **since 2010, a whopping 92% of claims filed with CICP were rejected, with no appeal permitted.** [2][3

The recent FDA authorization for COVID-19 vaccines is for Emergency Use Authorization ONLY. Testing for these vaccines was not required to meet standards otherwise required by federal law for FDA approval. **According to the FDA, "There is no U.S. Food and Drug Administration (FDA) approved vaccine to prevent COVID-19."** [4

Rushing a questionable vaccine into public use has fatally backfired before. A similar hurried vaccine rollout led to the death of numerous Filipino children who received a dengue vaccine during a declared epidemic, before long-term risks were understood. [6] No one yet knows how the new COVID-19 vaccines will affect people with autoimmune disease, people with cancer, pregnant women and unborn babies, or what impact the vaccine may have on fertility.

mRNA is still an unproven technology, never before used in vaccines for humans.[7] Previous coronavirus mRNA vaccine trials resulted in ferrets with liver damage,[8] mice with enhanced respiratory disease,[9] and monkeys with ADE lung damage. [10]

Current COVID-19 vaccines have not proven to prevent disease transmission.[11] [12] They may reduce symptoms without preventing infection.

COVID-19 vaccine mandates violate the basic human righ to informed consent.

[[1] https://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx
[2] https://www.hrsa.gov/cicp/filing-benefits
[3] https://www.mctlaw.com/vaccine-injury/vaccinations/coronavirus-covid-19
[4] https://www.fda.gov/media/144412/download
[5] https://www.fda.gov/media/144414/download
[6] https://www.sciencemag.org/news/2019/04/dengue-vaccine-fiasco-leads-criminal-charges-researcher-philippines
[7] https://www.fastcompany.com/90573488/how-pfizers-covid-19-vaccine-works-mrna
[8] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7115540/
[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1716185/
[10] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7075522/
[11] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html
[12] https://www.nytimes.com/2020/11/17/health/coronavirus-immunity.html

PCIC
InformedConsentPA.or

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

July 29, 2020

SENT VIA EMAIL

Elizabeth Brehm
Siri & Glimstad
200 Park Avenue, 17th Floor
New York, 10166
Via email: foia@sirillp.com

Dear Ms. Brehm:

This letter is in response to your Centers for Disease Control and Prevention and Agency for Toxic Substances and Disease Registry (CDC/ATSDR) Freedom of Information Act (FOIA) request of July 13, 2020, for:

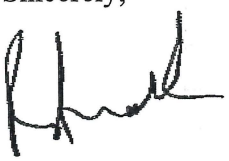
> "All documents in the CDC's possession which compare the health outcomes between children that have received vaccines and children that have never received any vaccines."

A search of our records failed to reveal any documents pertaining to your request. The CDC has not conducted a study of health outcomes in vaccinated vs unvaccinated populations.

You may contact our FOIA Public Liaison at 770-488-6277 for any further assistance and to discuss any aspect of your request. Additionally, you may contact the Office of Government Information Services (OGIS) at the National Archives and Records Administration to inquire about the FOIA mediation services they offer. The contact information for OGIS is as follows: Office of Government Information Services, National Archives and Records Administration, 8601 Adelphi Road-OGIS, College Park, Maryland 20740-6001, e-mail at ogis@nara.gov; telephone at 202-741-5770; toll free at 1-877-684-6448; or facsimile at 202-741-5769.

If you are not satisfied with the response to this request, you may administratively appeal by writing to the Deputy Agency Chief FOIA Officer, Office of the Assistant Secretary for Public Affairs, U.S. Department of Health and Human Services, Hubert H. Humphrey Building, 200 Independence Avenue, Suite 729H, Washington, D.C. 20201. You may also transmit your appeal via email to FOIARequest@psc.hhs.gov. Please mark both your appeal letter and envelope "FOIA Appeal." Your appeal must be postmarked or electronically transmitted by November 2, 2020.

Sincerely,



Roger Andoh
CDC/ATSDR FOIA Officer
Office of the Chief Operating Officer
Phone: (770) 488-6399
Fax: (404) 235-1852

#20-02002-FOIA

HOUSE HUMAN SERVICES
ROBIN WEISZ, CHAIRMAN JANUARY 19, 2021

TESTIMONY BY
ALEXIS WANGLER
RE: HOUSE BILL NO. 1320

Mr. Chairman and members of the House Human Services, my name is Alexis Wangler. I am the Co-Founder and President of the 501(c)(3) nonprofit Health Freedom North Dakota. This is my written testimony in regard to House Bill No. 1320.

I am strongly in favor of this bill. As stated in my written testimony for House Bill No. 1307, vaccinations are not one size fits all. Did you know that vaccines by law are classified as an "unavoidably unsafe" product? An unavoidably unsafe product is a product that is incapable of being made safe for its intended and ordinary use. No one should be mandated to ingest or inject and unavoidably unsafe product.

Vaccines can cause injury and death. The Vaccine Injury Compensation Program (VICP) acknowledges and compensates for injury and death as a result of vaccination. Many peer reviewed studies evidence severe adverse events that can occur from vaccination. The National Childhood Vaccine Injury Act of 986 was in response to failing vaccine manufacturers overrun with injury and death lawsuits from vaccines, namely DPT.

Another reason I am strongly in favor of this bill is because people have the God-given right to bodily autonomy. Vaccine mandates violate bodily autonomy via coercion. When one is forced to choose between removal of their basic liberties or to unwilling consent to a medical procedure, this amounts to coercion.

Lastly, I am strongly in favor of this bill because it would prohibit making receipt of a vaccine a condition for entry, education, employment, or services. Again, to prohibit a person from anything based on vaccination status is discrimination. This component of the bill would help parents with the struggle of finding daycare, keep his or her job, etc.

I urge you to agree to pass this bill. It would do so much good. Thank you for your time & consideration.

IN FAVOR: HB 1320

Relating to immunization records and data; and relating to immunizations required for entry to school or day care

Dear House Members of the Human Service Committee,

I urge you to **support HB 1320.**

I have been following laws pertaining to medical freedoms in other parts of the US. What has happened in states like California and New York is extremely concerning to me. I trust that you, our elected decision-makers, are willing to protect our children and secure our medical freedoms here in North Dakota.

As you may already know, vaccines are not safe for everyone. All vaccines have potential side effects and risks. While some adverse events of vaccines may be mild, like pain and swelling at the injection site, some are severe and can be significantly life-altering. These risks include, but are not limited to: (Sources: vaers.hhs.gov and CDC.gov)

Death, SIDS
anaphylaxis, anaphylactic shock, other allergic reactions
Guillain-Barré Syndrome, transverse myelitis, paralysis
autoimmune diseases, arthritis, gastrointestinal disorders, eczema
myocardial infarction (heart attack)
long-term seizures
strokes, coma, lowered consciousness, or permanent brain damage
pneumonia, respiratory illness, asthma, ear infections
swelling of the brain and/or spinal cord covering
temporary low platelet count which can cause unusual bleeding or bruising

Because vaccines are "unavoidably unsafe," and come with potential risk, I believe vaccines should always, always be optional. Therefore, everyone should have the right to opt out of a vaccine or other health-related decision for any applicable reason including: medical, moral, ethical, religious, or philosophical concerns.

The unvaccinated population, including children, poses no true risk to the general public, including daycares and school settings.

Thank you very much for your time and consideration. Sources and links included on page 2 of this letter.

Tara Dukart
Hazen, ND

https://pubmed.ncbi.nlm.nih.gov/32537156/

https://vaccine.guide/effectiveness-outbreaks-herd-immunity/herd-immunity/herd-immunity-and-compulsory-vaccination-does-the-theory-justify-the-law/

https://www.icandecide.org/wp-content/uploads/2020/05/1-PAGE-INTRO-VAX-SAFETY.pdf

https://www.icandecide.org/wp-content/uploads/2019/09/Publications-Regarding-Vaccine-Safety-1.pdf

https://childrenshealthdefense.org/news/research-reviews/fully-vaccinated-vs-unvaccinated-a-summary-of-the-research/

Written Testimony of Edward F. Fogarty, MD in regards to HB1307, HB1320 and HB1306 prepared for the North Dakota House Human Services Committee 01/19/2021.

Dear HHS Committee Members,

I am strongly in favor of the passage of HB1307, HB1320 and HB1306. These there bills revolve around the matters of protection of our citizens from participation in fraudulent medical and healthcare marketplaces in my opinion as a physician.

My experience as a North Dakota physician who has been a leading researcher in hyperbaric medicine and recovery of various forms of acute and chronic brain injury also informs my opinion on the importance of these bills who's passage would serve as a firewall to greater potential harms of our citizenry from product liabilities of vaccines of any sort.

Our federal government in 1986 gave immunity to all vaccine manufacturers for liability of any sort relating to their products. This has led to an entire industry running amok on matters of safety. In 2020, with our nation in a declared state of war on SARS-CoV2, I believe we have all seen how powerful the medical/pharmaceutical lobby really is and its impact on our public health department in ND as well as the very governance of our state through the executive branch.

These three bills will provide some "relief" for the encroachment of the amalgams of government/public health and global pharmaceutical companies into our most sacred decision making over our own health and immune system modifications as well as those of our children's health, well being and development.

HB1307 provisions prohibiting public facilities to demand proof of vaccination is critically important to prevent the further encroachment for what many see as a medical tyranny fed by the current pandemic. Proof of IMMUNITY rather than proof of compliance in a corrupt marketplace is the more medically sound course for any of these considerations. The marketplace of healthcare does not want to lose the opportunity to "over-vaccinate" American populations who may already be immune to diseases such as COVID19 through prior infection or vaccination. Sadly many of my own colleagues in medicine fail to understand that diagnostic laboratory studies can show that a particular vaccine is not only unnecessary but a fraudulent waste of health care resources. I addressed some of these concerns in a Bismarck Tribune Opinion piece on 03/23/2008:
https://bismarcktribune.com/news/opinion/mailbag/a-proposal-on-vaccinations/article_e41b2f91-d75f-511d-92d7-eeef199e8f91.html

HB320 is extremely important for North Dakota's citizens as state and local government mandates on vaccination might technically be unconstitutional under the laws of North Dakota itself in regards to the employment doctrine set forth in our constitution. The ND Constitution under Article VIII, section 1 indicates that all public schools are open to all children of the state. Our citizens who see the corruptions of medicine, government and law at the federal level in these matters, should be afforded the sanctuary of refusal of vaccination under prior ND laws giving philosophical, medical and religious exemptions in this arena. Behavioral economics issues have begun to show our nation and our state that we have significant percentage of people questioning the safety and need for some of these medical products that have no liability for causing harm. I believe we need this law in ADDITION to the free will provisions of exemptions, this law will send a message to government bodies who would rather their needs whether honest or fraudulent be met before the people of North Dakota's rights are protected.

I have seen MANY coercive manipulations of my fellow North Dakotans in these matters of vaccine mandates. There is a nurse in Jamestown who has loss of consciousness with every vaccination for influenza, ostensibly this person is going through this safety racket to keep her job?

I fear that many of you on this committee may have family members or yourself as well placed under duress for standing up for your right to medical decision making over vaccines and in the future, now that we have a class of vaccines that is manipulating genomics at the ribosomal level, when will the state/medical/industrial complex start mandating even greater modifications of our very being in service to the "greater good" or indirectly the billionaire cronies of elected officials? On February 20, 2019, I published this Open Letter to the State of Washington which also reiterates that state officials ought to be careful regarding their own needs to protect their own health freedoms in this realm.
https://informedchoicewa.org/education/an-open-letter-from-edward-f-fogarty-md/

It should be noted that I also called into question the use of ND taxpayer dollars for the "aid package through ND Public Health" in the containment of the 2019 Washington measles outbreak. Why did our state tax dollars go to another state's response to a measly generally non-fatal disease of childhood that engendered infection "parties" in the 1960s which some of you no doubt are old enough to have participated in for contracting mother natures version of an important immunological conditioning agent. Mayo Clinic is working on research to use measles infections therapeutically against untreatable cancers. Merck, which makes MMR under FDA licensure in America has been in a decade long battle for maintaining this licensure as the live attenuated corporate viruses here are not provoking a strong enough repsonse anymore to maintain the licensure under scientific titer checking protocols that many US physicians are now using in their clinical practices. Yes, many of my Integrative Medicine colleagues around the country are doing titer checks on the MMR series and finding that the mumps component is not provoking a safe level of antibodies after 2 doses. This is the crux of a Federal False Claims Act lawsuit in Eastern Pennsylvania filed by whistleblower scientists and several physicians against Merck.
https://www.courthousenews.com/class-says-merck-lied-about-mumps-vaccine/

The news piece above is from June of 2012. As some of you who may have read many of my emails to you and the Governor in the last 3 months may know, I am a proponent of education of many issues in the interface of law, medicine and government. One of th emore important SCOTUS decisions in this nation's history is that of Throckmorton (1878) wherein the doctrine of 'fraud vitiates all" was introduced. Please stand strong for yourselves, your families and your fellow North Dakotans and pass all three of these bills. HB1306 is needed for your grandchildren and great grandchildren to develop under a more natural milieu. As the leading state expert who is a physician/scientist that has reversed cognitive declines in a few of our state's elders via a gentle detoxification process of mild hyperbaric air and oxygen therapies, I can show you dozens of scientific studies that show infant mammals have an exquisitely sensitive respiratory drive center that lies in close proximity to the bloodstream for carbon dioxide sampling. When CO2 levels increase in the bloodstream, babies especially have a fine tuned response to increasing the respiratory rate so that CO2 (a metabolic toxin) is off-gassed to the atmosphere quickly through the lungs. As the sampling of science below shows, mammalian infants can have other toxins, including aluminum and mercury from vaccines interfere with the development of the tiny cluster of important neurons developing in these respiratory center drives.

But if you cannot understand the science below (see appendix), that is okay as we have a grand opportunity from the 2020 pandemic experiences to see how many SIDS deaths did not occur in 2020 during the pandemic as 0-12 month old American children were, on the whole basically in a delayed CDC vaccination schedule. This experiment by the hand of God and mother nature has already happened and we should now commit some limited funds to a simple epedimiology study (IN THE RIGHT HANDS) that can show the decline of SIDS rates in our children corresponding to the delay of vaccinations in our family's children. A paired relative risk could be obtained temporally by looking at the 2017, 2018, and 2019 birth cohorts on a month by month basis. The null hypothesis would be that the ND Babies born in April of the 3 years prior had the same risk of SIDS as though born in April 2020, and the other major months of access restrictions to medical facilities in 2020 for moms and their newborns would likely disprove the "null" hypothesis.

In summary, as many of you surely may have guessed from my communications with you over the last 3 months, I believe as a physician who's understanding of economic wellness that carries into my practice of medical education, communication and real world procedural and diagnostic medicine - we would be remiss as a political body to fail our grandchildren by failing to pass all three of these bills. Thank you for your time and attention.

Respectfully submitted,

Edward "Ted" Fogarty, MD
800 MUNICH DR
BISMARCK, ND
01/19/2021
1245 PM

APPENDIX:
https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc?2013vv0611-73-0
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3170075/
https://pubmed.ncbi.nlm.nih.gov/28918379/

https://bismarcktribune.com/news/opinion/mailbag/a-proposal-on-vaccinations/article_e41b2f91-d75f-511d-92d7-eeef199e8f91.html

Now that the courts have recognized a link between vaccinations and autism, we need to revisit public policy. Individual vaccines can't get much safer, but vaccine protocols can. The 2008 Centers for Disease Control protocol for pediatric vaccines is not the safest way to accomplish the goal of immunity to multiple infectious diseases in an individual.
A vast majority of children will not be affected by the administration of vaccinations. But if epidemiological purposes can be met with a more directed approach, there is no reason to endanger a genetically vulnerable child with unneeded boosters. Titer checking protocols are inherently safer for individuals, especially in the at-risk families for autism.

A simple lab test to check titers can tell you whether an additional "booster" is needed. The vast majority of kids, 95 percent, are immune for life to measles-mumps and rubella after one dose. Multi-shot vaccine protocols are a boon to vaccine companies, not North Dakota families. Pediatricians using titer checks would shift resources from multinational vaccine corporations to North Dakota hospitals via laboratory services utilization.

The argument against this approach has always been, "It's too troublesome," and "What if we lose the patient to follow-up?" These are legitimate concerns, but is it fair to make the social assumptions that no one in this state sees their pediatrician after the first few months of a baby's life?

As the art moves forward in vaccinomics, the future will show how easily we can do this better. We now have simple finger-stick titer checking technology for HIV antibodies. This could be ported into titer checking systems for vaccine efficacy, and the University of North Dakota School of

Medicine could be the institution that leads the charge on this innovative research. It will take some time to calibrate such systems, but we can do it here better than anywhere because of our high compliance with vaccination in this state and our close-knit medical and governmental communities. Even current policy needs some modification in light of the growing public concerns in vaccine safety due to the Hanna Poling case. She is the child of parents who hold M.D., Ph.D., R.N. and J.D. degrees. They would probably advocate as I, after their experience, that parents need to be made aware of better ways to vaccinate. The first modification of law and policy that should occur is a disclosure on consent forms for vaccine boosters. A child may already be immune for life in certain series after one dose of vaccine (live virus vaccines have incredible long-lived titers and high first response rates). A titer check can obviate the need for an unneeded booster; shouldn't the public be made away of this? This is particularly important in families with high rates of autoimmune disease.

In my own experience, I lost my vaccine records, and in order to get into medical school, I had a whole series titer (antibody) check to prove that I was immune to the diseases we all need protection from in this incredibly helpful arm of medicine.

To ensure that this is done appropriately for your child is to be a loving parent, and to push your colleagues in medicine and government is to be a certain kind of patriot. To fail to educate parents on this option is engendering the socialistic mentality of a cradle-to-grave caretaker federalist system. Governments and school districts would be better served to require titer levels, not written records of vaccine shots. Titer levels are scientific evidence of immunity. A vaccine record actually isn't, as it can be forged.

All U.S. physicians and state legislators should thoroughly read the Simpsonwood Transcripts (www .nationalautismassociation.org /library.php). This is the most honest assessment of the relationship of vaccines to autism and shows a clear signal of "uncertain" strength.

The CDC conveniently "forgets" to publish the transcript as part of the timeline of understanding the relationship of vaccines to autism. This is clearly a lack of transparency at the federal level of health policy, a timely discussion in light of John Irby's front-page piece in the March 16 Tribune. Federal mandates turn a blind eye to the at-risk child harmed by vaccines. We are abusing the molecular machinery of some of our more fragile children to protect vaccine companies, it's a deal with the devil that all of us in medicine hate having to make; I make it every day as a member of the medical specialty, radiology, that deals the most heavy metals and known teratogens to U.S. citizens.

The integrity and smarts of our state level public health officers is getting usurped by the federal government whose agencies are drunk on the influence of multinational corporations, especially in medicine and pharmaceuticals. As a father of an autistic child, I will fight the federal government's continuing to abuse certain vulnerable children in this nation's war against disease. We don't send everyone to the front line of other wars, why aren't we more discriminating in this one?

North Dakota physicians know how to better vaccinate the children of this state than the CDC. We all need to get behind the pediatrics and public health community of North Dakota to improve this art in scientific ways. It may be a decade before that happens, but we can do it.

(*Dr. Edward "Ted" Fogarty is a Bismarck radiologist. - Editor*)

https://informedchoicewa.org/education/an-open-letter-from-edward-f-fogarty-md/

Excerpts below:

"This is not only a costly loss of worker productivity, influenza vaccines are a yearly unethical experiment because of the lack of any safety studies on these medical products. Influenza vaccines are distributed within weeks of their development and have repeatedly been found contaminated aftermarket release in the last 20 years. Our national healthcare security through the workforce of physicians, nurses, laboratory and radiology technologists is placed at risk for political espionage even as more vaccines are manufactured in jurisdictions that could use these products as Trojan horses for slow viruses or prions. Epidemiologically, my colleagues in public health, Neurology or Infectious Disease will need years and many exposures to identify a signal if such covert biological warfare is occurring even now."

"We do not have the ability to easily understand who is at risk of vaccine injury in children, especially our newborns, we pour billions into individualized care of the legislative-age crowd on pharmacogenomic safety studies so that products like Vioxx do not destroy lives of our learned elders. As we have never done anything of the sort in public health and policy for our most developmentally and eugenically vulnerable wildcards of mixed genes in American families, we practice tacit genetic discrimination in the access to public education. Our school budgets are skyrocketing on the increasing numbers of special needs children.

"If removing philosophical exemptions to participation in fraudulent unregulated markets are what your collective actions bring to bear in your state, you may find liabilities that you did not anticipate. I can say this without reservation, the most pervasive molecular crime against humanity in the last 20 years has been the use of aluminum injections on day one of life which have no medical indication. Diagnostic medicine has long ago marked the crime of medical assault on American babies whose mothers' obstetric laboratory panels have shown millions of times over that they are delivering antibodies against the Hep B vaccine itself to their fetuses. There is no medical indication for a vaccine on day one of life outside of active infection of the mother. The rest of my colleagues in medicine would be sued or lose their license for serial billing of the state or insurance companies on completely worthless un-indicated interventions like Hep B on day one, or for that matter, at 2 months of life.

“With growing whistleblower cases coming out of the woodwork in scientific fraud are you really ready to cast this lot towards your constituents’ children and families. The U.S. Department of Justice has a case against Merck in Pennsylvania for the scandalous corporate racketeering of scientists that were told to spike the data for mumps to pass the bar of 95% efficacy, ostensibly so that Merck would not lose the monopoly on MMR in this country. I believe you can all see now that the only check and balance in the system against fraud in vaccine science is a public consumer (parents) becoming aware within our nation discourse regarding these issues. Please hold the line on the philosophical exceptions for the greater good of Washington’s political well-being. Forcing your youngest citizens to participate in a fraud and racketeering scheme is a violation of basic human rights. We first need ethical corporate leadership in the vaccine industry before we can trust our genetically-disabled to the gross negligence of entire generations of humans being treated like cattle. Thank you for your time and attention, may the wisdom of the great decision makers of history help you discern the best for your state regarding philosophical exemptions.”

2/20/2019

EFF3MD

Grant Final Report

Grant ID: R18 HS 017045

Electronic Support for Public Health–Vaccine Adverse Event Reporting System (ESP:VAERS)

Inclusive dates: 12/01/07 - 09/30/10

Principal Investigator:
Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Team members:
Michael Klompas, MD, MPH

Performing Organization:
Harvard Pilgrim Health Care, Inc.

Project Officer:
Steve Bernstein

Submitted to:
The Agency for Healthcare Research and Quality (AHRQ)
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Abstract

Purpose: To develop and disseminate HIT evidence and evidence-based tools to improve healthcare decision making through the use of integrated data and knowledge management.

Scope: To create a generalizable system to facilitate detection and clinician reporting of vaccine adverse events, in order to improve the safety of national vaccination programs.

Methods: Electronic medical records available from all ambulatory care encounters in a large multi-specialty practice were used. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions were evaluated for values suggestive of an adverse event.

Results: Restructuring at CDC and consequent delays in terms of decision making have made it challenging despite best efforts to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial and comparison of ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. However, Preliminary data were collected and analyzed and this initiative has been presented at a number of national symposia.

Key Words: electronic health records, vaccinations, adverse event reporting

Final Report

Purpose

This research project was funded to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS), via the following aims:

Aim 1. Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration.

Aim 2. Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS).

Aim 3. Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.

Aim 4. Distribute documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems.

Scope

Public and professional confidence in vaccination depends on reliable postmarketing surveillance systems to ensure that rare and unexpected adverse effects are rapidly identified. The goal of this project is to improve the quality of vaccination programs by improving the quality of physician adverse vaccine event detection and reporting to the national Vaccine Adverse Event Reporting System (VAERS). This project is serving as an extension of the Electronic Support for Public Health (ESP) project, an automated system using electronic health record (EHR) data to detect and securely report cases of certain diseases to a local public health authority. ESP provides a ready-made platform for automatically converting clinical, laboratory, prescription, and demographic data from almost any EHR system into database tables on a completely independent server, physically located and secured by the same logical and physical security as the EHR data itself. The ESP:VAERS project developed criteria and algorithms to identify important adverse events related to vaccinations in ambulatory care EHR data, and made attempts at formatting and securely sending electronic VAERS reports directly to the Centers for Disease Control and Prevention (CDC).

Patient data were available from Epic System's Certification Commission for Health Information Technology-certified EpicCare system at all ambulatory care encounters within Atrius Health, a large multispecialty group practice with over 35 facilities. Every patient receiving a vaccine was automatically identified, and for the next 30 days, their health care diagnostic codes, laboratory tests, and medication prescriptions are evaluated for values

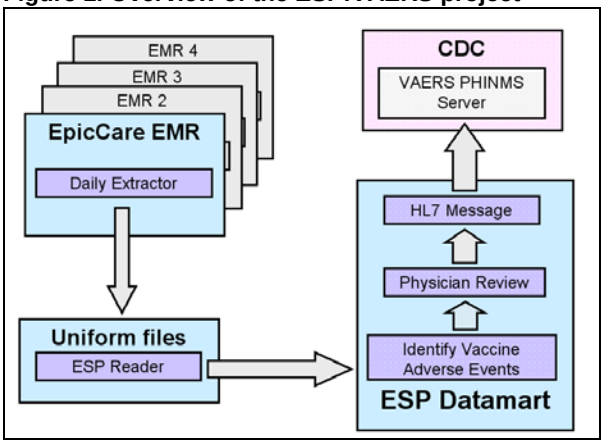
suggestive of an adverse vaccine event. When a possible adverse event was detected, it was recorded, and the appropriate clinician was to be notified electronically.

Clinicians in-basket messaging was designed to provide a preview a pre-populated report with information from the EHR about the patient, including vaccine type, lot number, and possible adverse effect, to inform their clinical judgment regarding whether they wish to send a report to VAERS. Clinicians would then have the option of adding free-text comments to pre-populated VAERS reports or to document their decision not to send a report. The CDC's Public Health Information Network Messaging System (PHIN-MS) software was installed within the facilities so that the approved reports could be securely transferred to VAERS as electronic messages in an interoperable health data exchange format using Health Level 7 (HL7).

Methods

The goal of Aim 1: *Identify required data elements, and develop systems to monitor ambulatory care electronic medical records for adverse events following vaccine administration,* and Aim 2: *Prepare, and securely submit clinician approved, electronic reports to the national Vaccine Adverse Event Reporting System (VAERS),* was to construct the below flow of data in order to support the first two Aims:

Figure 1. Overview of the ESP:VAERS project



Existing and functioning ESP components are shown on the left, and Aims 1 and 2 on the right. ESP:VAERS flags every vaccinated patient, and prospectively accumulate that patient's diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions. A main component of Aim 1 was to *Develop AE criteria to assess these parameters for new or abnormal values that might be suggestive of an adverse effect.* A reporting protocol & corresponding algorithms were developed to detect potential adverse event cases using diagnostic codes, and methods were tested to identify prescriptions or abnormal laboratory values that might be suggestive of an adverse effect. These algorithms were designed to seek both expected and unexpected adverse effects.

This reporting protocol was approved by both internal & external partners. We initially prepared a draft document describing the elements, algorithms, interval of interest after vaccination, and actions for broad classes of post-vaccination events, including those to be reported immediately without delay (such as acute anaphylactic reaction following vaccination), those never to be reported (such as routine check-ups following vaccination) and those to be reported at the discretion and with additional information from the attending physician through a feedback mechanism. The draft was then widely circulated as an initial / working draft for comment by relevant staff in the CDC and among our clinical colleagues at Atrius. In addition to review by the internal CDC Brighton Collaboration liaison, this protocol has also received review & comment via the CDC's Clinical Immunization Safety Assessment (CISA) Network.

The goal of Aim 2 was the *Development of HL7 messages code for ESP:VAERS to ensure secure transmission to CDC via PHIN-MS*. The HL7 specification describing the elements for an electronic message to be submitted to Constella, the consultants engaged by CDC for this project was implemented. Synthetic and real test data was been generated and transmitted between Harvard and Constella. However, real data transmissions of non-physician approved reports to the CDC was unable to commence, as by the end of this project, the CDC had yet to respond to multiple requests to partner for this activity.

The goal of Aim 3 was to *Comprehensively evaluate ESP:VAERS performance in a randomized trial, and in comparison to existing VAERS and Vaccine Safety Datalink data.*

We had initially planned to evaluate the system by comparing adverse event findings to those in the Vaccine Safety Datalink project—a collaborative effort between CDC's Immunization Safety Office and eight large managed care organizations. Through a randomized trial, we would also test the hypothesis that the combination of secure, computer-assisted, clinician-approved, adverse event detection, and automated electronic reporting will substantially increase the number, completeness, validity, and timeliness of physician-approved case reports to VAERS compared to the existing spontaneous reporting system; however, due to restructuring at CDC and consequent delays in terms of decision making, it became impossible to move forward with discussions regarding the evaluation of ESP:VAERS performance in a randomized trial, and compare ESP:VAERS performance to existing VAERS and Vaccine Safety Datalink data. Therefore, the components under this particular Aim were not achieved.

Aim 4 *Distribution of documentation and application software developed and refined in Aims 1 and 2 that are portable to other ambulatory care settings and to other EMR systems* has been successfully completed. Functioning source code is available to share under an approved open source license. ESP:VAERS source code is available as part of the ESP source code distribution. It is licensed under the LGPL, an open source license compatible with commercial use. We have added the ESP:VAERS code, HL7 and other specifications and documentation to the existing ESP web documentation and distribution resource center http://esphealth.org, specifically, the Subversion repository available at:
http://esphealth.org/trac/ESP/wiki/ESPVAERS.

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average of 890 possible events, an average of 1.3 events per clinician, per month. These data were presented at the 2009 AMIA conference.

In addition, ESP:VAERS investigators participated on a panel to explore the perspective of clinicians, electronic health record (EHR) vendors, the pharmaceutical industry, and the FDA towards systems that use proactive, automated adverse event reporting.

Adverse events from drugs and vaccines are common, but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of "problem" drugs and vaccines that endanger public health. New surveillance methods for drug and vaccine adverse effects are needed. Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting: reporting is not part of clinicians' usual workflow, takes time, and is duplicative. Proactive, spontaneous, automated adverse event reporting imbedded within EHRs and other information systems has the potential to speed the identification of problems with new drugs and more careful quantification of the risks of older drugs.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Inclusion of AHRQ Priority Populations

The focus of our project was the Atrius Health (formerly HealthOne) provider & patient community. This community serves several AHRQ inclusion populations, specifically low-income and minority populations in primarily urban settings.

Atruis currently employs approximately 700 physicians to serve 500,000 patients at more than 18 office sites spread throughout the greater Metropolitan Boston area. The majority of Atruis physicians are primary care internal medicine physicians or pediatricians but the network also includes physicians from every major specialty.

The entire adult and pediatric population served by Atruis was included in our adverse event surveillance system (ESP:VAERS). Atruis serves a full spectrum of patients that reflects the broad diversity of Eastern Massachusetts. A recent analysis suggests that the population served by Atruis is 56% female, 16.6% African American, 4% Hispanic. The prevalence of type 2 diabetes in the adult population is 5.7%. About a quarter of the Atruis population is under age 18.

List of Publications and Products

ESP:VAERS [source code available as part of the ESP source code distribution]. Licensed under the GNU Lesser General Public License (LGPL), an open source license compatible with commercial use. Freely available under an approved open source license at: http://esphealth.org.

Lazarus, R, Klompas M, Hou X, Campion FX, Dunn J, Platt R. Automated Electronic Detection & Reporting of Adverse Events Following Vaccination: ESP:VAERS. The CDC Vaccine Safety Datalink (VSD) Annual Meeting. Atlanta, GA; April, 2008.

Lazarus R, Klompas M Automated vaccine adverse event detection and reporting from electronic medical records. CDC Public Health Informatics Network (PHIN) Conference August 27, 2008.

Klompas M, Lazarus R ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 17th.

Lazarus R, Klompas M, Kruskal B, Platt R Temporal patterns of fever following immunization in ambulatory care data identified by ESP:VAERS Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

Linder J, Klompas M, Cass B, et al. Spontaneous Electronic Adverse Event Reporting: Perspectives from Clinicians, EHR Vendors, Biopharma, and the FDA. Presented at the American Medical Informatics Association Annual Symposium; 2009 November 14–18: San Francisco, CA.

International Journal of
Environmental Research and Public Health

MDPI

Article

Relative Incidence of Office Visits and Cumulative Rates of Billed Diagnoses Along the Axis of Vaccination

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Received: 23 October 2020; Accepted: 18 November 2020; Published: 22 November 2020

Abstract: We performed a retrospective analysis spanning ten years of pediatric practice focused on patients with variable vaccination born into a practice, presenting a unique opportunity to study the effects of variable vaccination on outcomes. The average total incidence of billed office visits per outcome related to the outcomes were compared across groups (Relative Incidence of Office Visit (RIOV)). RIOV is shown to be more powerful than odds ratio of diagnoses. Full cohort, cumulative incidence analyses, matched for days of care, and matched for family history analyses were conducted across quantiles of vaccine uptake. Increased office visits related to many diagnoses were robust to days-of-care-matched analyses, family history, gender block, age block, and false discovery risk. Many outcomes had high RIOV odds ratios after matching for days-of-care (e.g., anemia (6.334), asthma (3.496), allergic rhinitis (6.479), and sinusitis (3.529), all significant under the Z-test). Developmental disorders were determined to be difficult to study due to extremely low prevalence in the practice, potentially attributable to high rates of vaccine cessation upon adverse events and family history of autoimmunity. Remarkably, zero of the 561 unvaccinated patients in the study had attention deficit hyperactivity disorder (ADHD) compared to 0.063% of the (partially and fully) vaccinated. The implications of these results for the net public health effects of whole-population vaccination and with respect for informed consent on human health are compelling. Our results give agency to calls for research conducted by individuals who are independent of any funding sources related to the vaccine industry. While the low rates of developmental disorders prevented sufficiently powered hypothesis testing, it is notable that the overall rate of autism spectrum disorder (0.84%) in the cohort is half that of the US national rate (1.69%). The practice-wide rate of ADHD was roughly half of the national rate. The data indicate that unvaccinated children in the practice are not unhealthier than the vaccinated and indeed the overall results may indicate that the unvaccinated pediatric patients in this practice are healthier overall than the vaccinated.

Keywords: pediatrics; vaccines; adverse events; relative incidence of office visit

1. Introduction

Vaccines are widely regarded as safe and effective within the medical community and are an integral part of the current American medical system. While the benefits of vaccination have been estimated in numerous studies, negative and nonspecific impact of vaccines on human health have not been well studied. Most recently, it has been determined [1,2] that variation exists in individual responses to vaccines, that differences exist in the safety profile of live and inactivated vaccines, and that simultaneous administration of live and inactivated vaccines may be associated with poor outcomes. Studies have not been published that report on the total outcomes from vaccinations, or the increase or decrease in total infections in vaccinated individuals.

Pre-licensure clinical trials for vaccines cannot detect long-term outcomes since safety review periods following administration are typically 42 days or less [3]. Long-term vaccine safety science relies on post-market surveillance studies using databases such as the US Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC's) Vaccine Adverse Events Reporting System (VAERS) and the Vaccine Safety Datalink. VAERS [4] is a passive reporting system in which, according to Ross 2011 [5], "fewer than 1% of vaccine adverse events are reported." The Vaccine Safety Datalink (VSD) can, in principle, according to the Institute of Medicine (IOM, 2013) [6], be used to compare outcomes of vaccines and unvaccinated children. Based on the IOM's recommendation, in 2016, the CDC published a white paper (CDC, 2016 [7]; Glanz et al., 2016 [8]) on studying the safety of their recommended pediatric vaccine schedule. Unfortunately, to date, no studies have been published comparing a diversity of outcomes of vaccinated and unvaccinated children using the VSD.

There are serious limitations inherent to long-term vaccine safety studies as currently implemented. Post-licensure studies on vaccine safety typically employ an "N vs. $N + 1$" design of analysis, meaning they compare fully vaccinated children with fully vaccinated children missing only one vaccine. Despite reports of increases in vaccine cessation, virtually none of the post licensure-vaccine safety studies have included comparisons to groups completely unexposed to vaccines.

A few independent (non-CDC) studies do exist that have compared outcomes between vaccinated and unvaccinated children. A small survey study of 415 families with homeschooled children by Mawson et al., 2017 [9] that compared vaccinated with completely unvaccinated children reported increased risk of many diagnoses among the vaccinated children including (condition, fold-increase): allergic rhinitis (30.1), learning disabilities (5.2), attention deficit hyperactivity disorder (ADHD) (4.2), autism (4.2), neurodevelopmental disorders (3.7), eczema (2.9), and chronic illness (2.4). The increased risk of neurodevelopmental disorders appeared to be higher in cases of preterm births. A study from Germany (Schmitz et al., 2011) [10] reported no increases in adverse outcomes other than atopy.

A limitation of both of these studies is that they relied on parental surveys, and both had a small unexposed group. A further limitation in the German study [10] is that they also defined a child as unexposed to vaccines even if they received vaccination for varicella, rotavirus, pneumococcal, meningococcal, influenza, and/or others; the study, therefore, is not "vaccinated vs. unvaccinated". Studies of Diphtheria, Pertussis, and Tetanus (DTP) vaccine that had an unexposed group found an increased risk of mortality (Mogensen et al., 2017) [11] and asthma (McDonald et al., 2008) [12] in the vaccine exposed group. Gallagher and Goodman, 2008 [13] reported increased ASD in a hepatitis B vaccine-exposed group. Studies funded by the pharmaceutical industry or conducted by the CDC typically tend to find no harm associated with vaccination, while studies conducted without pharmaceutical industry funding have often found harm.

Hooker and Miller 2020 [14] recently found an increase in odds ratio (OR) in developmental delay (OR 2.18), asthma (OR 4.49), and ear infection (OR 2.13) in vaccinated children compared to unvaccinated children in a study using data from three practices. In the current study, we assess the total outcomes of patients ranging in age from 2 months to 10.4 years of all children in a pediatric practice that have not been vaccinated compared to those who have been variably vaccinated based on medical records using a novel measure, the Relative Incidence of Office Visit (RIOV), and compare results from that measure to results obtained using odds ratios of incidence of diagnoses.

2. Materials and Methods

2.1. Data Source and Provenance

A detailed proposal for a retrospective study was submitted to an Institutional Review Board (IRB), and was approved (Pro00031853 letter dated 7 May 2019). The data source for this study was all billing and medical records of Integrative Pediatrics, a private pediatric practice located in Portland, Oregon. Data collected from True North Data (Mill Creek, WA, USA) were de-identified by trained and honest brokers with the Institute for Pure and Applied Knowledge (IPAK) affiliation

who were certified to de-identify patient data as required under the Health Insurance Portability and Accountability Act (HIPAA), thus ensuring that the data analysts never saw identified data. Outcomes were represented by International Classification of Diseases (ICD) codes (See Supplementary Materials Table S1). Coded data were matched back to the identified medical and billing record to provide a data parity check by our honest brokers team.

2.2. Inclusion/Exclusion Criteria

All patients that were born into the practice between 1 June 2008 and 27 January 2019, with a first visit before 60 days of life and a last visit after 60 days. All inclusion/exclusion criteria applied are outlined in Figure 1.

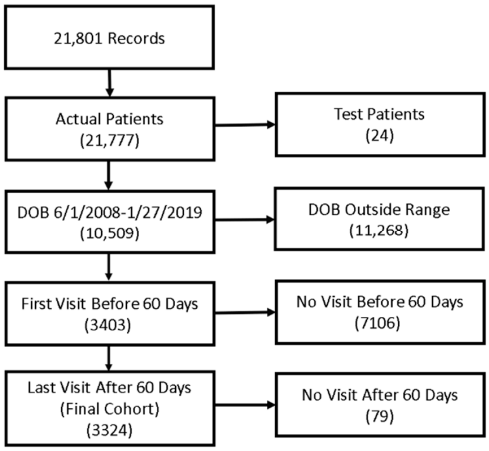

Figure 1. Inclusion criteria diagram.

2.3. Study Population

The inclusion/exclusion criteria lead to 3324 patients, of which 2763 were variably vaccinated, having received 1 to 40 vaccines (Figure 1).

2.4. Demographics

The study population had similar proportions of males and females (Table 1). Nearly all patients had been breastfed in both the vaccinated (96.6%) and the unvaccinated (98%) conditions. Among the vaccinated, 25.16% had a family history of autoimmunity, whereas among the unvaccinated, 31% had the same characteristic. Functionally, this also likely reflects the net effects of decisions between the patient/doctor dyad in determining risk of long-term poor outcomes sometimes associated with vaccination.

Table 1. Demographic variables in the analyzed data set.

Category	Unvaccinated (N = 561)	Vaccinated (N = 2763)	χ^2	*p*
Male (N,%)	279 (49.7%)	1432 (51.8%)	0.819	0.365
Female (N,%)	282 (50.3%)	1331 (48.2%)		
Breastfed (N,%)	550 (98%)	2670 (96.6%)	3.037	0.081
			T-test	
FHA (any)	174 (31%)	695 (25.16%)	28.239	<0.00001
Mean DOC	741	1525	17.69	<0.00001
DOC matched	741	741 (N = 561)	0	1.0
Mean BW (kg) unmatched	3.3	3.28	0.509	0.305

DOC = "Days of Care" = (day of age at last record − day of age at first record); FHA = family history of autoimmunity (at least one condition); Mean BW = average body weight (day 1). The "**T-test**" is in bold in the table because it is a column subheader.

2.5. Variation in Vaccination

The study population has a great diversity in vaccination uptake (Figure 2), reflecting the combined outcome of the patient/physician dyad considering vaccine risk information leading to informed consent on the part of the patients in the practice.

Given the potential of a cohort effect leading to time-based trends in vaccination and to protect against health-care seeking behavior, we calculated for each patient the number of days of care (DOC) as the number of days between the last and first office visits. Importantly, DOC is the range from first to last recorded visits for each patient and is not expected to be influenced overall by healthcare seeking behavior. Among the vaccinated, the mean DOC was 1525 days; among the unvaccinated, the mean DOC was 741 days. This reflects age of patient, not healthcare seeking behavior (prior to matching, unvaccinated: min age, 2 months, mean age 2 years 1 month, and max age 10 years 1 month; vaccinated: min age 2 months, mean age 4 years 3 months, and max age 10 years 6 months; after DOC matching, average age in the vaccinated was also 2 years 1 month). The difference in DOC between the vaccinated and unvaccinated groups was highly significant prior to DOC matching (Student's t, $p < 0.0001$). The patient populations did not differ in mean predicted birthweight (unvaccinated 3.3 kg; vaccinated 3.28 kg, $p = 0.61$ (Student's t)).

From this analysis, only DOC could be a potential confounding variable, potentially collinear with patient age, given full consideration by a matched analysis (see below).

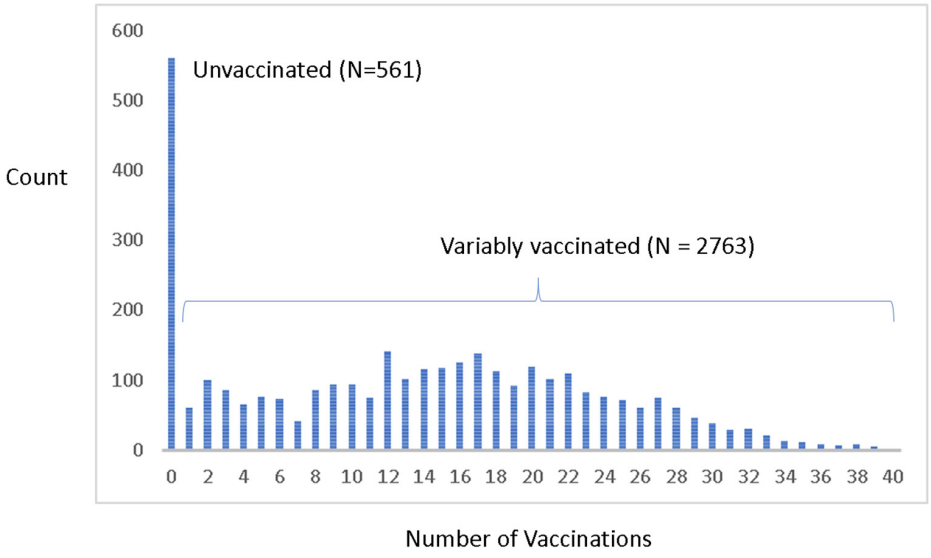

Figure 2. Distribution of vaccination across the patient cohort.

2.6. Analysis 1. Relative Incidence of Average Billed Visitation Rates in Percentile Vaccinating vs. Unvaccinated (Aka "Whole Cohort" Analysis: Unblocked and Unmatched)

2.6.1. Relative Incidence of Office Visit (RIOV)

Typical retrospective analyses of association of outcomes and vaccine exposure rely on the incidence of conditions, which is the percentage of a group with a particular diagnosis of interest. This is the equivalent of "at least one billed office visit", which is a specific form of "at least n office visits" related to a diagnosis. Use of incidence-only is therefore an arbitrary decision on data representation. We generalized the approach by considering the incidence of office visits over each patients' record related to a diagnosis. First, patients were ranked by the number of vaccines accepted. For controls, the average incidence of billed visitations per conditions was calculated within percentiles ranging from the 5th (least vaccinated) to the 90th percentile of vaccination acceptance (Figure 3). For the study outcomes, data were represented as quartiles.

Average incidence of office visit ratio (RIOV) plots for the vaccinated (OV_V) and unvaccinated (OV_{UV}) groups were used to provide assurance of the robustness of the results in the study design and design of analysis. In some cases, the percentile groups in the non-vaccinating end of the immunization axis had zero patients; in those cases, the value of the least vaccinating percentile was used as the denominator for the relative incidence to avoid division by zero. In contrast therefore to "most vaccinated" ("MV") to "unvaccinated" ("UV"), such analyses were therefore "most vaccinated" vs. "least vaccinated" ("LV") patients. This modification had to be applied to the billed diagnoses of "developmental speech delay" and "pain". The *y*-axis in the graphical representation of the data in the percentile analysis is the average incidence of related visitations per condition at a given percentile of vaccination/the average incidence of the related visitations per condition in the unvaccinated (OV_V/OV_{UV}). Incidence ratios were calculated as a ratio of average incidence per patient in each percentile compared to the un- or least-vaccinated group (the latter to avoid division by zero, e.g., ADHD); they are equivalent to an expression of relative risk of diagnosis for each study outcome.

2.6.2. Natural Positive and Negative "Controls"

It is well known that "fever" is a side effect of vaccination. In this analysis, we therefore used incidence of "fever" as positive controls on trends in the data. Similarly, "Well Child" visits can be considered a type of negative control given that they were regularly scheduled events and that they set a comparator value of RIOV for other outcomes (Figure 3).

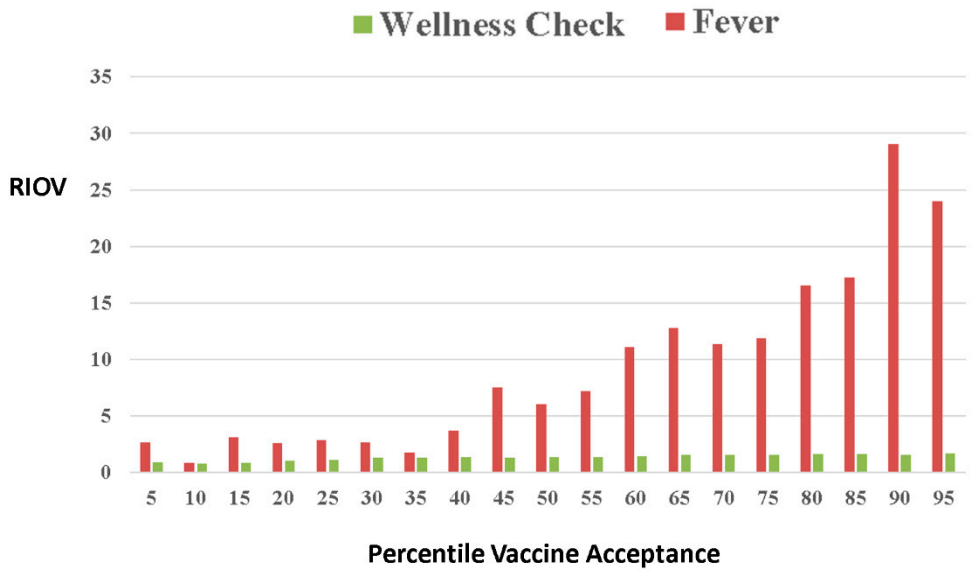

Figure 3. Relative Incidence of Office Visit (RIOV) percentile vaccinated vs. unvaccinated design of analysis: power decreases from left to right; thus, a stable trend (increase or decrease) becomes noteworthy. The data shown are for the Relative Incidence of Office Visits (RIOVs) to average incidence ratio of billed office visits related to fever in the vaccinated compared to the unvaccinated (OV_V/OV_{UV}) conditions and for "Well Child" visit on the right. For all the clinical conditions studied, RIOV reflects the total number of billed office visits per condition per group, reflecting the total disease burden on the group and the population that it represents.

2.7. Analysis 2. Odds Ratio Analysis of Incidence of Diagnoses

For comparison to the RIOV method, the same data were also analyzed using a classical odds ratio of incidence of diagnoses using the rates of diagnosis of each condition in the vaccinated and unvaccinated groups using 95% confidence interval testing. Odds ratios per each ith diagnosis were calculated as the standard ratio of the rate of exposure in those with the diagnosis ($p_{1,i}$) to the rate of exposure in those without diagnosis ($p_{2,i}$), i.e.,

$$OR_i = \frac{p_{1,i} \Big/ (1 - p_{1,i})}{p_{2,i} \Big/ (1 - p_{2,i})} \quad (1)$$

Relative risk ratios for each of the ith conditions with n_{1i} vaccinated in D_1 diagnosed and n_{2i} vaccinated among D_2 without diagnosis was calculated as

$$RR_i = \frac{n_{1,i} \Big/ (D_{1,i})}{n_{2,i} \Big/ (D_{2,i})} \quad (2)$$

Z-tests of proportion were conducted to provide p-values. Effect size was estimated with absolute risk difference (ARD), calculated as (vaccinated diagnosis rate − unvaccinated diagnosis rate).

2.8. Analysis 3. Days-of-Care (DOC)-Matched Vaccinated vs. Unvaccinated RIOV Analysis

Because this is an observational retrospective study, a potential limitation of the time-agnostic analysis is that more recent and younger patients' parents in the practice have opted to vaccinate less frequently and, being younger, have fewer office visits. Thus, fewer diagnoses may be expected to be related to lower exposures due to the combined effects of age (less time) and vaccine choice behaviors. Given this shift occurring in vaccination choices over time, it is possible that a false signal may be embedded due to temporal population-wide shifts due to unmeasured factors, such as cultural shifts in attitudes toward vaccination unrelated to personal outcomes or specific risk. Therefore, an additional analysis was conducted to assess the signal in Days-of-Care (DOC)-matched groups. For each unvaccinated patient, a patient with identical or closest DOC values was selected (without bias) from among the more numerous vaccinated patients. RIOV analysis was conducted on the resulting two groups.

2.9. Analysis 4. DOC-Matched OR on Incidence of Diagnoses. Vaccinated vs. Unvaccinated

As a comparison to analysis 3, odds ratios of incidence using diagnoses were calculated on the same data resulting from the matching of patients for DOC.

2.10. Analysis 5. Cumulative Office Visit Risk (COV Relative Risk)

To provide another view on the data considering the dimension of time, we calculated for all vaccinated patients and separately for the unvaccinated the number of diagnoses of all of the conditions studied at each day of life considering the vaccinated patients born into the practice (N = 2763) compared to the unvaccinated patients (N = 561). We also then calculated the cumulative office visits per each day of life. It is important to note that, in these analyses, a patient can have office visits related to the same diagnosis multiple times. These two representations of the data provide a clear graphical representation of the comparison of the vaccinated and unvaccinated and seem to also provide some insight into the typical timing of onset of a study outcome. Cumulative incidence of risk of office visit (RIOV) would be the cumulative numbers divided by the number of patients per group and would thus also reflect age-specific cumulative probabilities (risk of diagnosis-related office visit). Due to the imbalance in study design, the COV curve for the unvaccinated are expressed as the adjusted number

of office visits expected if the study had been balanced with equal numbers to make the two curves directly comparable in scale when expressed as numbers of office visits (multiplier factor 4.9).

2.11. Analysis 6. Family History Blocked RIOV Analysis

Data on family history of autoimmune disorders or autism were used to block patients into those who had a family history on record (FH+) and those who did not (FH−; blocked design). Average RIOV ratios were calculated to determine whether increased vaccination was associated with increased relative incidence of office visitations in both clinical groups (similar to analysis 1), given family history (FH+ and FH−). The results are not otherwise matched or blocked.

2.12. Analysis 7. RIOV vs. OR Incidence of Diagnoses Power Simulation Comparison

A comparison of the power of the test statistics RIOV and OR on incidence is provided to demonstrate the relative power of RIOV to detect differences and associations compared to odds ratio of diagnoses. Poisson variables drawn from distinct theoretical populations were analyzed using both RIOV (full values of x_i) and OR on incidence ($x_i > 0$). For the simulation, 1000 measurement sets $X = \{x_1, x_2, x_3 \ldots x_n\}$ drawn from a Poisson distribution of 400,000 random values were used to simulate two groups (each of size N = 400) for each Poisson λ value ranging from 1 to 1.1 (step 0.01). The null data ($\lambda = 1$) were used to represent the unvaccinated with no effect.

We simulated an increased effect of vaccines on office visits by increasing λ from 1.01 to 1.1 (step 0.01), with 400,000 values at each level of λ. Increased levels of λ represent increased numbers of office visits due to negative effects of vaccines. The data were analyzed using OR of incidence counting each individual value of $x_i > 0$ as a positive diagnosis and again using RIOV, leaving the generated values of x_i in both simulated groups intact.

2.13. Analysis 8. Gender Blocks

We blocked the cohort data into gender blocks (males and females). RIOV analysis was conducted on the vaccinated vs. unvaccinated in both gender blocks.

2.14. Analysis 9. Age (Youngest Third and Oldest Third) Blocks

One of the honest brokers ranked the patients by date of birth and sent a set of age-ranked identifiers to the analyst (J.L.-W.). The data were blocked into the youngest 1/3 and the oldest 1/3. RIOV analysis was conducted on the vaccinated vs. unvaccinated in both age blocks.

2.15. Analysis 10

We compiled and presented the number of diagnoses for infections targeted by vaccines (considering the CDC pediatric schedule) in the vaccinated and unvaccinated groups in the full cohort. We evaluated each vaccine targeted infection individually and analyzed the association between vaccination status and overall occurrence of vaccine-targeted infections using vaccine-targeted diagnoses. We studied the incidence of vaccine-targeted diagnoses in the vaccinated and unvaccinated groups using the χ^2 test.

3. Results

The overall full-cohort RIOV analysis of the vaccinated (N = 2763) vs. unvaccinated (N = 561) groups are presented in Table 2. There were no cases of ADHD in the unvaccinated group.

Table 2. RIOV and test of proportions of office visits per condition for the fully vaccinated (N1 = 2763) vs. (never) unvaccinated (N2 = 561) groups comparison: these results are not adjusted for days of care. CI = confidence interval.

Condition	Vaxxed	Unvaxxed	RIOV	95% CI	Z	*p*
Fever	759	17	9.065	8.801	12.476	<0.0001
"Well Child" Visits	32,826	4987	1.336	1.149	6.540	<0.0001
Ear Pain	269	16	3.414	3.232	5.310	<0.0001
Otitis media	3105	216	2.919	2.518	23.441	<0.0001
Conjunctivitis	1018	87	2.376	1.935	9.783	<0.0001
Eye Disorders (Other)	277	31	1.814	1.586	3.350	0.0008
Asthma	336	13	5.248	5.065	6.693	<0.0001
Allergic Rhinitis	405	12	6.853	6.662	8.158	<0.0001
Sinusitis	107	5	4.345	4.240	3.566	0.00036
Breathing Issues	621	44	2.866	2.561	7.898	<0.0001
Anemia	979	36	5.522	5.181	13.603	<0.0001
Eczema	512	23	4.520	4.281	8.479	<0.0001
Urticaria	174	17	2.078	1.908	3.027	0.00244
Dermatitis	742	105	1.435	0.992	4.034	<0.0001
Behavioral Issues	343	17	4.097	3.900	6.087	<0.0001
Gastroenteritis	688	30	4.656	4.374	6.543	<0.0001
Weight/Eating Disorders	1115	90	2.515	2.056	10.264	<0.0001
Seizure	43	8	1.091	0.985	0.229	0.8181

RIOVs were calculated using the number of patients as the sample size in each group (Vaxxed and Unvaxxed) with the exception of well-child visits and otitis media visits, both of which were greater in number than the number of patients.

3.1. Analysis 1 Results, Unmatched and Unblocked

RIOV analysis views across deciles provide a graphical view on the trends in the data (e.g., Figure 3). Recalling that the data are represented as the average incidence of billed office visits for patients in each percentile of the vaccine acceptance/unvaccinated groups, the statistic is the incidence of office visits in each percentile relative to the non-vaccinating portion of the population, but it is not relative risk of diagnosis. Results for outcomes were presented by study outcome cluster in quartiles for clarity.

Examination of the unmatched, unblocked results shows widespread increased RIOV among outcomes with all but seizures, and the developmental delay outcomes were significant. Those results are consistent with low power due to low overall incidence in the cohort. These results are not adjusted for days of care.

R1.1. Group A: Autoimmune Respiratory Illnesses. Large increases in office visits were found among the vaccinated group in this group of respiratory illnesses. Our quartile representation shows consistent increases in the incidence of office visits for allergy, allergic rhinitis, asthma, sinusitis, and breathing issues with increased vaccine acceptance compared to the unvaccinated group (Figure 4A). In the most vaccinated quartile compared to unvaccinated comparison, the relative risks (and lower CI) of office visits related to these conditions were estimated for asthma (16.01), allergic rhinitis (20.64), sinusitis (11.32), and breathing issues (6.52); all were highly significant in univariate analysis ($p < 0.0001$).

R1.2. Group B: Attention Deficit/Hyperactive Disorder and Behavioral Issues. Because there were no cases of ADHD in the unvaccinated group, the quartile analysis uses a comparison to the least vaccinated decile to avoid division by zero. Large increases were found in office visits among the vaccinated compared to the unvaccinated groups in outcomes in this group as well. The quartile representation shows large increases in ADHD and moderately large increases in behavioral issues (Figure 4B). Both of these conditions had highly significant relative incidences of office visit (ADHD, RIOV = 53.74; behavioral issues, 10.28) ($p < 0.00001$).

R1.3 Group C: Ear Pain, Otitis media, and Eye Disorders. Issues with the ear showed a range of increases with vaccine acceptance over the quartiles; in the last quartile, the differences were all

significant (ear pain (RIOV = 10.37), otitis media (RIOV = 7.03), and eye disorders (5.53) (Figure 4C) ($p < 0.00001$).

R1.4. Group D: Autoimmune Conditions of the Skin and Blood. Skin reactions commonly observed and sometimes attributed to vaccination showed consistent, moderate increases in RIOV in the last quartile of eczema (2.315), urticaria (4.81), and dermatitis (2.72) (Figure 4D); $p < 0.0001$.

R1.5. Group E: Gastroenteritis, Weight/Eating Disorders, and Seizure. The RIOV of both gastroenteritis and weight/disorders increased over the quartiles with increased vaccine uptake, as did seizure (Figure 4E).

R1.6. Group F: speech, language, social, and learning delays showed variable but nonsignificant response over the axis of vaccination. Autism was only significant at the third quartile (Figure 4F).

Sensitivity analysis for multiple hypothesis testing in the full cohort data did not change the outcome of analyses for most comparisons. Specifically, an increase of the critical value of Z on the test of proportions from 9.98 to 18 resulted in no loss of significance except for seizure; when increased to 19, dermatitis and behavioral issues lost significance.

Associations were found comparing the most vaccinated quartile for most of the outcomes (Table 3) with the exception of developmental delays and autism spectrum disorders (Figure 4). Following the same analysis protocol for all other conditions, the rate of autism was found to be higher at the third quartile of vaccine uptake compared to unvaccinated (Figure 4F). This is expected given that families with children with autism may be inclined to opt out of the vaccination program, potentially reflecting a signal of informed choice by families excluding them from the higher vaccinated quartile.

Table 3. RIOV analysis of outcomes of the vaccinated vs. unvaccinated groups, matched for Days of Care (DOC) matched comparison (N1 = 561 and N2 = 561).

					Test of Proportions	
Condition	**Vaxxed**	**Unvaxxed**	**RIOV**	**95% CI**	**Z**	**P(Z)**
Fever	78	17	4.596	4.412	6.547	<0.00001
"Well Child" Visit	5204	4989	1.045	1.041	2.156	0.0307
Ear Pain	18	16	1.127	1.022	0.354	0.726
Otitis media	355	216	1.646	1.001	8.312	<0.00001
Conjunctivitis	113	87	1.301	1.023	2.042	0.04136
Eye Disorders—Other	38	31	1.228	1.076	0.877	0.3788
Asthma	20	13	1.541	1.437	1.317	0.186
Allergic Rhinitis	21	12	1.753	1.649	1.600	0.1096
Sinusitis	6	5	1.202	1.143	0.306	0.756
Breathing Issues	75	44	1.708	1.502	3.015	0.00252
Anemia	130	36	3.618	3.361	7.912	<0.00001
Eczema	64	23	2.788	2.613	4.581	<0.00001
Urticaria	14	17	0.825	0.925	−0.541	0.5892
Dermatitis	86	105	0.821	1.090	−1.459	0.1443
Behavioral Issues	54	17	3.182	3.026	4.452	<0.00001
Gastroenteritis	89	30	2.972	2.763	5.728	<0.00001
Weight/Eating Disorders	147	92	1.601	1.288	4.023	<0.00001
Seizure	10	8	0.798	0.067	0.874	0.6312
Respiratory Infection	703	382	2.682	1.134	51.85	<0.00001

The calculation of Z for "Well Child" visits compared the proportion of number of office visits per group to the total number of days of care (length of time in practice; per group: vaccinated = 416,101, unvaccinated 416,056) in this DOC-matched analysis.

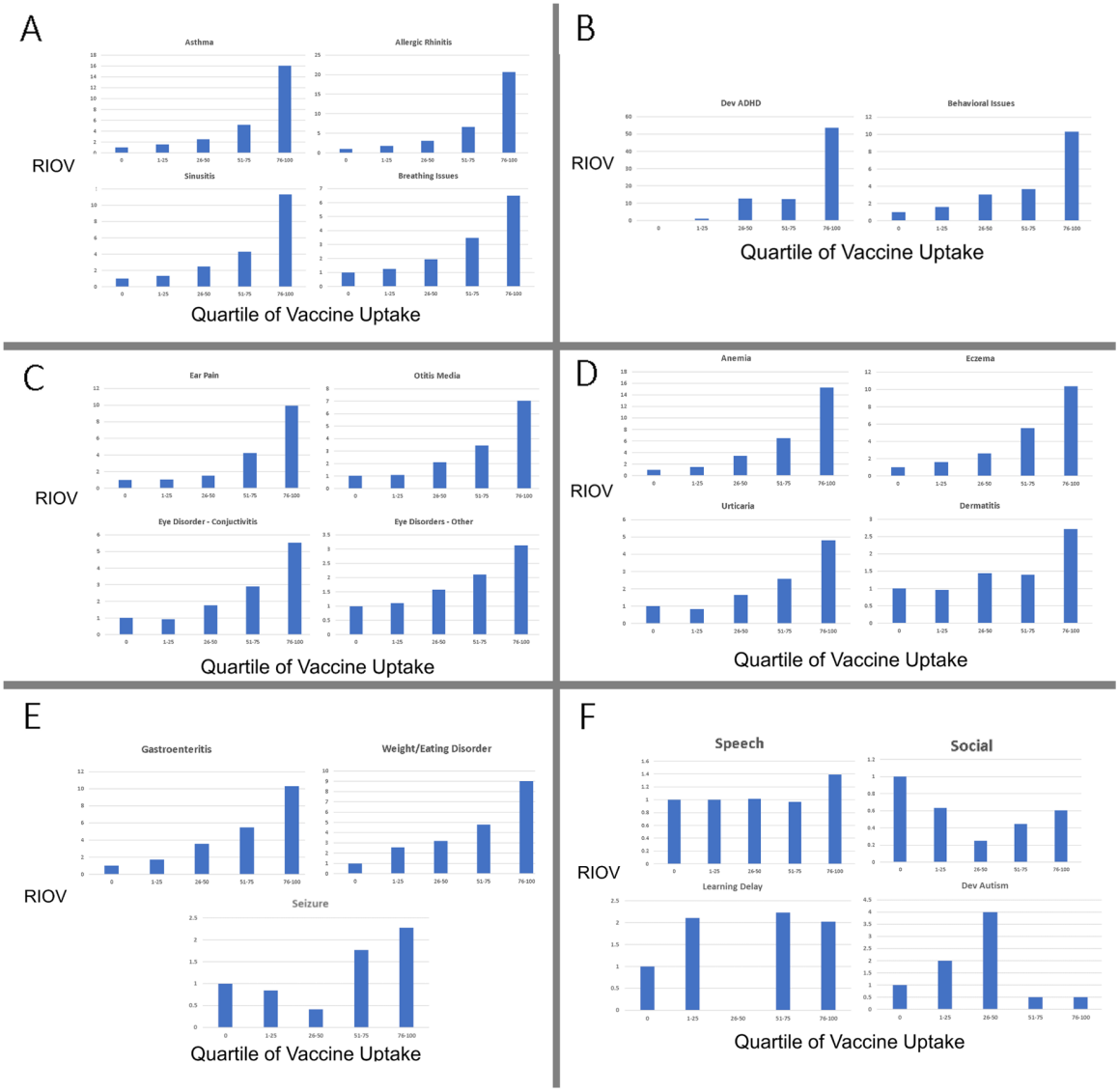

Figure 4. RIOV axis of vaccination percentile vaccine uptake analysis: incidence of study outcome-related office visits relative to that found in the 2763 variably vaccinated compared to the 561 unvaccinated groups for each percentile of vaccine uptake on the *x*-axis. (**A**) Autoimmune respiratory illnesses; (**B**) attention deficit/hyperactive disorder and behavioral issues; (**C**) ear pain, otitis media, and eye disorders; (**D**) autoimmune conditions of the skin and blood; (**E**) gastroenteritis, weight/eating disorders, and seizure; and (**F**) development delays in speech, learning, and social interactions and autism spectrum disorder.

3.2. Analysis 2 Results. Odds Ratio on Incidence of Diagnoses

When the data are represented as the number of patients in each group who had at least one record of an office visit related to a given condition, the signals remain (Table 4). Incidence of diagnoses of each condition was compared between the 561 unvaccinated and the 2763 vaccinated individuals. This result is similar overall to the RIOV analysis; we present the odds ratio, relative risk, lower than 95% of each, along with the absolute risk difference (vaccinated − unvaccinated) in Table 4. Among all of the outcomes, allergic rhinitis and anemia had the highest OR; anemia, weight/eating disorders, and respiratory infection showed the highest absolute risk difference (ARD; all increased in the vaccinated).

Table 4. Incidence of diagnoses of conditions in the vaccinated vs. unvaccinated groups in the population under study.

Outcome	OR	RR	Relevant 95% CI	ARD *	Significant
Fever	9.57	8.08	5.35/7.45	0.15	+/+
Ear Pain	4.11	3.87	2.22/3.40	0.06	+/+
Otitis media	3.11	2.2	2.49/2.11	0.12	+/+
Otitis externa	3.832	3.756	1.395/3.000	0.02	+/+
Conjunctivitis	2.67	2.21	2.04/2.08	0.15	+/+
Eye Disorders (Other)	1.9	1.82	1.24/1.61	0.04	+/+
Ear Disorders	2.359	2.32	1.08/1.86	0.02	+/+
Asthma	3.496	3.361	1.77/2.87	0.04	+/+
Allergic Rhinitis	6.479	5.595	3.31/5.31	0.08	+/+
Sinusitis	3.529	3.451	1.42/2.79	0.02	+/+
Breathing Issues	2.46	2.238	1.74/2.04	0.08	+/+
Anemia	6.334	4.482	4.68/4.6	0.21	+/+
Eczema	4.763	4.301	2.86/3.89	0.09	+/+
Urticaria	2.258	2.183	1.29/1.87	0.03	+/+
Dermatitis	1.591	1.482	1.22/1.37	0.06	+/+
Behavioral Issues	3.13	1.8	1.80/2.60	0.05	+/+
Gastroenteritis	4.479	3.587	2.98/3.56	0.13	+/+
Weight/Eating Disorders	3.146	2.489	2.41/2.35	0.183	+/+
Allergy—Food	2.24	2.23	0.52/1.47	0.004	−/+
Pain	2.569	2.236	1.759/2.147	0.0754	+/+
Respiratory Infection	1.716	1.365	1.351/1.255	0.131	+/+

* ARD = absolute risk difference, calculated as (vaccinated diagnosis rate − unvaccinated diagnosis rate). Odds ratios and relative risk ratios were calculated as described in the Methods section (Equations (1) and (2), respectively). The +, − symbols represent the significance of the OR and RR statistics for each condition for the relevant (upper or lower) 95% CI.

3.3. Analysis 3 Results. Days of Care (DOC) Matched Vaccinated vs. Unvaccinated RIOV Analysis

Due to the likelihood of confounding on DOC, DOC-matched results inform on the robustness of associations. DOC matching also led to matching by age; the average rank of age in both the vaccinated and unvaccinated groups was nearly identical (Student's t, $p = 0.919$). Average age at last office visit was also not significantly different (Student's t, $p = 0.95$). The average age of first office visit differed only by 2 days (6 days vs. 8 days, Student's t, $p < 0.001$).

3.4. Analysis 4 Results. DOC-Matched Incidence

In the analysis of days-of-care-matched data represented as incidence, many of the conditions for which associations were found in the RIOV analysis were found to be undetectable by OR and Relative Risk analysis (Table 5). This included ear pain, eye disorders, ear disorders, asthma, allergic rhinitis, sinusitis, and urticaria (Table 5). Otitis externa, anemia, and respiratory virus infection had the highest absolute risk differences.

While RIOV is reduced in the DOC-matched analysis, the significance of an increased proportion of cases in the vaccinated individuals compared to unvaccinated individuals remains for most outcomes. Risk of seizure was significant for confidence interval testing in this matched analysis but not for Z-test ($p = 0.6321$). Some comparisons had too few counts in the DOC-matched analysis to be reliable (e.g., food allergy had 1 case in the vaccinated group and 2 in the unvaccinated group).

Table 5. Analysis 4: DOC-matched incidence analysis.

Outcome	OR	RR	95% CI	ARD	Significance
Fever	3.88	3.66	2.02/2.75	0.057	+,+
Ear Pain	1.559	1.57	0.723/0.966	0.01	−,−
Otitis media	1.551	1.4	1.17/1.22	0.078	+,+
Otitis externa	2.01	1.996	0.602	1	+,+
Conjunctivitis	1.323	1.273	0.942/1.05	0.033	−,+
Eye Disorders—Other	1.25	1.24	0.729/0.879	0.011	−,−
Ear Disorders	1.29	1.28	0.476/0.671	0.003	−,−
Asthma	1.224	1.22	0.503/0.679	0.003	−,−
Allergic Rhinitis	1.452	1.44	0.615/0.842	0.007	−,−
Sinusitis	1.2	1.2	0.364/0.540	0.008	−,−
Breathing Issues	1.614	1.549	1.504/1.217	0.037	+,+
Anemia	3.216	2.865	2.098/2.368	0.103	+,+
Eczema	2.822	2.682	1.57/2.01	0.047	+,+
Urticaria	1	1	0.471/0.595	0	−,−
Dermatitis	0.884	0.898	1.27/1.13	−0.012	+,+
Behavioral Issues	2.13	2.067	1.11/1.45	0.0266	+,+
Gastroenteritis	2.785	2.572	1.74/2.054	0.073	+,+
Weight/Eating Disorders	1.915	1.721	1.386/1.47	0.089	+,+
Allergy—Food	0.498	0.499	5.51/3.53	−0.001	−,−
Seizure	1.756	1.746	0.511/0.836	0.0053	−,−
Infection—Respiratory	1.716	1.365	1.351/1.255	0.131	+,+
Pain	1.274	1.255	0.783/0.927	0.014	−,−

The symbols "+, – " denote the significance of the relevant (upper or lower) 95% CI analysis for OR and RR.

3.5. Analysis 5 Results. Cumulative Office Visits

The visual impact of the cumulative office visit plots is striking; more so than other plots, the time element (day of life) provides an index by which to compare the accumulation of human pain and suffering from potential vaccine side effects (Figure 5). These results are worth studying closely and noticing the variation among the cumulative office visits per condition and the stark differences between the rates of billed office visits in the most and unvaccinated patients born into the practice.

False discovery sensitivity analysis performed by increasing of the critical of value of Z (test of proportions) from 9.98 to 18 caused a loss of significance for ear and eye conditions only. All other conditions were robustly significant to $Z_{crit} < 19.2$ (behavioral issues). The remainder of the conditions retained significance well beyond $Z_{crit} = 24$.

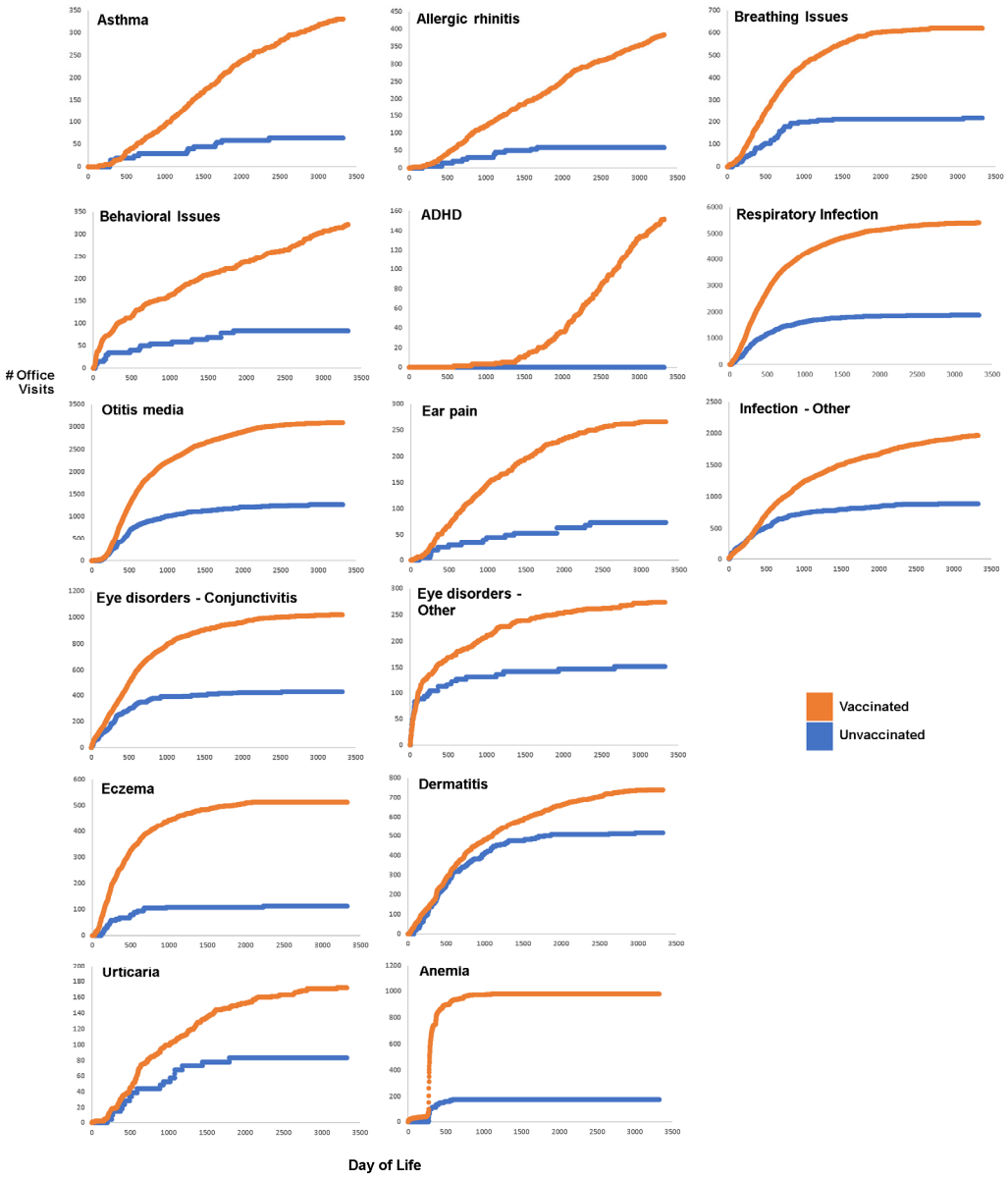

Figure 5. Analysis 5. Cumulative office visits in the vaccinated (orange) vs. unvaccinated (blue) patients born into the practice: the clarity of the age-specific differences in the health fates of individuals who are vaccinated (2763) compared to the 561 unvaccinated in patients born into the practice over ten years is most strikingly clear in this comparison of the cumulative numbers of diagnoses in the two patient groups. The number of office visits for the unvaccinated is adjusted by a sample size multiplier factor (4.9) to the expected value as if the number of unvaccinated in the study was the same as the number of vaccinated.

3.6. Analysis 6 Results. Family History-Blocked RIOV Analysis

The relative incidence of visitation per condition for patients with family history of autoimmune conditions and those patients with no record of family history of autoimmune conditions indicate variation among conditions in the likelihood of family history playing a role, either biologically or by influencing patient choice, in the association of vaccine uptake and outcome (Table 6). Within the pattern (Score FH+ >> Score FH−), family history of autoimmunity itself is consistent with a biological risk factor of the outcome. This was the pattern for fever, sinusitis, and potentially anemia. Within the pattern (Score FH+ << Score FH−), this is consistent with the signal of vaccine choice, implying that further vaccine uptake may have increased the risk of the condition in the unvaccinated. This was

the case in otitis externa, asthma, allergic rhinitis, and dermatitis. In this analysis: FH + N1 = 175 vaccinated, N2 = 88 unvaccinated; FH−, N1 = 385 vaccinated, and N2 = 186 unvaccinated.

Table 6. RIOV score blocked by family history and implication for co-factor status.

Condition	FH+	FH−	Pattern *	Consistent w/Risk Cofactor? **
Fever	21.826	3.818	+,+	yes
"Well Child" Visit	2.690	1.009	+,−	yes
Ear Pain	10.500	13.427	+,+	no
Otitis externa	0.988	9.242	−,+	yes
Otitis media	30.500	21.715	+,+	maybe
Conjunctivitis	19.266	13.443	+,+	maybe
Other Eye Disorder	2.343	3.902	+,+	maybe
Asthma	8.143	19.030	+,+	yes
Allergic Rhinitis	18.382	54.339	+,+	yes
Sinusitis	27.316	8.282	+,+	yes
Breathing Issues	9.524	10.188	+,+	no
Anemia	29.302	20.027	+,+	maybe
Eczema	17.292	13.718	+,+	maybe
Urticaria	4.135	4.404	+,+	no
Dermatitis	1.470	4.922	−,+	yes
Sezure	0.989	0.634	−,−	no
Respiratory Infection	4.556	5.396	+,+	no

* +,+ CI testing significant in both comparisons, +,− significant under FH+ block but not FH- block, etc. ** Yes = FH is a likely co-risk factor for outcome. Numerators (N1 and N2) for both groups were adjusted in fever and "Well Child" visits by a factor of 20; Otitis externa, anemia, and Otitis externa (factor of 2) and Otitis media (factor of 3). This does not change the RIOV score but allows the Z-test score to estimated.

3.7. Analysis 7 Results. Power Simulation

The resulting 1000 comparison sets at each value of λ (N1 = 400 λ = 1.0 vs. N2 = 400 $\lambda = 1.x$ for each $\{x = 0.01, 0.02, 0.03 \ldots 0.50\}$ were analyzed twice, first as an odds ratio of "diagnosis" ("0" = no diagnosis vs. ">0" = diagnoses). The second analysis conducted was a ratio of relative incidence of office visits, with each groups' sum of values within each comparison group representing the total number of office visits being compared.

The simulations were not intended to precisely model the data from the current study; instead, it is intended to demonstrate the principle that the loss of information caused by using the incidence of health condition rather than the more sensitive measure of the number of office visits results in a loss of power to detect adverse events.

Over the range studied, the average increase in power achieved from the analysis using RIOV compared to the odds ratio of diagnoses was doubled over that of odds ratio on incidence of diagnoses (133%) (Figure 6). RIOV was more powerful compared to OR on rates of diagnosis over the simulated range. Our results demonstrate that drug and vaccine safety studies should employ RIOV rather than OR on rates of diagnosis of health conditions that might be attributable to the treatment, therapy, or vaccine.

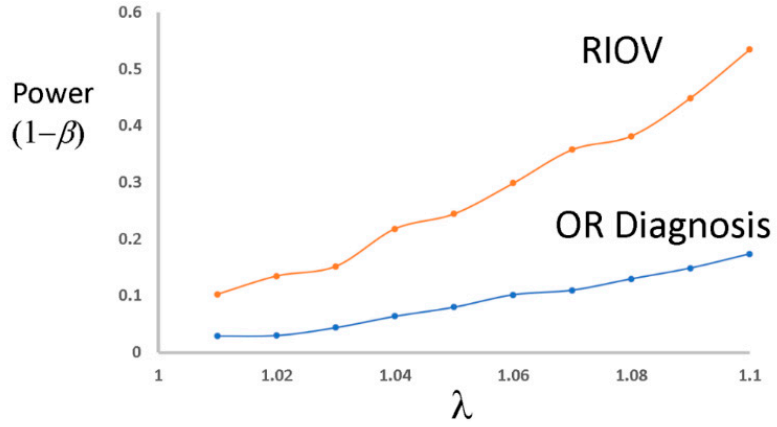

Figure 6. Simulated demonstration of increased power of RIOV (number of office visits) relative to the power of odds ratio of incidence of diagnoses (at least one office visit).

3.8. Analysis 8. Gender Blocks

In the gender block analysis, the following conditions were significant in both the male and female ROIV comparisons: fever, "Well Child" visits, ear pain, otitis media, conjunctivitis, eye disorders (other), asthma, sinusitis, breathing issues, anemia, eczema, behavioral, gastroenteritis, and weight/eating disorder. The developmental delays were largely underpowered for robust analysis due to low overall rates in the practice, but two conditions were significantly lower in the vaccinated females (autism) and males (social development). These results, provided as a table with RIOV values and exact *p*-values of Z in Supplementary Materials Table S2, were not DOC- or age-matched.

3.9. Analysis 9 Age Blocks: Oldest Third and Young Third Blocked Analysis

The following conditions were significantly increased ($p < 0.05$) in the vaccinated group in both age blocks: fever, otitis media, conjunctivitis, sinusitis, breathing issues, anemia, gastroenteritis, and weight/eating disorder. The following conditions were significantly increased in the vaccinated group in the younger (more recent) age block only: asthma and allergic rhinitis. The following conditions were significantly increased in the older age block only: "Well Child" visit and eczema. None of the developmental delay categories were significantly increased in either the older or younger age blocks, likely due to low power. Social delay was significantly increased in the unvaccinated older age block. Two health outcomes, pain and respiratory infection, were increased in the unvaccinated group under the older block but were not significantly different in the younger block. These results, requested by a peer reviewer, demonstrate robustness of many associations to blocking by age and by gender and are provided as tables in Supplementary Materials Table S3 (including RIOV values and exact *p*-values of Z).

3.10. Analysis 10 Results—Vaccine-Targeted Diagnoses

There was a total of 41 vaccine-targeted diagnoses in patients born into the practice, mostly (by far) in varicella (29) and less so in pertussis (10). Overall, the groups show differences in vaccine-targeted diagnoses (Table 7; $\chi^2 = 0.292$, $p = 0.588$). The rates of any diagnosis were vaccinated, 7/2647 (0.00264) and unvaccinated, 34/561 (0.0499). The odds ratio of having a diagnosis of any vaccine-targeted infection (Dx_V/Dx_{UV}) was 0.054 (0.114), *Z*-score, 7.155, $p < 0.0001$. Relative risk of any vaccine-targeted diagnosis was 0.053 (0.119), $Z = 7.117$, $p < 0.0001$, number needed to treat (NNT) = 21.15 (17.72 to 26.225 (benefit)).

Table 7. Incidence of vaccine-targeted diagnoses in the study cohort.

Vaccine Targeted Diagnosis	Vaccinated	Unvaccinated	Deaths
Diphtheria	0	0	0
Hepatitis A	0	0	0
Hepatitis B	0	0	0
HiB *	0	0	0
Measles	0	0	0
Meningococcus	0	0	0
Mumps	0	0	0
Pertussis	1	9	0
Pneumococcal	0	0	0
Rotavirus	0	2	0
Rubella	0	0	0
Tetanus	0	0	0
Varicella	6	23	0
Total **	7	34	0

* Haemophilus influenzae type B; ** Overall for all $\chi^2 = 99.51$. $p < 0.00001$.

The overall probability (risk) of a vaccine-targeted diagnosis in the unvaccinated, however, was only 0.0123, among 13 conditions. It is important to note that zero deaths have been attributed to any vaccine-targeted diagnosis in this practice over the study period.

4. Discussion

The analysis of total outcomes related to vaccine and drug exposures is rarely conducted. It is made complex due to factors such as changes in trends in vaccine or drug acceptance, and the very signal sought—indication of adverse events from vaccines—can be changed by decisions made to avoid vaccine injury by those at risk. We have shown that the outcome of observational studies is sensitive to the choice of test of association and have presented a test (RIOV) more powerful than odds ratios on incidence (Figure 6).

Matching on DOC provides protection against healthcare-seeking behavior because each patient in the vaccinated group is matched to a person in the unvaccinated group with nearly identical length of records in the practice. This also led to matching on age, adding protection against incidental temporal confounds in changes over time in vaccination trends or schedules: both the vaccinated and unvaccinated matched samples are representative of the entire age range of the study cohort. Most of the differences in ratios persist comparing the full cohort analysis when the data were matched for DOC (Analysis 2; Table 3). All RIOV were >1, indicating increased risk of office visit for a specific outcome, except seizure, urticaria, and dermatitis. The change in direction of seizure likely points to "cessation of vaccination signal" following initial events. The difference between the vaccinated and unvaccinated groups was no longer significant for dermatitis following matching for DOC.

The variation in vaccination was the outcome of the final decisions on the part of the patients after consulting with their physicians in the practice. This adherence to the tenets of informed consent, as required by federal regulations for both medical practice and for post-market surveillance studies, is also a key element built into "The Vaccine Friendly Plan" (VFP), developed in a manner to space aluminum-containing vaccines out and to avoid aluminum-containing vaccines (ACVs) whenever a non-ACV is available. The net effects of these changes on aluminum accumulation in children is described in [15]. Children on the CDC schedule would have on average received more vaccines in total; considering the most vaccinated of the VFP compared to the CDC schedule reveals that CDC-scheduled children receive 14 more vaccines by age 2 compared to those most vaccinated on the VFP; by age 5 years, children receive 4 more vaccines (CDC 6, VFP 2), and by ten years, children receive six more vaccines under the CDC schedule compared to the VFP (CDC + 8, VFP, +2). This represents a

total of 24 additional vaccines those on the CDC schedule would have received in 2019 compared to the most vaccinated individuals in this retrospective study. Children on the CDC schedule also would have received more instances of more than one ACV per visit and a larger number of ACVs.

We have found higher rates of office visits and diagnoses of common chronic ailments in the most vaccinated children in the practice compared to children who are completely unvaccinated. The data clearly show different odds of developing many of these adverse health conditions. We have demonstrated in many ways that most of the statistical associations found tend to be robust to age in cohort (days of care), vaccination range, and family history. The first of these is the contrast in the increase in fever cf. "Well Child" visit (Figure 3). The second is robustness of the results to adjustment to days of care provided and of course robustness to the age-matched design as well.

Vaccination appears to have had the largest impact on anemia and respiratory virus infection on the number of office visits in the vaccinated compared to the unvaccinated groups. Due to a small number of cases and corresponding low power, neurodevelopmental conditions and seizures are not well studied using the data available. Autism, at a study-wide rate of 8 per 1000, is far lower than the national rate (18.5–21 per 1000). Speech, learning, and social delays were found to have different full-cohort practice-wide incidences of 0.023, 0.003. and 0.009, respectively. Future studies with less restrictive inclusion criteria that also avoid temporal confounding by matched DOC may help us better characterize these populations in the practice.

Our family history of autoimmune conditions analysis points to numerous conditions likely carrying a genetic risk of vaccine-related adverse health effects. This, however, is only one study from data from a single practice, so any absence of a pattern consistent with a genetic risk of adverse health effects should not be taken as evidence of absence of a role of genetic risk. Larger studies able to estimate the interaction term between family history and vaccine exposure should be undertaken.

Previous studies such as the Mawson study (2017) [9] reported high odds ratios for allergic rhinitis (30.1), learning disabilities (5.2), ADHD (4.2), autism (4.2), neurodevelopmental disorders (3.7), eczema (2.9), and chronic illness (2.4) but were limited because they were based on survey data. While not necessarily fatal to a study, the highly charged nature of the vaccine risk research brings a special concern over survey respondents who might, for the sake of advocacy, seek or unintentionally emphasize their unvaccinated child's lack of diagnoses or amplify their vaccinated child's larger number of diagnoses. Recall bias is a potential factor in this setting, and therefore, our results go a long way to validate those on the Mawson (2017) [9] study. The age range in that study was also restricted to 6- to 12-year-olds, precluding the comparison of the cumulative rates from day 1 of life. Survey studies in the future should obtain HIPAA permissions to access at least a portion of patients' medical records to at least estimate the accuracy of responses compared to medical records from a sample. Despite limitations of survey studies, our results validate many of these results.

Numerous studies conducted in the past have found an association of vaccination with adverse health effects. Numerous studies reporting an association of individual vaccines with adverse study outcomes are too numerous to cite here; many more such studies are reviewed online [16]. For example, a prior study reported a vaccination association with asthma and allergy (e.g., Hurwitz and Morgenstern, 2000) [17].

Concerned over healthy user bias (HUB), i.e., healthier individuals accepting more vaccines leading to differences in study outcome are alleviated in this practice, the physicians and patients overtly came to a joint decision on whether to vaccinate on a patient-by-patient and vaccine-by-vaccine basis. As originally described, if "healthy user bias" was the explanation problem, we would see more illness in the unvaccinated; we found the opposite. We do see the potential signal of informed avoidance of vaccine injury with informed consent and without coercion potentially weakening associations of vaccine injury. This type of effect has historically been interpreted as a form of healthy user bias, but it can be equally interpreted as the signal of avoidance of vaccine injury due to informed consent. Our design of analysis allows the detection of some potential instances (e.g., autism, in which

some individuals at risk of adverse outcome who otherwise would have been in quartiles 3 and 4 stopped vaccinating).

Glanz et al., 2003 [18] found that parents who tended to not accept all vaccines or who delayed vaccines were 2 times more likely to report that they began thinking about vaccines before their child was born and were also 8 times more likely to report that they constantly reevaluate their vaccine decisions than parents who accepted all vaccines. Notably, the signal of change in vaccination behavior following adverse events via informed consent would appear to be detectable as a reduction in the overall incidence of adverse outcomes in the unvaccinated group and fewer office visits related to those outcomes. This opposing trend is the opposite of the expectation that physicians may be more likely to admit the unvaccinated for health issues than the vaccinated (described by [18]). Lifestyle differences between the vaccinated and unvaccinated groups in this practice cannot explain the large difference in outcomes, and if they do, then it would be objective to conclude that everyone should adopt the lifestyle followed by the unvaccinated if they want healthier children. That lifestyle choice includes, for many families, avoiding some or all vaccines, and thus, the lifestyle choice concern is inextricably linked to vaccine exposure.

Because we are considering the potential effects of cumulative vaccination, the potential problem of reverse temporal association with appropriately juxtaposed association is undefined in our study. The RIOV design of analysis makes the reverse temporal association irrelevant, as in the vaccinating population, the cumulative number of vaccinations over the course of a decade is the independent variable. For reverse temporal association concern to manifest, all or most of the diagnoses would have had to had occur prior to the first vaccine, which is extremely unlikely (and are not at all what our data show). Our accumulation diagrams make clear the general tendencies toward requiring medical attention for outcomes in vaccinated vs. unvaccinated segments of the patient population in a distinctly age-specific manner. We have focused on the cumulative effects of vaccines on overall health and therefore, this concern cannot logically apply to the study as it is designed.

4.1. Caveat on Applicability of Results (Generalizability)

Data from this single and unique practice provides a unique opportunity to examine variation in outcomes associated with variation in vaccination. A number of unique factors may limit the generalizability of these findings to other practices, including the fact that patients in the practice appear to be, on average, becoming healthier over time with less chronic illness and seem to have lower frequencies of certain health issues compared to national trends. Under the Vaccine Friendly Plan, parental choice leads to cessation of vaccination more frequently if certain health indications present following vaccination, leading, by observation, to a reduction in identifiable adverse health conditions. Therefore, our results may or may not generalize to other practices but could be expected to apply to practices that adopt the Vaccine Friendly Plan over the next ten years. Our results are likely conservative compared to practices that do not screen actively for patients who might experience further health complications due to vaccines. We conducted our analyses and present our results and interpretation with these caveats in mind.

We have been keenly aware of the brewing political controversies around vaccination studies, including the public's increased awareness of the dearth of long-term randomized prospective clinical studies that use inert placebos such as saline. Many studies have failed to detect the association of vaccines with adverse outcomes; however, they have mostly used correlative retrospective studies focused on odds ratios of mere incidence and have largely been agnostic to intrinsic methodological power. A white paper for conducting retrospective studies on vaccines [6,7] suggests adjusting/correcting for variables that correlate with vaccination status and/or outcomes. This is an incorrect and risky strategy; in a situation with highly collinear independent variables, adjusting for co-risk factors can remove variation in the model important to finding accurate interpretive context of the main variable of interest and prevents the development of risk models to avoid adverse vaccine outcomes. The CDC's white paper has fostered the widespread practice of selecting a subset of available

variables as confounders for adjusted analyses when the functional relationships among collinear variables are not well established, a feat that Vansteelandt et al., 2010 [19] consider "impossible". The protocol introduces serious risks of model misspecification due to adjusting for variables that correlate with outcomes and overadjustment of highly and sometimes multicollinear variables without formal model selection protocols and should be discontinued.

The use of objective criteria for model selection is rare, and the common practice of arbitrary selection of potential confounders could conflate signals when study outcome measures or measurements collinear with study outcome measures are treated as confounders. This increases the risk of overadjustment bias (See Schisterman et al., 2009 [20]). Not all potential confounders are in fact confounders; they may in fact represent a co-risk factor that could be used to predict risk of adverse events. "Adjusting" for risk factors of vaccine adverse events would undo signals expected to be functionally related to risk of vaccine toxicity; these include birthweight, gestational age, mother's income, and mother's age, all variables that are likely multicollinear and may well be important functional indicators of specific risk to vaccine adverse events. Repeated rounds of analysis of the same data set following observation of results to achieve a desired result (toward or away from statistical significance) without showing all the stages of analysis is now understood to increase the likelihood of bias and can be seen as "*p*-hacking" (George et al., 2016) [21] or "results-peeking". Such activities undertaken to achieve a desired result and failure to bring forward the full set of alternative or interim results should be discouraged by scientific journals publishing any type of observational research studies on any subdiscipline of research.

We recommend stratification and blocking with RIOV, which makes explicit the robustness of the association in different subpopulations. It also makes transparent the effect of subgroup sample size on power. Underpowered designs and methods should not yield presented hypothesis testing results (negative or positive) as definitive as they can have misleading and potentially disastrous effects on public health policies.

Given the massive abundance of electronic medical record data, the dearth of independent studies such as ours on vaccine safety is conspicuous. The value of any vaccination program must be seen as a product of the total net health effects of the individual vaccines in the program, and negative findings should provide an agency for a shift in their use, respect for patient choice, and regulation of their excipients and vaccine formulation.

It is little appreciated that the results of observational studies—including retrospective vaccine safety studies—can depend to a large degree on the statistical method(s) selected and the variables used to "adjust for" variation as found in an observational data set. We have introduced a new measure—RIOV—as a more powerful alternative to the commonly used odds ratios of incidence of diagnosis. We have shown OR on incidence of diagnosis to be, via our simulations (Analysis 7), a less powerful test than RIOV. OR on incidence is in fact a de facto lossy transform (binarization of a continuous variable office visits) of RIOV. Office visits carry more information than diagnoses; specifically, measures based on the number of office visits will carry information on severity in addition to the number of yes/no ever-diagnoses. Our days-of-care-matched incidence (diagnosis only) analysis appears to be the least powerful analysis when odds ratio using incidence is considered; reduced power of OR on incidence relative to RIOV analysis may explain the failure of many prior studies to detect an association between exposure to vaccines and adverse health effects. The realization that studies of the relative occurrence of office visits is a more powerful measure than incidence of diagnoses means that future vaccine studies can be made more capable of detecting real associations of adverse outcomes associated with vaccination.

Many families across the United States who are not vaccinating or who have stopped vaccinating their child or children or who choose to partially vaccinate often choose to opt out as a direct result of adverse health observations following vaccination, including health conditions that to date have not been attributed to vaccination based on epidemiological studies. Parents are almost universally told by their child's health care provider that the health issue was not due to the vaccine, in spite of growing

evidence in the scientific literature that supports both plausible mechanisms of action for chronic illnesses including epidemiological associations. It is now apparent that the commonly reported lack of association of adverse events may be due to the use of a test statistic with low intrinsic power and due to problems including model misspecification and overadjustment bias and that further research is needed to update guidelines and recommendations via additional studies.

We attribute the relative dearth of epidemiological findings similar to ours to a number of factors, including the use of incidence of diagnoses, which is clearly likely to be (on first principles) a less sensitive measure of differences in vaccine-induced disease burden. Importantly, RIOV is a readily accessible measure that likely has a higher power to detect associations than ratios of incidence or odds ratio. The underreporting of adverse events to VAERS is also a factor precluding the detection of adverse events that can be attributed to vaccines. According to the US CDC (CDC, 2020) [22] and the US Department of Health and Human Services (HHS) [23], healthcare providers should report to VAERS (a) any adverse event listed in the VAERS Table of Reportable Events Following Vaccination that occurs within the specified time period after vaccinations and (b) an adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine. Also, the CDC reports that healthcare providers are strongly encouraged to report to VAERS (a) any adverse event that occurs after the administration of a vaccine licensed in the United States, whether it is or is not clear that a vaccine caused the adverse event and (b) vaccine administration errors. Finally, the CDC reports that vaccine manufacturers are required to report to VAERS all adverse events that come to their attention; they are also required to pass on such reports to the Food and Drug Administration.

Regardless of such recommended reporting, the inquiry by Harvard Pilgrim (Ross et al., 2011) [5] on underreporting found that vaccine adverse events are underreported to VAERS by a factor of 100. If doctors are not reporting events because they believe they are not attributable to vaccines and VAERS is the primary resource by which new adverse events are detected, heretofore, undetected adverse events are not discovered. Families experiencing vaccine-induced chronic illnesses not yet recognized by science as adverse outcomes to vaccination are going to object strenuously to mandatory vaccination policies, and science will lag behind the public awareness of vaccine-induced human pain and suffering. This lag is currently undermining trust in public health vaccine policies, government regulating and licensing agencies, vaccine makers, and proponents of vaccination—including most of mainstream media in the US—who insist all vaccines are universally "safe and effective."

This study, and others, indicates that the correct path forward should include the enforceable requirement of all physicians to report all adverse health events recorded in medical records over an extended period to capture those adverse events that are latent, whether they are already recognized by the HHS or not, so as to empower users of the VAERS system to be better able to detect adverse outcomes associated with vaccination. Mandatory adoption of an ESP-VAERS-like adverse event detection system embedded in electronic medical record systems in practices and clinics would be beneficial toward a full understanding of vaccine-related morbidity and mortality in our populations and could lead to a significant increase in overall health. This study also provides information on diagnosed infections targeted by pediatric vaccines.

4.2. Strengths and Limitations

Factors such as sample size limitations, likely due to changes in vaccine acceptance following initial adverse events, limit our ability to robustly test hypotheses of association for some outcomes, especially in neurodevelopmental disorders and vaccination and seizures. If a link does exist, the absence of clear associations is likely due the small number of patients in the practice with neurodevelopmental disorders and seizures, which, ironically, may be due in part to the respect for patient preference, leading to informed choices by families at potential risk.

A related potential limitation includes that, because the data used were from billed diagnoses (in the case of outcomes) or billed vaccination, there may be some occurrences that were missed if insurance did not cover those events for a given patient (e.g., ASD diagnosed via a family

counselor/psychologist/psychiatrist). Similarly, diagnoses of developmental delay outside of the office may have not made it into the medical record for some patients. However, given that part of our data representation of such diagnoses was a per-patient count of reports of such diagnoses, the effects of these possible sampling limitations is likely mostly restricted to neurodevelopmental delays, and such an effect is more likely in outcomes related to data for a limited number of diagnoses than on vaccination data.

A criticism of association studies that detect negative health effects of vaccines is that some unknown, unmeasured confounder, or set of confounders might offer an alternative explanation. An example is the concern that our results may be explicable by other, unmeasured, healthier lifestyle choices made by families who also do not vaccinate. This seems highly unlikely given the relationships between increased adverse outcomes and vaccine acceptance, and lifestyle choices do not seem to be plausible explanations for many of the outcomes we have measured, although exposures to environmental substances such as cigarette smoke and acetaminophen (paracetamol), and malnutrition, which are known to impact negatively the immune system and development, cannot be ruled out as additive or multiplicative risk factors to vaccine adverse reactions and to the examined outcomes. The positive control outcome "fever" (Figure 3) points to a pattern expected following vaccination with no known or suspected relationship to lifestyle choices. However, if it were so, it would appear that our collective priority as a medical community should not be the pursuit of complete vaccination across the population but instead studies on what those other lifestyle choices might include and massive recommendations toward improving the lifestyle choices across the population.

Our study also has numerous strengths: the sample is fully representative of the practice population, and our design protocol had robust data provenance (parity checking) and rigorous data analysis. We avoided overadjustment bias and used a more powerful test to detect adverse events, demonstrated the robustness of the results to analysis assumptions, and have been careful to avoid overdrawn conclusions.

5. Conclusions

We could detect no widespread negative health effects in the unvaccinated other than the rare but significant vaccine-targeted diagnosis. We can conclude that the unvaccinated children in this practice are not, overall, less healthy than the vaccinated and that indeed the vaccinated children appear to be significantly less healthy than the unvaccinated.

We concur with Mawson et al., 2017 [9], who reported: "Further research involving larger, independent samples is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health."

We also concur with Hooker and Miller 2020 [14], who wrote: "Further study is necessary to understand the full spectrum of health effects associated with childhood vaccination".

Other pediatric practices with variably vaccinating populations should be studied using a methodology similar to ours to attempt to refute or validate our findings and those of Mawson et al., 2017 [9], Hooker and Miller 2020 [14], and the numerous studies that have reported adverse health following vaccination. We are particularly interested in further study of the relationship between specific vaccines and combination of vaccines on specific outcomes as well as the relationship between the uptake of specific types of vaccines—inactivated, live virus, and aluminum-adjuvanted—with specific outcomes. Larger studies using electronic medical records from major medical institutions should be undertaken by research teams with no financial interest in the outcome of the studies (e.g., revenue from vaccination and from treatment of vaccine-related adverse outcomes).

Unintended and nonspecific consequences of vaccination, such as increased risk of chronic health conditions from vaccine exposures, must also be examined to determine if for any vaccine-targeted infection alternative methods of infection-avoidance or effective treatments that reduce disease sequela are available and preferable to vaccination in various circumstances, as has been reported by Cowling

et al., 2012 [24] and by Wolff (Wolff, 2020) [25]. Our findings are consistent with the concern that vaccination may increase respiratory virus infection risk, clearly a grave concern in the age of COVID-19.

Our finding of a robust signal of anemia deserves follow up: aluminum is known to bind to transferrin [26] and, in so doing, may interfere with the proper deposition of iron in the bones of children. Iron deficiency can also contribute to febrile seizures, a known side effect of some vaccines. Our society should work to identify safer vaccine schedules and safer adjuvants [27–35] and to reduce autoimmunity risk by removing unsafe epitopes—peptide sequences from pathogens or human cell line remnants in vaccines that match human proteins in sequence or structure from any tissue [36]—would seem expeditious, kind, and wise.

Future studies should now focus on the relative incidence of billed office visits, now that it has been shown to be a more sensitive and powerful measure of outcomes with a larger dynamic range than binary yes/no incidence of diagnoses.

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/17/22/8674/s1: 'Table S1: ICD code mapping'; Table S2: 'LW and Thomas Supplemental S2 Gender Block Results 2.8.xlsx'; Table S3: 'LW and Thomas Supplemental S3 Age Blocks R2.9.xlsx'.

Author Contributions: P.T. directed the care of the patients in the study; P.T. conceived of the study concept; both J.L.-W. and P.T. designed the study; J.L.-W. designed the analysis strategy, and J.L.-W. conceived of and executed the data analysis including the power simulations and drafted the first manuscript; two anonymous honest brokers de-identified the data and provided a data parity check; all technical errors in the execution of analysis, if any, are the sole responsibility of J.L.-W. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by donations from the public to The Institute for Pure and Applied Knowledge (IPAK; http://ipaknowledge.org). None of the donors had any input into the scope or design of the study or the decision to publish. IPAK is a not-for-profit research organization.

Acknowledgments: We are indebted to the public for funding this study via donations to the Institute for Pure and Applied Knowledge. None of the donors had any influence on the scope or direction of the study. We are also deeply indebted to two anonymous honest brokers whose expertise in handling the deidentification and data parity checking made this study possible. Given negative social pressures and direct threats of undue consequences on individuals who participate in studies that cast any negative light on vaccines or the practice of vaccination, we respect their anonymity. We are also indebted to a spreadsheet checker for his time double- and cross-checking our many data analysis spreadsheets for errors or inconsistencies. All errors in the design or execution of analysis are the responsibility of J.L.W. We are especially grateful to three anonymous reviewers for their time and expertise and especially to reviewer #1 for providing in-depth critical and useful review of this study.

Conflicts of Interest: J.L.W. has, in the past, been but is no longer a compensated expert witness in cases in the US National Vaccine Injury Compensation Program. P.T. receives income in the form of royalties from the sale of his book, and he receives income from the sale and administration of vaccines in his practice. P.T. is the owner of Integrative Pediatrics, the population for this study, and is the author of the book "The Vaccine-Friendly Plan: Dr. Paul's Safe and Effective Approach to Immunity and Health—from Pregnancy Through Your Child's Teen Years" by Balantine Books 2016.

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Vaccines and Related Biological Products Advisory Committee Meeting
December 10, 2020

FDA Briefing Document

Pfizer-BioNTech COVID-19 Vaccine

Sponsor:
Pfizer and BioNTech

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Glossary

AE	adverse event
AIDS	acquired immunodeficiency syndrome
ARDS	acute respiratory distress syndrome
BNT162b2	Pfizer-BioNTech COVID-19 Vaccine
CBRN	chemical, biological, radiological, or nuclear
CDC	Centers for Disease Control and Prevention
CMC	Che
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
hACE2	human angiotensin converting enzyme 2
HHS	Health and Human Services
HIV	human immunodeficiency virus
IM	intramuscular
LNP	lipid nanoparticle
MERS-CoV	Middle Eastern respiratory syndrome
modRNA	nucleoside-modified messenger RNA
NAAT	nucleic acid amplification-based test
PVP	Pharmacovigilance Plan
RBD	receptor binding domain
RT-PCR	reverse transcription-polymerase chain reaction
SAE	serious adverse event
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
VE	vaccine efficacy
VRBPAC	Vaccines and Related Biological Products Advisory Committee

1. Executive Summary

On November 20, 2020, Pfizer and BioNTech (the Sponsor) submitted an Emergency Use Authorization (EUA) request to FDA for an investigational COVID-19 vaccine (BNT162b2) intended to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The vaccine is based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA and formulated in lipid nanoparticles (LNPs). The proposed use under an EUA is "for active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older." The proposed dosing regimen is 2 doses, 30 µg each, administered 21 days apart.

The EUA request includes safety and efficacy data from an ongoing phase 3 randomized, double-blinded and placebo-controlled trial of BNT162b2 in approximately 44,000 participants. The primary efficacy endpoint is incidence of COVID-19 among participants without evidence of SARS-CoV-2 infection before or during the 2-dose vaccination regimen. In a mid-November analysis of 36,621 participants randomized 1:1 to vaccine or placebo who were included in the per-protocol efficacy analysis population of participants without evidence of SARS-CoV-2 infection prior to 7 days after completion of the vaccination regimen, efficacy in preventing confirmed COVID-19 occurring at least 7 days after the second dose of vaccine was 95.0%, with 8 COVID-19 cases in the vaccine group and 162 COVID-19 cases in the placebo group. Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across age groups, genders, racial and ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19. Secondary efficacy analyses suggested benefit of the vaccine in preventing severe COVID-19, in preventing COVID-19 following the first dose, and in preventing COVID-19 in individuals with prior SARS-CoV-2 infection, although available data for these outcomes did not allow for firm conclusions.

Safety data from approximately 38,000 participants ≥16 years of age randomized 1:1 to vaccine or placebo with a median of 2 months of follow up after the second dose suggest a favorable safety profile, with no specific safety concerns identified that would preclude issuance of an EUA. Available safety data from all participants enrolled through the November 14, 2020 data cut-off (N=43,252, which includes late enrollment of additional adolescent and adult participants), was consistent with the safety profile for the approximately 38,000 participants with median follow-up of 2 months and also did not raise specific safety concerns. The most common solicited adverse reactions were injection site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%); severe adverse reactions occurred in 0.0% to 4.6% of participants, were more frequent after Dose 2 than after Dose 1, and were generally less frequent in participants ⩾55 years of age (⩽ 2.8%) as compared to younger participants (⩽4.6%). The frequency of serious adverse events was low (<0.5%), without meaningful imbalances between study arms. Among non-serious unsolicited adverse events, there was a numerical imbalance of four cases of Bell's palsy in the vaccine group compared with no cases in the placebo group, though the four cases in the vaccine group do not represent a frequency above that expected in the general population. Otherwise, there were no notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to BNT162b2 vaccine. With the exception of more frequent, generally mild to moderate reactogenicity in participants <55 years of age, the safety profile of BNT162b2 was generally similar across age groups, genders, ethnic and racial groups, participants with or without medical comorbidities, and participants with or without evidence of prior SARS-CoV-2 infection at enrollment.

This meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) is being convened to discuss and provide recommendations on whether:

- based on the totality of scientific evidence available, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 in individuals 16 years of age and older, and
- the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its known and potential risks for use in individuals 16 years of age and older.

The committee will also discuss what additional studies should be conducted by the vaccine manufacturer following issuance of the EUA to gather further data on the safety and effectiveness of this vaccine.

2. Background

2.1. SARS-CoV-2 Pandemic

The SARS-CoV-2 pandemic presents an extraordinary challenge to global health and, as of November 30, 2020, has caused more than 60 million cases of COVID-19 and claimed the lives of 1.5 million people worldwide. In the United States, over 13 million cases have been reported to the Centers for Disease Control and Prevention (CDC), with over 260,000 deaths. Confirmed cases and mortality continue to rise globally. On January 31, 2020, the U.S. Secretary of Health and Human Services (HHS) declared a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS. Following the World Health Organization's declaration of the novel coronavirus pandemic on March 11, 2020, the U.S. President declared a national emergency in response to COVID-19 on March 13, 2020. Vaccines to protect against COVID-19 are critical to mitigate the current SARS-CoV-2 pandemic and to prevent future disease outbreaks.

SARS-CoV-2 is a novel, zoonotic coronavirus that emerged in late 2019 in patients with pneumonia of unknown cause.[1] The virus was named SARS-CoV-2 because of its similarity to the coronavirus responsible for severe acute respiratory syndrome (SARS-CoV, a lineage B betacoronavirus).[2] SARS-CoV-2 is an enveloped, positive sense, single stranded RNA virus sharing more than 70% of its sequence with SARS-CoV, and ~50% with the coronavirus responsible for Middle Eastern respiratory syndrome (MERS-CoV).[3] The SARS-CoV-2 spike glycoprotein (S), which is a main target for neutralizing antibody, binds to its receptor human angiotensin converting enzyme 2 (hACE2) to initiate infection.[4] SARS-CoV-2 is the cause of COVID-19, an infectious disease with respiratory and systemic manifestations. Disease symptoms vary, with many persons presenting with asymptomatic or mild disease and some progressing to severe respiratory tract disease including pneumonia and acute respiratory distress syndrome (ARDS), leading to multiorgan failure and death.

In an attempt to prevent the spread of disease and to control the pandemic, numerous COVID-19 vaccine candidates are in development. These vaccines are based on different platforms including mRNA and DNA technologies and include viral vectored, subunit, inactivated, and live attenuated vaccines. Most COVID-19 candidate vaccines express the spike protein or parts of the spike protein, i.e., the receptor binding domain (RBD), as the immunogenic determinant.

2.2. EUA Request for the Pfizer and BioNTech COVID-19 Vaccine BNT162b2

Pfizer, in partnership with BioNTech Manufacturing GmbH, is developing a vaccine to prevent COVID-19 which is based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA and formulated in lipid nanoparticles (LNP). The Pfizer-BioNTech COVID-19 Vaccine (also referred to as BNT162b2) is administered intramuscularly as a 2-dose series spaced 21 days apart at a dose of 30 μg each. The vaccine is supplied as a multi-dose vial (5 doses) containing a frozen suspension (-80°C to -60°C) of BNT162b2 that must be thawed and diluted with 1.8 mL of sterile 0.9% sodium chloride, allowing for five 0.3 mL doses. The vaccine is preservative free.

A phase 3 randomized and placebo-controlled trial using BNT162b2 in approximately 44,000 participants is currently ongoing to evaluate the vaccine's safety and efficacy. Vaccine efficacy for the primary endpoint against confirmed COVID-19 occurring at least 7 days after the second dose was 95.0% with 8 COVID-19 cases in the vaccine group compared to 162 COVID-19 cases in the placebo group. Data from about 38,000 participants randomized 1:1 with a median of 2 months of follow-up after the second dose of vaccine showed a favorable safety profile at a dose of 30 μg in participants 16 years of age and older. On November 20, 2020, Pfizer and BioNTech submitted an EUA request to FDA for its investigational COVID-19 vaccine (BNT162b2) intended to prevent COVID-19 caused by SARS-CoV-2.

2.3. U.S. Requirements to Support Issuance of an EUA for a Biological Product

Based on the declaration by the Secretary of HHS that the COVID-19 pandemic constitutes a public health emergency with a significant potential to affect national security or the health and security of United States citizens living abroad, FDA may issue an EUA after determining that certain statutory requirements are met (section 564 of the FD&C Act (21 U.S.C. 360bbb-3)).[5]

- The chemical, biological, radiological, or nuclear (CBRN) agent referred to in the March 27, 2020 EUA declaration by the Secretary of HHS (SARS-CoV-2) can cause a serious or life-threatening disease or condition.
- Based on the totality of scientific evidence available, including data from adequate and well-controlled trials, if available, it is reasonable to believe that the product may be effective to prevent, diagnose, or treat such serious or life-threatening disease or condition that can be caused by SARS-CoV-2, or to mitigate a serious or life-threatening disease or condition caused by an FDA-regulated product used to diagnose, treat, or prevent a disease or condition caused by SARS-CoV-2.
- The known and potential benefits of the product, when used to diagnose, prevent, or treat the identified serious or life-threatening disease or condition, outweigh the known and potential risks of the product.
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the disease or condition.

If these criteria are met, under an EUA, FDA can allow unapproved medical products (or unapproved uses of approved medical products) to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions caused by threat agents. FDA has been providing regulatory advice to COVID-19 vaccine manufacturers regarding the data needed to determine that a vaccine's benefit outweigh its risks. This includes demonstrating that manufacturing information ensures product quality and consistency along with data from at least one phase 3 clinical trial demonstrating a vaccine's safety and efficacy in a clear and compelling manner.

In the event an EUA is issued for this product, it would still be considered unapproved and it would be under further investigation (under an Investigational New Drug Application) until it is licensed under a Biologics License Application (BLA). Licensure of a COVID-19 vaccine will be based on review of additional manufacturing, efficacy, and safety data, providing greater assurance of the comparability of licensed product to product tested in the clinical trials, greater assurance of safety based on larger numbers of vaccine recipients who have been followed for a longer period of time, and additional information about efficacy that addresses, among other questions, the potential for waning of protection over time.

2.4. Applicable Guidance for Industry

Risk and benefit considerations are unique for COVID-19 vaccines, given that an EUA may be requested to allow for a vaccine's rapid and widespread deployment for administration to millions of individuals, including healthy people. FDA published in October 2020 guidance for industry entitled "Emergency Use Authorization for Vaccines to Prevent COVID-19" (Appendix C, page 53) describing FDA's current recommendations regarding the manufacturing, nonclinical, and clinical data and information needed under section 564 of the FD&C Act to support the issuance of an EUA for an investigational vaccine to prevent COVID-19, including a discussion of FDA's current thinking regarding the circumstances under which an EUA for a COVID-19 vaccine would be appropriate.

2.5. Safety and Effectiveness Information Needed to Support an EUA

Effectiveness data

Issuance of an EUA requires a determination that the known and potential benefits of the vaccine outweigh the known and potential risks. For a preventive COVID-19 vaccine to be potentially administered to millions of individuals, including healthy individuals, data adequate to inform an assessment of the vaccine's benefits and risks and support issuance of an EUA would include meeting the prespecified success criteria for the study's primary efficacy endpoint, as described in the guidance for industry entitled "Development and Licensure of Vaccines to Prevent COVID-19" (i.e., a point estimate for a placebo-controlled efficacy trial of at least 50%, with a lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate of >30%).[6]

Safety data

An EUA request for a COVID-19 vaccine should include all safety data accumulated from studies conducted with the vaccine, with data from phase 1 and 2 focused on serious adverse events, adverse events of special interest, and cases of severe COVID-19 among study participants. Phase 3 safety data should include characterization of reactogenicity (common and expected adverse reactions shortly following vaccination) in a sufficient number of participants from relevant age groups and should include a high proportion of enrolled participants (numbering well over 3,000) followed for serious adverse events and adverse events of special interest for at least one month after completion of the full vaccination regimen. The phase 1 and 2 safety data likely will be of a longer duration than the available safety data from the phase 3 trial at the time of submission of an EUA request and thus, are intended to complement the available data from safety follow-up from ongoing phase 3 studies.

Phase 3 Follow-up

Data from phase 3 studies should include a median follow-up duration of at least 2 months after completion of the full vaccination regimen to help provide adequate information to assess a vaccine's benefit-risk profile. From a safety perspective, a 2-month median follow-up following completion of the full vaccination regimen will allow identification of potential adverse events that were not apparent in the immediate postvaccination period. Adverse events considered plausibly linked to vaccination generally start within 6 weeks of vaccine receipt.[7] Therefore, a 2-month follow-up period may allow for identification of potential immune-mediated adverse events that began within 6 weeks of vaccination. From the perspective of vaccine efficacy, it is important to assess whether protection mediated by early responses has not started to wane. A 2-month median follow-up is the shortest follow-up period to achieve some confidence that any protection against COVID-19 is likely to be more than short-lived. The EUA request should include a plan for active follow-up for safety (including deaths, hospitalizations, and other serious or clinically significant adverse events) among individuals administered the vaccine under an EUA in order to inform ongoing benefit-risk determinations to support continuation of the EUA.

2.6. Continuation of clinical trials following issuance of an EUA for a COVID-19 vaccine

FDA does not consider availability of a COVID-19 vaccine under EUA, in and of itself, as grounds for immediately stopping blinded follow-up in an ongoing clinical trial or grounds for offering vaccine to all placebo recipients. To minimize the risk that use of an unapproved vaccine under EUA will interfere with long-term assessment of safety and efficacy in ongoing trials, it is critical to continue to gather data about the vaccine even after it is made available under EUA. An EUA request should therefore include strategies that will be implemented to ensure that ongoing clinical trials of the vaccine are able to assess long-term safety and efficacy (including evaluating for vaccine-associated enhanced respiratory disease and decreased effectiveness as immunity wanes over time) in sufficient numbers of participants to support vaccine licensure. These strategies should address how ongoing trial(s) will handle loss of follow-up information for study participants who choose to withdraw from the study in order to receive the vaccine under an EUA.

FDA is aware that some COVID-19 vaccine developers may wish to immediately unblind their trials upon issuance of an EUA in order to rapidly provide vaccine to trial participants who received placebo. Some developers have proposed maintaining blinding in a crossover design that provides vaccine to previous placebo recipients and placebo to previous vaccine recipients. Such strategies would impact collection of longer-term placebo-controlled safety data and evaluation of the duration of vaccine efficacy. Ethical and scientific issues associated with offering vaccination to placebo recipients have been discussed in recent statements and articles.[8-10]

2.7. Previous Meetings of the VRBPAC to Discuss Vaccines to Prevent COVID-19

On October 22, 2020, the VRBPAC met in open session, to discuss, in general, the development, authorization and/or licensure of vaccines to prevent COVID-19. No specific application was discussed at this meeting. Topics discussed at the meeting included:

- FDA's approach to safety and effectiveness, and chemistry, manufacturing and control (CMC) data as outlined in the respective guidance documents

- Considerations for continuation of blinded Phase 3 clinical trials if an EUA has been issued for an investigational COVID-19 vaccine
- Studies following licensure and/or issuance of an EUA for COVID-19 vaccines to:
    - Further evaluate safety, effectiveness and immune markers of protection
    - Evaluate the safety and effectiveness in specific populations.

3. Topics for VRBPAC Discussion

The Vaccines and Related Biological Products Advisory Committee will convene on December 10, 2020, to discuss and provide recommendations on whether:

- based on the totality of scientific evidence available, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine may be effective in preventing COVID-19 in individuals 16 years of age and older, and
- the known and potential benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its known and potential risks for use in individuals 16 years of age and older.

The committee will also discuss what additional studies should be conducted by the vaccine manufacturer following issuance of the EUA to gather further data on the safety and effectiveness of this vaccine.

4. Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)

4.1. Vaccine Composition, Dosing Regimen

The Pfizer-BioNTech COVID-19 Vaccine is a white to off-white, sterile, preservative-free, frozen suspension for intramuscular injection. The vaccine contains a nucleoside-modified messenger RNA (modRNA) encoding the viral spike glycoprotein (S) of SARS-CoV-2. The vaccine also includes the following ingredients: lipids ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-distearoyl-sn-glycero-3-phosphocholine, and cholesterol), potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose.

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen [between -80°C to -60°C (-112°F to -76°F)] multi-dose (5-dose) vial. The vaccine must be thawed and diluted in its original vial with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to administration. After dilution, the vial contains 5 doses of 0.3 mL per dose. After dilution, the multiple-dose vials must be stored between 2°C to 25°C (35°F to 77°F) and used within 6 hours from the time of dilution.

The Pfizer-BioNTech COVID-19 Vaccine, BNT162b2 (30 µg), is administered intramuscularly (IM) as a series of two 30 µg doses (0.3 mL each) 21 days apart.

FDA has reviewed the CMC data submitted to date for this vaccine and has determined that the CMC information is consistent with the recommendations set forth in FDA's Guidance on Emergency Use Authorization for Vaccines to Prevent COVID-19. As such, FDA has determined that the Sponsor has provided adequate information to ensure the vaccine's quality and consistency for authorization of the product under an EUA.

4.2. Proposed Use Under EUA

The proposed indication and use of the vaccine under an EUA is “for active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older.”

5. FDA Review of Clinical Safety and Effectiveness Data

5.1. Overview of Clinical Studies

Data from two ongoing clinical studies were included in the EUA request, which are summarized in Table 1 below. Study C4591001 is a multi-center, multi-national Phase 1,2,3 randomized, blinded, placebo-controlled safety, immunogenicity, and efficacy study that is the focus of the EUA review. Study BNT162-01 is a Phase 1 study that explored various vaccine candidates and dose levels and will not be discussed in detail. A brief summary of the BNT162-01 study design and results to date is found in Appendix A, page 51.

Table 1: Clinical Trials Submitted in Support of Efficacy and Safety Determinations of the Pfizer-BioNTech COVID-19 Vaccine

Study Number/ Country	Description	BNT162b2 (30 μg)* participants (N)	Placebo participants (N)	Study Status
C4591001 USA, Argentina, Brazil, Germany, S. Africa, Turkey	Phase 1,2,3 randomized, placebo-controlled, observer-blind; to evaluate safety, immunogenicity and efficacy of COVID-19 vaccine	Phase 1: 24 Phase 2/3: 21823	Phase 1: 6 Phase 2/3: 21828	Ongoing
BNT162-01 Germany	Phase 1/2 randomized, open-label; to evaluate safety and immunogenicity, dose escalation	12	0	Ongoing

N= total number of randomized participants as of November 14, 2020. Placebo: saline.
*Phase 1 studies included additional participants vaccinated with other dose levels and other mRNA vaccine candidates.
Studies C4591001 and BNT162-01 started in April 2020 (first participant, first visit).

5.2. Study C4591001

5.2.1. Design

Study C4591001 is an ongoing, randomized, placebo-controlled, phase 1/2/3 study being conducted in the US, Argentina, Brazil, Germany, South Africa and Turkey. Initially the study was designed as a phase 1/2 study in healthy adults in the US for vaccine candidate and dosage selection, immunogenicity and preliminary efficacy, but the protocol was revised to expand the study design for inclusion of a phase 2/3 portion to evaluate clinical disease endpoint efficacy in individuals 12 years of age and older in the US and additional sites outside of the US.

In phase 1, two age groups were evaluated in separate cohorts, younger participants 18 through 55 years of age (N=45) and older participants 65 through 85 years of age (N=45). The study population included healthy men and women and excluded participants at high risk of SARS-CoV-2 infection or with serological evidence of prior or current SARS-CoV-2 infection. Two different vaccine candidates were evaluated, and younger participants received escalating dose levels with progression to subsequent dose levels and evaluation of escalating dose levels in the older age group (65 through 85 years), based on recommendations from an internal review committee that reviewed safety and immunogenicity data. For each vaccine candidate and dose

level, participants were randomized 4:1, such that 12 participants received the vaccine candidate and 3 participants received placebo. Review of the safety and immunogenicity from phase 1, in combination with data from Study BNT162-01 (See Section 10), supported the final vaccine candidate and dose level (BNT162b2 at 30 µg, given 21 days apart) to proceed into phase 2/3.

In phase 2/3, participants were enrolled with stratification by age (younger adults: 18 through 55 years of age; older adults: over 55 years of age) and a goal of 40% enrollment in the older adult age group. Adolescents were added to the protocol, based on review of safety data in younger adults enrolled in the ongoing study, so the age strata were revised as follows: 12 through 15 years of age, 16 through 54 years of age, and 55 years of age and older. The study population for phase 2/3 includes participants at higher risk for acquiring COVID-19 and at higher risk of severe COVID-19 disease, such as participants working in the healthcare field, participants with autoimmune disease, and participants with chronic but stable medical conditions such as hypertension, asthma, diabetes, and infection with HIV, hepatitis B or hepatitis C. Participants were randomized 1:1 to receive 2 doses of either BNT162b2 or placebo, 21 days apart. The phase 2 portion of the study evaluated reactogenicity and immunogenicity for 360 participants enrolled early-on, and these participants also contribute to the overall efficacy and safety data in the phase 3 portion. The ongoing phase 3 portion of the study is evaluating the safety and efficacy of BNT162b2 for the prevention of COVID-19 disease occurring at least 7 days after the second dose of vaccine. Efficacy is being assessed throughout a participant's follow-up in the study through surveillance for potential cases of COVID-19. If, at any time, a participant develops acute respiratory illness, an illness visit occurs. Assessments for illness visits include a nasal (midturbinate) swab, which is tested at a central laboratory using a reverse transcription-polymerase chain reaction (RT-PCR) test (e.g., Cepheid; FDA authorized under EUA), or other sufficiently validated nucleic acid amplification-based test (NAAT), to detect SARS-CoV-2. The central laboratory NAAT result is used for the case definition, unless it is not possible to test the sample at the central laboratory. In that case, the following NAAT results are acceptable: Cepheid Xpert Xpress SARS-CoV-2Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001) Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001).

The study design includes planned interim analyses of the first primary efficacy endpoint at pre-specified numbers of COVID-19 cases (at least 62, 92, and 120 cases), and all primary and secondary efficacy endpoints were analyzed in the final efficacy analysis after at least 164 COVID-19 cases were accrued (see Statistical Analysis section, below). Participants are expected to participate for a maximum of approximately 26 months.

Primary Efficacy Endpoints

Study C4591001 has two primary endpoints:

First primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Second primary endpoint: COVID-19 incidence per 1000 person-years of follow-up in participants with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥7 days after Dose 2

Secondary Efficacy Endpoints

Study C4591001 has secondary endpoints based on different approaches to COVID-19 case evaluation criteria as follows:

COVID-19 confirmed at least 14 days after Dose 2: COVID-19 incidence per 1000 person-years of follow up in participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed ≥14 days after Dose 2

Severe COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2

CDC-defined COVID-19: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2.

For the primary efficacy endpoint, the case definition for a confirmed COVID-19 case was the presence of at least one of the following symptoms and a positive SARS-CoV-2 NAAT within 4 days of the symptomatic period:

- 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;
- Vomiting.

For a secondary efficacy endpoint, a second definition, which may be updated as more is learned about COVID-19, included the following additional symptoms defined by CDC (listed at https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html):

- Fatigue;
- Headache;
- Nasal congestion or runny nose;
- Nausea.

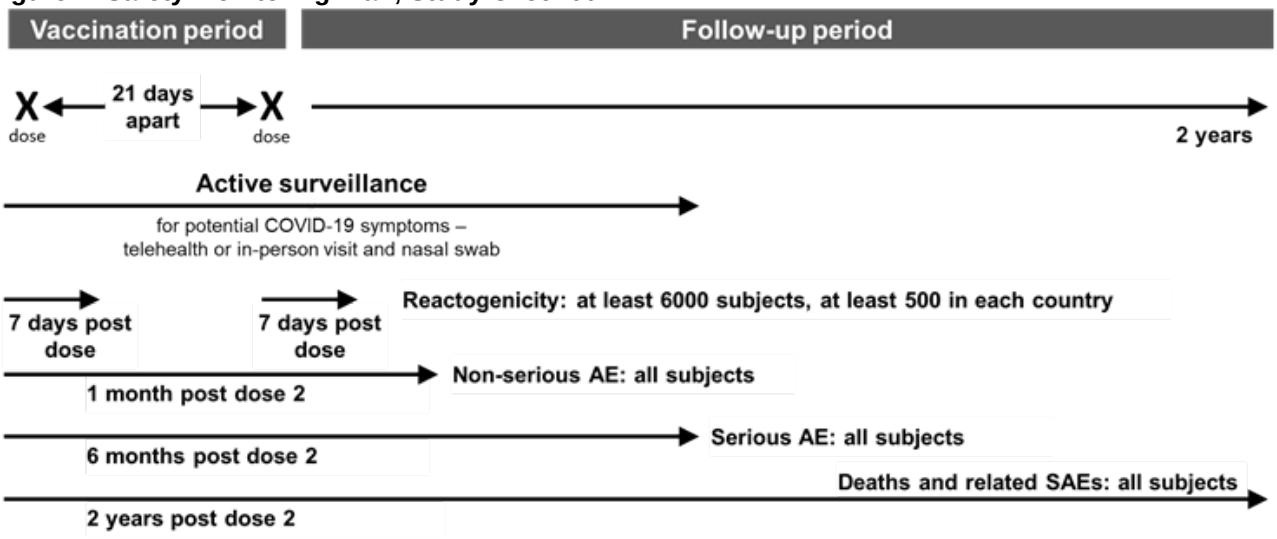
For another secondary endpoint, the case definition for a severe COVID-19 case was a confirmed COVID-19 case with at least one of the following:

- Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO2 ≤93% on room air at sea level, or PaO2/FiO2 <300 mm Hg);
- Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO);
- Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors)
- Significant acute renal, hepatic, or neurologic dysfunction;
- Admission to an ICU;
- Death.

Evaluation of Safety

The primary safety objective for all phases was to describe the safety of BNT162 vaccine(s) in healthy adults after 1 or 2 doses. All phase 1 participants (n=30), and then 6653 U.S. participants (360 phase 2, 6293 phase 3) and the first ~500 phase 3 participants/per country with enrollment through October 9, 2020 (Argentina, Brazil and South Africa) recorded local reactions, systemic events, and antipyretic/pain medication usage from Day 1 through Day 7 after each dose. Unsolicited adverse events (AEs) are collected from Dose 1 to 1 month after the last dose and serious AEs (SAEs) from Dose 1 to 6 months after the last dose. Figure 1 below shows the study safety monitoring plan.

Figure 1. Safety Monitoring Plan, Study C4591001



Reactogenicity assessments included solicited injection site reactions (pain, redness, swelling) and systemic AEs (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain), and antipyretic/pain medication use were recorded in an e-diary. At the data cutoff date for the EUA, reactogenicity events were not collected from adolescents 16 to 17 years of age (enrolled prior to the implementation of Protocol Amendment 9, finalized on 29 October 2020) using an e-diary but were detected and reported as unsolicited AEs. For any phase 3 participants who were not in the reactogenicity subset, local reactions and systemic events consistent with reactogenicity were detected and reported as unsolicited AEs. HIV-positive participants and adolescents 12 through 15 years of age were included in the reactogenicity subset with implementation of protocol amendment 6 (finalized on September 8, 2020) and amendment 7 (finalized on October 6, 2020), respectively. Solicited reactogenicity data in adolescents 16-17 years of age are not available for the reporting period. Reactogenicity data from a total of 100 adolescents 12 through 15 years of age enrolled in C4591001 phase 2/3 were provided in the EUA submission. However, the Sponsor did not request inclusion of this age group in the EUA because the available data, including number of participants and follow-up duration, were insufficient to support favorable a benefit-risk determination at this time. Therefore, the reactogenicity data for participants 12 through 15 years of age are not presented in this document.

Clinical laboratory tests were assessed in phase 1 at 1-week postvaccination. The planned safety follow-up for currently enrolled adolescents and adults is through 24 months after vaccination #2.

Potential COVID-19 illnesses and their sequelae were not to be reported as AEs, with the exception of illnesses that met regulatory criteria for seriousness and were not confirmed to be COVID-19. These illnesses were evaluated and reported as SAEs.

In phase 2/3, monitoring for risk of vaccine-enhanced disease was performed by an unblinded team supporting the Data Monitoring Committee that reviewed cases of severe COVID-19 as they were received and reviewed AEs at least weekly for additional potential cases of severe COVID-19. The stopping rule was triggered when the 1-sided probability of observing the same or a more extreme case split was 5% or less when the true incidence of severe disease was the same for vaccine and placebo participants, and alert criteria were triggered when this probability was less than 11%.

Analysis Populations

For the purposes of analysis, the following populations are defined:

Population	Description
Enrolled	All participants who have a signed informed consent document.
Randomized	All participants who are assigned a randomization number.
Evaluable efficacy	All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window and have no other important protocol deviations as determined by the clinician.
All-available efficacy	1. All randomized participants who receive at least 1 vaccination. 2. All randomized participants who complete 2 vaccination doses.

Phase 2/3 safety analysis populations were as follows:

- Phase 2/3 all-enrolled population: composed of a total of 43,448 (21720 vaccine, 21728 placebo) participants ≥16 years of age, regardless of duration of follow-up, for whom written informed consent was obtained. Initial enrollment included individuals 18 years and older, then included individuals as young as 16 years of age and individuals with known HIV (protocol amendment 6; finalized on September 8, 2020). As of November 14, 2020, 43.9% and 79.5% of vaccine recipients completed at least 2 months (≥8 weeks) and at least 1 month (≥4 weeks), respectively, of safety follow-up after Dose 2. The percentages of placebo recipients completing at least 2 months (≥8 weeks) and at least 1 month (≥4 weeks) were similar to the vaccine group.

- Phase 2/3 safety population (median follow-up time of 2 months after vaccination #2): comprised of a total of 37586 (18801 vaccine,18785 placebo) participants >16 years of age enrolled by October 9, 2020 and received at least 1 dose of study vaccine or placebo; overall, 98.1% of participants completed the 2-dose series. As of November 14, 2020, 50.6% and 91.6% of vaccine recipients completed at least 2 months (>8 weeks) and at least 1 month (>4 weeks), respectively, of safety follow-up after Dose 2. The percentages of placebo recipients completing at least 2 months (>8 weeks) and at least 1 month (>4 weeks) were similar to the vaccine group. A total of 283 (138 vaccine,145 placebo) individuals were 16 to <18 years of age. HIV-positive individuals were included in the all-enrolled population, but not the phase 2/3 safety population because the number of participants enrolled by October 9, 2020 was small (n=120) and the median duration of safety follow-up was short.

5.2.2. FDA Assessment of Phase 2/3 Follow-Up Duration

Study C4591001 initially enrolled approximately 30,000 participants and then several months later began enrollment of approximately 14,000 additional participants, including adolescents and participants with chronic, stable HIV, hepatitis B, or hepatitis C infections. Because of the gap in enrollment, the entire enrolled study population had a median follow-up of less than 2 months as of the EUA submission data cut-off date of November 14, 2020. However, the analyses submitted to support this EUA request meet the expectation for median duration of follow-up time, as follows:

- Submitted safety analyses for participants enrolled through October 9, 2020, and followed through November 14, 2020 (referred to by Pfizer and in this document as the phase 2/3 safety population and including a total of 37,586 participants), represent a median follow-up of 2 months. Additionally, this safety database is larger than for the initial planned enrollment of approximately 30,000 participants.

- The date for data cut-off for the first interim analysis for efficacy was November 4, 2020, when a total of 94 confirmed COVID-19 cases were accrued. All of the participants included in the first interim efficacy analysis had at least 7 days of follow-up after Dose 2, and thus were enrolled no later than October 7, 2020. All participants in the first interim efficacy analysis were therefore included in the phase 2/3 safety population defined above. Although the median follow-up duration for participants included in the first interim efficacy analysis was slightly less than 2 months as of November 4, 2020, these participants were also included in the final efficacy analyses with data cut-off of November 14, 2020, which extended the median follow-up for these participants to greater than 2 months. The results of the final efficacy analysis on data to November 14, 2020, indicate that the conclusions from the first interim efficacy analysis would not change when including additional follow-up to November 14, 2020.

The date for data cut-off for the final efficacy analysis was November 14, 2020, when a total of 170 confirmed COVID-19 cases were accrued. As noted above, the median follow-up duration after completion of the full vaccination regimen for all participants enrolled at that time was less than 2 months for both safety and efficacy populations, due to a gap in enrollment. Because the data for the final efficacy analysis could be submitted in support of the EUA request and could provide data from a greater number of participants than from the interim analysis, FDA has focused its review on the efficacy data from the final efficacy analyses. Additional safety analyses from this larger database of all enrolled participants were also reviewed to evaluate for differences compared with the smaller phase 2/3 safety population.

5.2.3. Subject Disposition and Inclusion in Analysis Populations

Disposition tables are presented below in Table 2 (efficacy analysis populations) and Table 3 (phase 2/3 safety population). Overall, few participants were discontinued or lost to follow-up, and these and other analysis population exclusions were generally balanced between treatment groups. Of 43,448 participants in the phase 2/3 all-enrolled population, 94.2% of vaccine recipients and 94.1% of placebo recipients completed 2 doses (data not shown).

Table 2. Efficacy Populations, Treatment Groups as Randomized

	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
Randomized[b]	21823 (100.0)	21828 (100.0)	43651 (100.0)
Dose 1 all-available efficacy population	21768 (99.7)	21783 (99.8)	43551 (99.8)
Participants without evidence of infection before Dose 1	20314 (93.1)	20296 (93.0)	40610 (93.0)
Participants excluded from Dose 1 all-available efficacy population	55 (0.3)	45 (0.2)	100 (0.2)
Reason for exclusion[c]			
Did not receive at least 1 vaccination	54 (0.2)	45 (0.2)	99 (0.2)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Dose 2 all-available efficacy population	20566 (94.2)	20536 (94.1)	41102 (94.2)
Participants without evidence of infection prior to 7 days after Dose 2	18701 (85.7)	18627 (85.3)	37328 (85.5)
Participants without evidence of infection prior to 14 days after Dose 2	18678 (85.6)	18563 (85.0)	37241 (85.3)
Participants excluded from Dose 2 all-available efficacy population	1257 (5.8)	1292 (5.9)	2549 (5.8)
Reason for exclusion[c]			
Did not receive 2 vaccinations	1256 (5.8)	1292 (5.9)	2548 (5.8)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Evaluable efficacy (7 days) population	20033 (91.8)	20244 (92.7)	40277 (92.3)
Evaluable efficacy (14 days) population	20033 (91.8)	20243 (92.7)	40276 (92.3)
Participants excluded from evaluable efficacy (7 days) population	1790 (8.2)	1584 (7.3)	3374 (7.7)
Participants excluded from evaluable efficacy (14 days) population	1790 (8.2)	1585 (7.3)	3375 (7.7)
Reason for exclusion[c]			
Randomized but did not meet all eligibility criteria	36 (0.2)	26 (0.1)	62 (0.1)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1)	1550 (7.1)	1561 (7.2)	3111 (7.1)
Had other important protocol deviations on or prior to 7 days after Dose 2	311 (1.4)	60 (0.3)	371 (0.8)
Had other important protocol deviations on or prior to 14 days after Dose 2	311 (1.4)	61 (0.3)	372 (0.9)

[a]n = Number of participants with the specified characteristic.
[b]These values are the denominators for the percentage calculations.
[c]Participants may have been excluded for more than 1 reason.
Note: 100 participants 12 through 15 years of age with limited follow-up are included in the randomized population (49 in the vaccine group and 51 in the placebo group). Some of these subjects were included in the denominators of efficacy analyses, depending on the population analyzed, but did not contribute primary endpoint cases and do not affect efficacy conclusions for ages 16 years and above.

Table 3. Disposition of All Randomized Participants, Phase 2/3 Safety Population

Treatment Group	BNT162b2 N=18904 n (%)	Placebo N=18892) n (%)	Total N=37796 n (%)
Randomized	18904 (100.0)	18892 (100.0)	37796 (100.0)
Vaccinated			
Completed 1 dose	18858 (99.8)	18849 (99.8)	37707 (99.8)
Completed 2 doses	18555 (98.2)	18533 (98.1)	37088 (98.1)
Withdrawn from Study	180 (1.0)	259 (1.4)	439 (1.2)
Reason for Withdrawal			
Adverse Event	8 (0.0)	5 (0.0)	13 (0.0)
Death	2 (0.0)	4 (0.0)	6 (0.0)
Withdrawal by Subject	84 (0.4)	157 (0.8)	241 (0.6)
Lost to Follow-up	80 (0.4)	86 (0.5)	166 (0.4)
No longer meets eligibility criteria	1 (0.0)	2 (0.0)	3 (0.0)
Refused further study procedures	0	1 (0.0)	1 (0.0)

Source: EUA 27036, amendment 3, Table 2; c4591001-safety-tables-cos-reacto.pdf, page 43.
Note: One participant was randomized but did not sign informed consent and therefore not included in any analysis population.
Note: 120 HIV-positive participants included in this table. HIV population analyses were summarized separately from analyses based on the phase 2/3 safety population, but included in the all-enrolled poplation analyses presented in this briefing document.
%:n/N. n = number of subjects with the specified characteristic. N = number of participants ≥16 years of age enrolled by October 9, 2020, including 120 HIV-positive participants, and received at least 1 dose of study vaccine or placebo. N is the denominator used for the percentage calculations.
Data analysis cutoff date: November 14, 2020

The numbers of randomized participants contributing to efficacy analyses presented in this document include 100 participants 12 through 15 years of age (49 in the vaccine group and 51 in the placebo group) who had limited follow-up at the time of the November 14, 2020 data cut-off. However, the sponsor did not include this age group in the EUA request. The numbers of participants presented and used as denominators for efficacy calculations were not adjusted to remove participants 12 through 15 years of age. Because the number of participants 12 through 15 years of age is very small relative to the overall efficacy analysis populations, and no primary endpoint COVID-19 cases occurred in this age group, the vaccine efficacy conclusions are not impacted. No participants 12 through 15 years of age are included in the safety analyses. However, the safety disposition table includes 120 HIV-positive participants who were not included in the phase 2/3 safety population analyses.

5.2.4. Demographics and Other Baseline Characteristics

Overall, the phase 2/3 evaluable efficacy population included 49.4% females, 81.9% White, 9.8% African American, 4.4% Asian participants, and <3% from other racial groups; 26.2% of participants were Hispanic/Latino; 21.4% of participants were ≥65 years of age. The median age was 51 years. The most frequently reported comorbidities were obesity (35.1%), diabetes (with and without chronic complications, 8.4%) and pulmonary disease (7.8%). Geographically, 76.7% of participants were from the US, 15.3% from Argentina, 6.1% from Brazil, and 2% from South Africa.

The demographic characteristics among vaccine and placebo participants in the all-available efficacy population were similar to the evaluable efficacy population. Please refer to the table below.

Table 4. Demographic Characteristics, Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy (7 Days) Population

Characteristic	BNT162b2 (N[a]=20033) N[b] (%)	Placebo (N[a]=20244) N[b] (%)	Total (N[a]=40277) N[b] (%)
Sex: Female	9794 (48.9)	10107 (49.9)	19901 (49.4)
Sex: Male	10239 (51.1)	10137 (50.1)	20376 (50.6)
Age at Vaccination: Mean years (SD)	50.3 (15.73)	50.1 (15.78)	50.2 (15.76)
Age at Vaccination: Median (years)	51.0	51.0	51.0
Age at Vaccination: Min, max (years)	(12, 89)	(12, 91)	(12, 91)
Age Group: 16 to <18 years	77 (0.4)	76 (0.4)	153 (0.4)
Age Group: 16 to 55 years	11589 (57.8)	11743 (58.0)	23332 (57.9)
Age Group: >55 years	8396 (41.9)	8454 (41.8)	16850 (41.8)
Age Group: ≥65 years	4294 (21.4)	4319 (21.3)	8613 (21.38)
Age Group: ≥75 years	860 (4.3)	852 (4.2)	1712 (4.3)
Race: American Indian or Alaska Native	131 (0.7)	122 (0.6)	253 (0.6)
Race: Asian	880 (4.4)	883 (4.4)	1763 (4.4)
Race: Black or African American	1957 (9.8)	1972 (9.7)	3929 (9.8)
Race: Native Hawaiian or Other Pacific Islander	54 (0.3)	29 (0.1)	83 (0.2)
Race: White	16387 (81.8)	16619 (82.1)	33006 (81.9)
Race: Multiracial	523 (2.6)	493 (2.4)	1016 (2.5)
Race: Not reported	101 (0.5)	126 (0.6)	227 (0.6)
Ethnicity: Hispanic or Latino	5272 (26.3)	5281 (26.1)	10553 (26.2)
Ethnicity: Not Hispanic or Latino	14652 (73.1)	14847 (73.3)	29499 (73.2)
Ethnicity: Not reported	109 (0.5)	116 (0.6)	225 (0.6)
Comorbidities[c]: Yes	9278 (46.3)	9314 (46.0)	18592 (46.2)
Comorbidities: No	10755 (53.7)	10930 (54.0)	21685 (53.8)
Comorbidity: Obesity	6934 (34.6)	7093 (35.0)	14027 (34.8)

[a].N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
[b].n = number of participants with the specified characteristic.
[c]. Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as patients who had at least one of the Charlson comorbidity index (Appendix B, page 52) category or obesity only (BMI ≥30 kg/m^2).

Overall, the phase 2/3 safety population included 83.1% White, 9.1% African American, 4.3% Asian participants, and <3% from other racial groups; 28.0% of participants were Hispanic/Latino; 21.6% of participants were >65 years of age. The median age was 52 years, and safety data from a total of 103 participants 16 and 17 years of age were included in this submission. The most frequently reported comorbidities were obesity (35.1%), diabetes (without chronic complications, 7.8%) and chronic pulmonary disease (7.8%). Geographically, 76.7% of participants were from the US, 15.3% from Argentina, 6.1% from Brazil, and 2.0% from South Africa.

The demographic characteristics among vaccine and placebo participants in the all-enrolled population were similar and were also enrolled from sites in Germany (1%) and Turkey (1%). There were no significant imbalances in demographic and other baseline characteristics between the all-enrolled population and phase 2/3 safety population with median 2-month follow-up.

Table 5. Demographics and Other Baseline Characteristics, Phase 2/3 Safety Population

Characteristic	BNT162b2 N=18801 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	Placebo N=18785 n (%)	Placebo n (%)	Placebo n (%)	Placebo n (%)	Total N=37586 n (%)
Age (years)	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	
Age (years)									
Mean [SD]	16.40 [0.49]	44.99 [12.66]	68.84 [2.80]	78.07 [2.78]	16.36 [0.48]	44.78 [12.72]	68.84 [2.78]	78.10 [2.81]	50.38 [15.70]
Median	16	46	68	77	16	46	69	77	52
Min, max	16-17	18-64	65-74	75-89	16-17	18-64	65-74	75-91	16-91
Sex									
Male	33 (0.2)	7385 (39.3)	1714 (9.1)	470 (2.5)	24 (0.1)	7153 (38.1)	1724 (9.2)	498 (2.7)	19001 (50.6)
Female	20 (0.1)	7305 (38.9)	1513 (8.0)	361 (1.9)	26 (0.1)	7539 (40.1)	1511 (8.0)	310 (1.7)	18585 (49.4)
Race									
White	37 (0.2)	11895 (63.3)	2908 (15.5)	775 (4.1)	38 (0.2)	11891 (63.3)	2930 (15.6)	756 (4.0)	31230 (83.1)
African American	11 (0.1)	1477 (7.9)	186 (1.0)	20 (0.1)	7 (0.0)	1505 (8.0)	189 (1.0)	21 (0.1)	3416 (9.1)
Asian	0 (0.0)	693 (3.7)	81 (0.4)	26 (0.1)	0 (0.0)	715 (3.8)	72 (0.4)	19 (0.1)	1606 (4.3)
Multiracial	3 (0.0)	417 (2.2)	21 (0.1)	7 (0.0)	3 (0.0)	379 (2.0)	18 (0.1)	5 (0.0)	853 (2.3)
Not reported	0 (0.0)	82 (0.4)	11 (0.1)	0 (0.0)	1 (0.0)	98 (0.5)	10 (0.1)	5 (0.0)	207 (0.6)
American Indian or Alaska native	0 (0.0)	84 (0.4)	15 (0.1)	2 (0.0)	1 (0.0)	83 (0.4)	11 (0.1)	2 (0.0)	198 (0.5)
Nat. HI or other Pac. Isl.	2 (0.0)	42 (0.2)	5 (0.0)	1 (0.0)	0 (0.0)	21 (0.1)	5 (0.0)	0 (0.0)	76 (0.2)
Ethnicity									
Hispanic or Latino	6 (0.0)	4595 (24.4)	549 (2.9)	103 (0.5)	5 (0.0)	4616 (24.6)	558 (3.0)	90 (0.5)	10522 (28.0)
Non-Hispanic/non-Latino	47 (0.2)	10009 (53.2)	2658 (14.1)	722 (3.8)	44 (0.2)	10004 (53.3)	2652 (14.1)	707 (3.8)	26843 (71.4)
Not reported	0 (0.0)	86 (0.5)	20 (0.1)	6 (0.0)	1 (0.0)	72 (0.4)	25 (0.1)	11 (0.1)	221 (0.6)
Baseline Body Mass Index (BMI)									
Obese	3 (0.0)	5200 (27.7)	1079 (5.7)	248 (1.3)	14 (0.1)	5242 (27.9)	1147 (6.1)	235 (1.3)	13168 (35.0)
Overweight	14 (0.1)	4901 (26.1)	1278 (6.8)	368 (2.0)	9 (0.0)	4857 (25.9)	1255 (6.7)	340 (1.8)	13022 (34.6)

Characteristic	BNT162b2 N=18801 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	Placebo N=18785 n (%)	Placebo n (%)	Placebo n (%)	Placebo n (%)	Total N=37586 n (%)
Age (years)	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	
Baseline Evidence of Prior SARS-CoV-2 Infection									
Negative	48 (0.3)	13879 (73.8%)	3109 (16.5)	805 (4.3)	47 (0.3%)	13858 (73.8%)	3115 (16.6%)	788 (4.2%)	35649 (94.8%)
Positive	3 (0.0)	473 (2.5%)	53 (0.3)	16 (0.1)	3 (0.0%)	520 (2.8%)	52 (0.3%)	5 (0.0%)	1125 (3.0%)
Missing	2 (0.0)	338 (1.8%)	65 (0.3)	10 (0.1)	0 (0.0%)	314 (1.7%)	68 (0.4%)	15 (0.1%)	812 (2.2%)
Comorbidities									
No	48 (0.3)	12353 (65.7%)	2081 (11.1)	444 (2.4)	37 (0.2%)	12412 (66.1%)	2118 (11.3%)	470 (2.5%)	29963 (79.7%)
Yes	5 (0.0)	2337 (12.4%)	1146 (6.1)	387 (2.1)	13 (0.1%)	2280 (12.1%)	1117 (5.9%)	338 (1.8%)	7623 (20.3%)
Diabetes Without Chronic Complication	0 (0.0)	814 (4.3%)	497 (2.6)	156 (0.8)	1 (0.0%)	849 (4.5%)	491 (2.6%)	132 (0.7%)	2940 (7.8%)
Chronic Pulmonary Disease	5 (0.0)	1093 (5.8%)	286 (1.5)	89 (0.5)	12 (0.1%)	1060 (5.6%)	309 (1.6%)	66 (0.4%)	2920 (7.8%)
Myocardial Infarction	0 (0.0)	82 (0.4%)	71 (0.4)	41 (0.2)	0 (0.0%)	73 (0.4%)	83 (0.4%)	31 (0.2%)	381 (1.0%)
Peripheral Vascular Disease	0 (0.0)	26 (0.1%)	67 (0.4)	31 (0.2)	0 (0.0%)	29 (0.2%)	52 (0.3%)	33 (0.2%)	238 (0.6%)
Liver Disease (mild, moderate or severe)	0 (0.0)	83 (0.4%)	34 (0.2)	7 (0.0)	0 (0.0%)	67 (0.4%)	17 (0.1%)	6 (0.0%)	214 (0.6%)
Diabetes With Chronic Complication	0 (0.0)	47 (0.2%)	36 (0.2)	15 (0.1)	0 (0.0%)	47 (0.3%)	47 (0.3%)	18 (0.1%)	210 (0.6%)
Congestive Heart Failure	0 (0.0)	44 (0.2%)	26 (0.1)	17 (0.1)	0 (0.0%)	36 (0.2%)	30 (0.2%)	16 (0.1%)	169 (0.4%)
AIDS/HIV	0 (0.0)	0 (0.0%)	0 (0.0)	0 (0.0)	0 (0.0%)	1 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)

Characteristic	BNT162b2 N=18801 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	BNT162b2 n (%)	Placebo N=18785 n (%)	Placebo n (%)	Placebo n (%)	Placebo n (%)	Total N=37586 n (%)
Age (years)	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	**16 to <18**	**18 to <65**	**65 to <75**	**≥75**	
Hypertension only	0 (0.0)	2569 (13.7%)	1528 (8.1)	488 (2.6)	1 (0.0%)	2621 (14.0%)	1569 (8.4%)	432 (2.3%)	9208 (24.5%)

Source: FDA-generated table.
Abbreviations: n = number of participants with the specified characteristic; N = number of participants ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo, N is denominator for the percentage calculations; SD = standard deviation; min, max = minimum, maximum; Nat. HI = Native Hawaiian; Pac. Isl. = Pacific Islander
Data analysis cutoff date: November 14, 2020.

5.2.5. Vaccine Efficacy

Primary Efficacy Analyses

Efficacy Results – Primary Endpoint (Evaluable Efficacy Population)

For the first primary efficacy endpoint, vaccine efficacy (VE) for BNT162b2 against confirmed COVID-19 was evaluated in participants without evidence of prior SARS-CoV-2 infection prior to 7 days after Dose 2. For the second primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants with and without evidence of prior SARS-CoV-2 infection prior to 7 days after Dose 2. Cases were counted from 7 days after Dose 2 for both endpoints. The criterion for success was met if the posterior probability that true vaccine efficacy >30% conditioning on the available data was >99.5% at the final analysis.

For participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%. The case split was 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group (Table 6). The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability, which met the pre-specified success criterion.

Table 6. Final Analysis of Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants Without Evidence of Prior SARS-CoV-2 Infection - Evaluable Efficacy Population

Pre-specified Age Group	BNT162b2 N[a] = 18198 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a] =18325 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)	Met Predefined Success Criterion*
All participants	8 2.214 (17411)	162 2.222 (17511)	95.0 (90.3, 97.6)[e]	Yes
16 to 55 years	5 1.234 (9897)	114 1.239 (9955)	95.6 (89.4, 98.6)[f]	NA
> 55 years and older	3 0.980 (7500)	48 0.983 (7543)	93.7 (80.6, 98.8)[f]	NA

*Success criterion: the posterior probability that true vaccine efficacy > 30% conditioning on the available data is >99.5% at the final analysis

[a] N = number of participants in the specified group.

[b] n1 = Number of participants meeting the endpoint definition.

[c] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

[d] n2 = Number of participants at risk for the endpoint.

[e] Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time.

[f] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

For participants with and without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 94.6%, with 9 and 169 cases in the BNT162b2 and placebo groups respectively (Table 7). The posterior probability was >99.99% for the true VE being greater than 30%. The 95% credible interval for the vaccine efficacy was 89.9% to 97.3%, indicating that the true VE is at least 89.9% with a 97.5% probability given the available data.

Table 7. Efficacy of BNT162b2 Against Confirmed COVID-19 From 7 Days After Dose 2 in Participants With And Without Evidence of Prior SARS-CoV-2 Infection, Evaluable Efficacy Population

Pre-specified Age Group	BNT162b2 N[a] = 19965 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a] =20172 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)	Met Predefined Success Criterion*
All participants	9 2.332 (18559)	169 2.345 (18708)	94.6 (89.9, 97.3)[e]	Yes
16 to 55 years	6 1.309 (10653)	120 1.317 (10738)	95.0 (88.7, 98.2)[f]	NA
>55 years and older	3 1.022 (7892)	49 1.028 (7956)	93.8 (80.9, 98.8)[f]	NA

*Success criterion: the posterior probability that true vaccine efficacy >30% conditioning on the available data is >99.5% at the final analysis
[a] N = number of participants in the specified group.
[b] n1 = Number of participants meeting the endpoint definition.
[c] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
[d] n2 = Number of participants at risk for the endpoint.
[e] Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time.
[f] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Subgroup Analyses of Vaccine Efficacy

Subgroup analyses of the second primary efficacy endpoint provide additional information about the VE for participants with and without evidence of infection prior to vaccination in specific populations enrolled, which is the endpoint considered to represent the general population who may receive the vaccine, as baseline evidence of prior infection may not be known by all people who might receive the vaccine. The results are displayed below in Table 8. The VE point estimates for the subgroup analyses were comparable to results for the first primary efficacy endpoint.

VE point estimates were uniformly high across the subgroups examined with the exception of participants identifying as multiracial and participants with evidence of prior SARS-CoV-2 infection at enrollment, for which too few COVID-19 cases occurred to interpret efficacy data for these subgroups. Additionally, the numbers of participants and cases in some other specific subgroups, such as the adolescent age group and racial subgroups, limits the interpretability of the VE results because of the wide credible intervals, but are displayed for completeness.

Table 8: Subgroup Analyses of Second Primary Endpoint: First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup, Participants With and Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy (7 Days) Population

Efficacy Endpoint Subgroup	BNT162b2 N[a]=19965 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20172 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Overall	9 2.332 (18559)	169 2.345 (18708)	94.6 (89.6, 97.6)
Age group (years)			
16 to 17	0 0.003 (58)	1 0.003 (61)	100.0 (-3969.9, 100.0)
18 to 64	8 1.799 (14443)	149 1.811 (14566)	94.6 (89.1, 97.7)
65 to 74	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)
≥75	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)
At risk[f]			
Yes	4 1.083 (8584)	87 1.084 (8609)	95.4 (87.8, 98.8)
No	5 1.250 (9975)	82 1.261 (10099)	93.8 (85.0, 98.1)
Age group (years) and at risk			
16-64 and not at risk	5 1.012 (8172)	75 1.019 (8239)	93.3 (83.6, 97.9)
16-64 and at risk	3 0.790 (6329)	75 0.794 (6388)	96.0 (87.8, 99.2)
≥65 and not at risk	0 0.238 (1794)	7 0.241 (1849)	100.0 (29.5, 100.0)
≥65 and at risk	1 0.293 (2250)	12 0.290 (2218)	91.7 (44.2, 99.8)
Obese[g]			
Yes	3 0.810 (6445)	68 0.832 (6582)	95.5 (86.2, 99.1)
No	6 1.522 (12108)	101 1.513 (12120)	94.1 (86.7, 97.9)
Age group (years) and obese			
16-64 and not obese	5 1.163 (9380)	89 1.162 (9422)	94.4 (86.4, 98.2)
16-64 and obese	3 0.637 (5116)	61 0.651 (5199)	95.0 (84.6, 99.0)
≥65 and not obese	1 0.358 (2715)	12 0.351 (2685)	91.8 (44.7, 99.8)
≥65 and obese	0 0.172 (1328)	7 0.180 (1382)	100.0 (27.4, 100.0)
Sex			
Female	5 1.149 (9102)	84 1.176 (9366)	93.9 (85.2, 98.1)
Male	4 1.183 (9457)	85 1.170 (9342)	95.3 (87.6, 98.8)
Ethnicity			
Hispanic or Latino	3 0.637 (5074)	55 0.638 (5090)	94.5 (83.2, 98.9)

Efficacy Endpoint Subgroup	BNT162b2 N[a]=19965 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=20172 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)[e]
Not Hispanic or Latino	6 1.681 (13380)	114 1.693 (13509)	94.7 (88.1, 98.1)
Race			
American Indian or Alaska native	0 0.011 (104)	1 0.010 (104)	100.0 (-3511.0, 100.0)
Asian	1 0.095 (796)	4 0.097 (808)	74.4 (-158.7, 99.5)
Black or African American	0 0.187 (1758)	7 0.188 (1758)	100.0 (30.4, 100.0)
Native Hawaiian or other Pacific Islander	0 0.006 (50)	1 0.003 (29)	100.0 (-2112.1, 100.0)
White	7 1.975 (15294)	153 1.990 (15473)	95.4 (90.3, 98.2)
Multiracial	1 0.047 (467)	1 0.042 (424)	10.4 (-6934.9, 98.9)
Not reported	0 0.010 (90)	2 0.013 (112)	100.0 (-581.6, 100.0)
Baseline SARS-CoV-2 Status			
Positive[h]	1 0.056 (526)	1 0.060 (567)	-7.1 (-8309.9, 98.6)
Negative[i]	8 2.237 (17637)	164 2.242 (17720)	95.1 (90.1, 97.9)
Unknown	0 0.039 (396)	4 0.043 (421)	100.0 (-68.9, 100.0)

[a.] N = number of participants in the specified group.
[b.] n1 = Number of participants meeting the endpoint definition.
[c.] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
[d.] n2 = Number of participants at risk for the endpoint.
[e.] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.
[f.] At risk is defined as having at least one of the Charlson comorbidity index (Appendix B, page 52) category or obesity (BMI ≥30 kg/m^2).
[g.] Obese is defined as BMI ≥30 kg/m^2.
[h.] Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
[i.] Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

The demographics of the participants with confirmed COVID-19 cases contributing to the primary efficacy analysis are displayed below in Table 9.

Table 9. Demographic Characteristics, Participants With Protocol Defined Case (Without Evidence of Infection Prior to 7 Days After Dose 2)

Characteristic	BNT162b2 (N[a]=8) N[b] (%)	Placebo (N[a]=162) N[b] (%)	Total (N[a]=170) N[b] (%)
Sex: Female	5 (62.5)	81 (50.0)	86 (50.6)
Sex: Male	3 (37.5)	81 (50.0)	84 (49.4)
Age at Vaccination: Mean years (SD)	51.4 (12.47)	47.4 (15.21)	47.6 (15.09)
Age at Vaccination: Median (years)	51	48	48
Age at Vaccination: Min, max (years)	(30, 69)	(18, 79)	(18, 79)
Age Group: 16 to < 18 years	0	0	0
Age Group: 18 to < 65 years	7 (87.5)	143 (88.3)	150 (88.2)
Age Group: ≥ 65 to < 75 years	1 (12.5)	14 (8.6)	15 (8.8)
Age Group: ≥ 75 years	0	5 (3.1)	5 (2.9)
Race: American Indian or Alaska Native	0	1 (0.6)	1 (0.6)
Race: Asian	1 (12.5)	4 (2.5)	5 (2.9)
Race: Black or African American	0	7 (4.3)	7 (4.1)
Race: Native Hawaiian or Other Pacific Islander	0	1 (0.6)	1 (0.6)
Race: White	7 (87.5)	146 (90.1)	153 (90.0)
Race: Multiracial	0	1 (0.6)	1 (0.6)
Race: Not reported	0	2 (1.2)	2 (1.2)
Ethnicity: Hispanic or Latino	3 (37.5)	53 (32.7)	56 (32.9)
Ethnicity: Not Hispanic or Latino	5 (62.5)	109 (67.3)	114 (67.1)
Ethnicity: Not reported	0	0	0
Comorbidities[c]: Yes	4 (50.0)	86 (53.1)	90 (52.9)
Comorbidities: No	4 (50.0)	76 (46.9)	80 (47.1)
Comorbidity: Obesity	3 (37.5)	67 (41.4)	70 (41.2)

[a] N = number of participants in the specified group, or the total sample. This value is the denominator for the percentage calculations.
[b] n = Number of participants with the specified characteristic.
[c] Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as patients who had at least one of the Charlson comorbidity index (Appendix B, page 52) category or obesity only (BMI ≥30 kg/m^2).

Only 3% of participants had evidence of prior infection at study enrollment, and additional analyses showed that very few COVID-19 cases occurred in these participants over the course of the entire study (9 in the placebo group and 10 in the BNT162b2 group, only 1 of which occurred 7 days or more after completion of the vaccination regimen – data not shown). The placebo group attack rate from enrollment to the November 14, 2020, data cut-off date was 1.3% both for participants without evidence of prior infection at enrollment (259 cases in 19,818 participants) and for participants with evidence of prior infection at enrollment (9 cases in 670 participants). While limited, these data do suggest that previously infected individuals can be at risk of COVID-19 (i.e., reinfection) and could benefit from vaccination.

Additional analyses of the first primary efficacy endpoint were conducted to evaluate the vaccine efficacy, by comorbidity status. VE point estimates were uniformly high across the comorbidities examined, though for some interpretation of the results is limited by small numbers of participants and/or cases.

Table 10. Vaccine Efficacy: First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status, Among Participants Without Evidence of Infection Prior to 7 Days After Dose 2, Evaluable Efficacy (7 Days) Population

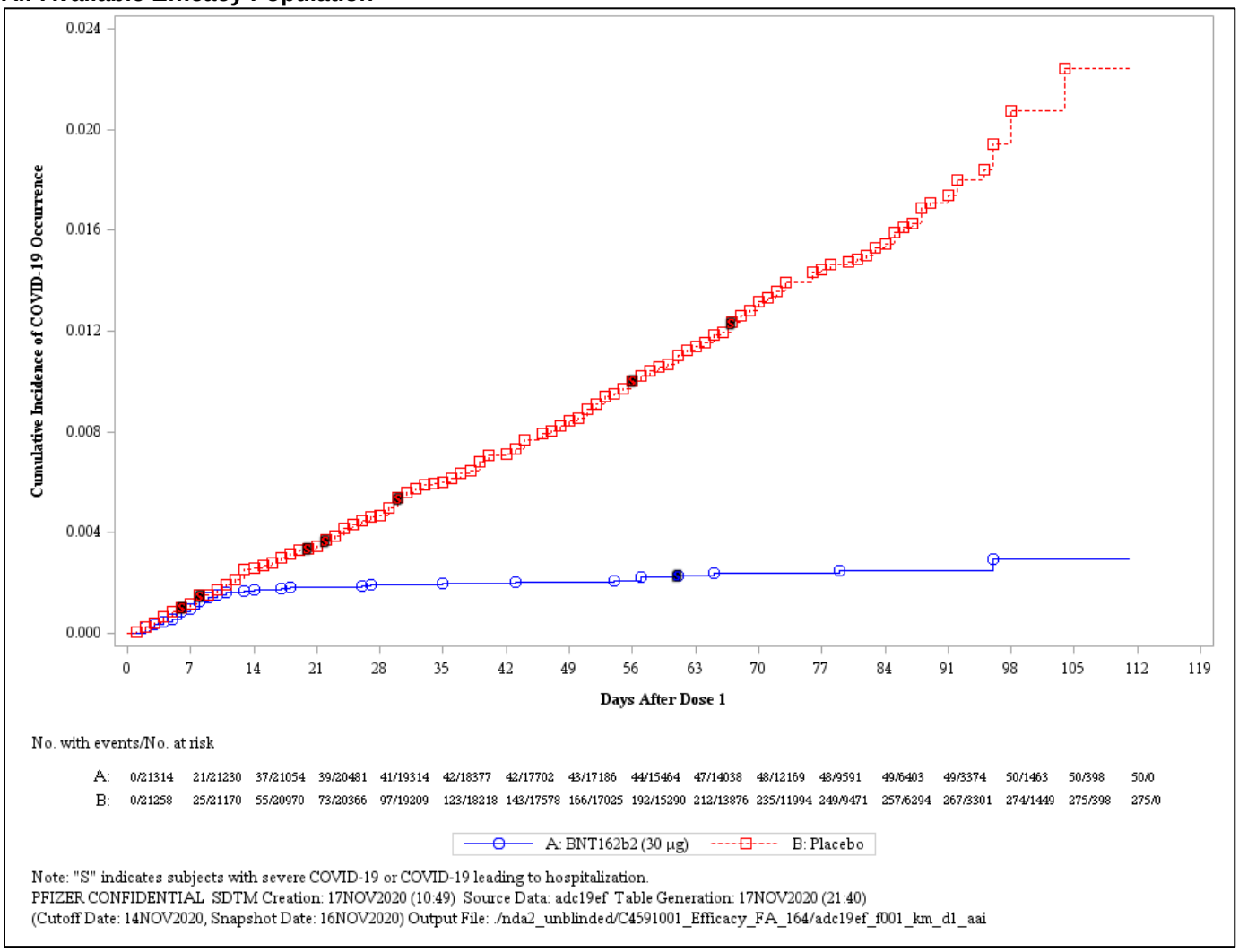
Efficacy Endpoint Subgroup	BNT162b2 (30 µg) N[a]=18198 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=18325 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI[e])
Overall	8 2.214 (17411)	162 2.222 (17511)	95.0 (90.0, 97.9)
Comorbidity			
No comorbidity	4 1.189 (9381)	76 1.197 (9482)	94.7 (85.9, 98.6)
Any comorbidity[f]	4 1.025 (8030)	86 1.025 (8029)	95.3 (87.7, 98.8)
Any malignancy	1 0.092 (704)	4 0.090 (681)	75.7 (-145.8, 99.5)
Cardiovascular	0 0.067 (534)	5 0.062 (492)	100.0 (-0.8, 100.0)
Chronic pulmonary disease	1 0.175 (1374)	14 0.171 (1358)	93.0 (54.1, 99.8)
Diabetes	1 0.176 (1372)	19 0.176 (1374)	94.7 (66.8, 99.9)
Obese (BMI≥30.0 kg/m^2)	3 0.763 (6000)	67 0.782 (6103)	95.4 (86.0, 99.1)
Hypertension	2 0.567 (4413)	44 0.567 (4437)	95.4 (82.6, 99.5)
Diabetes (including gestational diabetes)	1 0.177 (1381)	20 0.178 (1384)	95.0 (68.7, 99.9)

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein–binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Participants who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.
[a] N = number of participants in the specified group.
[b] n1 = Number of participants meeting the endpoint definition.
[c] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
[d] n2 = Number of participants at risk for the endpoint.
[e] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
[f] Subject who had 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as participants who had at least one of the Charlson comorbidity index (Appendix B, page 52) category or BMI ≥30 kg/m2.

Cumulative Incidence Curves

Based on the cumulative incidence curve for the all-available efficacy population after Dose 1, (Figure 2), COVID-19 disease onset appears to occur similarly for both BNT162b2 and placebo groups until approximately 14 days after Dose 1, at which time point, the curves diverge, with more cases accumulating in the placebo group than in the BNT162b2 group, and there does not appear to be evidence of waning protection during the follow-up time of approximately 2 months following the second dose that is being evaluated at this point in time.

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1 All-Available Efficacy Population



Secondary Efficacy Analyses

The secondary efficacy endpoints evaluate the VE of BNT162b2 for the prevention of COVID-19 disease from 14 days after Dose 2 and based on the CDC's definition of COVID-19 disease from 7 and 14 days after Dose 2. The case splits and VE for each of these secondary efficacy endpoints were each similar to the primary efficacy endpoints described above.

Severe COVID-19 Cases

In the final analysis of the evaluable efficacy population (7 days), four participants had severe COVID-19 disease at least 7 days after Dose 2 (one subject who received BNT162b2 and three participants who received placebo). The vaccine recipient who had severe COVID-19 disease met the severe case definition because oxygen saturation at the COVID-19 illness visit was 93% on room air. The subject was not hospitalized, did not seek further medical care, and did not have risk factors for severe disease. The three placebo recipients who had severe COVID-19 disease met the severe case definition for the following reasons: one subject had an oxygen saturation of 92% on room air without other severe disease criteria, one subject was

hospitalized for noninvasive positive pressure ventilation with bilateral pneumonia, and one subject had an oxygen saturation of 92% and ICU admission for heart block. One of these placebo recipients with severe disease also had a body mass index > 30 kg/m^2 as a risk factor, while the other two participants did not have any risk factors for severe disease. The vaccine efficacy of this secondary efficacy endpoint is shown in Table 11.

Table 11. First Severe COVID-19 Occurrence from 7 Days after Dose 2 - Evaluable Efficacy Population

Secondary Efficacy Endpoint	BNT162b2 N[a]=18198 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=18325 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)	Met Predefined Success Criterion*
First severe COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection	1 2.215 (17411)	3 2.232 (17511)	66.4 (-124.8, 96.3)[e]	No

*Success criterion: the posterior probability that true vaccine efficacy > 30% conditioning on the available data is >98.6% at the final analysis.
[a.] N = number of participants in the specified group.
[b.] n1 = Number of participants meeting the endpoint definition.
[c.] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 or 14 days after Dose 2 to the end of the surveillance period depending on specified endpoint.
[d]. n2 = Number of participants at risk for the endpoint.
[e] Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time.
[f] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

In the all-available efficacy population, ten participants had severe COVID-19 disease after Dose 1 (one subject who received BNT162b2 and nine participants who received placebo). Five of the remaining six placebo recipients who had severe COVID-19 disease were hospitalized, two of whom were admitted to an intensive care unit. Five of these remaining six placebo recipients who had severe disease had at least one risk factor for severe disease. The total number of severe cases is small, which limits the overall conclusions that can be drawn; however, the case split does suggest protection from severe COVID-19 disease.

Table 12. First Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

Secondary Efficacy Endpoint	BNT162b2 N[a]=21669 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21686 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)
First severe case occurrence after Dose 1	1 4.021 (21314)	9 4.006 (21259)	88.9 (20.1, 99.7)[f]
After Dose 1 to before Dose 2	0	4	100.0 (-51.5, 100.0)
Dose 2 to 7 days after Dose 2	0	1	100.0 (-3800.0, 100.0)
≥7 Days after Dose 2	1	4	75.0 (-152.6, 99.5)

[a] N = number of participants in the specified group.
[b] n1 = Number of participants meeting the endpoint definition.
[c] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 or 14 days after Dose 2 to the end of the surveillance period depending on specified endpoint.
[d] n2 = Number of participants at risk for the endpoint.
[e] Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time.
[f] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

Additional Efficacy Analyses

Additional analyses of the first primary efficacy endpoint were conducted to evaluate the all-available efficacy population, for all participants regardless of evidence of prior infection through 7 days after Dose 2 (Table 13).

Table 13. Primary Efficacy Endpoint –All-Available Efficacy Population

Efficacy Endpoint	BNT162b2 N[a]=21669 Cases n1[b] Surveillance Time[c] (n2[d])	Placebo N[a]=21686 Cases n1[b] Surveillance Time[c] (n2[d])	Vaccine Efficacy % (95% CI)
First COVID-19 occurrence after Dose 1 – Dose 1	50 4.015 (21314)	275 3.982 (21258)	82.0 (75.6, 86.9)[f]
After Dose 1 to before Dose 2	39	82	52.4 (29.5, 68.4)
Dose 2 to 7 days after Dose 2	2	21	90.5 (61, 98.9)
≥7 Days after Dose 2	9	172	94.8 (89.8, 97.6)

[a] N = number of participants in the specified group.
[b] n1 = Number of participants meeting the endpoint definition.
[c] Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 or 14 days after Dose 2 to the end of the surveillance period depending on specified endpoint.
[d] n2 = Number of participants at risk for the endpoint.
[e] Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time.
[f] Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.

VE in participants in the all-available efficacy population was similar to results in the evaluable efficacy population. The VE for the prevention of COVID-19 disease after Dose 1 is 82%, in the all-available efficacy population. Based on the number of cases accumulated after Dose 1 and before Dose 2, there does seem to be some protection against COVID-19 disease following one dose; however, these data do not provide information about longer term protection beyond 21 days after a single dose.

Efficacy Summary

The data submitted in this EUA request were consistent with the recommendations set forth in the FDA Guidance on Emergency Use Authorization for Vaccines to Prevent COVID-19 and met the prespecified success criteria established in the protocol. In the planned interim and final analyses, vaccine efficacy after 7 days post Dose 2 was 95%, (95% CI 90.3; 97.6) in participants without prior evidence of SARS-CoV-2 infection and >94% in the group of participants with or without prior infection. Efficacy outcomes were consistently robust (⩾93%) across demographic subgroups.

Efficacy against severe COVID-19 occurring after the first dose was 88.9% (95% CI 20.1, 99.7), with an estimated VE of 75.0% (95% CI -152.6, 99.5) (1 case in BNT162b2 group and 4 cases in placebo group) against severe COVID-19 occurring at least 7 days after Dose 2.

Among all participants (regardless of evidence of infection before or during the vaccination regimen), 50 cases of COVID-19 occurred after Dose 1 in the BNT162b2 group compared with 275 cases in the placebo group, indicating an estimated VE of 82% (95% CI: 75.6%, 86.9%) against confirmed COVID-19 occurring after Dose 1, with VE of 52.4% (95% CI: 29.5%, 68.4%) between Dose 1 and Dose 2. The efficacy observed after Dose 1 and before Dose 2, from a post-hoc analysis, cannot support a conclusion on the efficacy of a single dose of the vaccine, because the time of observation is limited by the fact that most of the participants received a

second dose after three weeks. The trial did not have a single-dose arm to make an adequate comparison.

5.2.6. Safety

Overview of Adverse Events

Table 14 below presents an overview of all adverse events in the phase 2/3 safety population. A higher proportion of vaccine recipients reported adverse events compared with placebo recipients, and this imbalance was driven by reactogenicity (solicited adverse events) reported in the 7 days following vaccination and unsolicited adverse events corresponding to reactogenicity symptoms among participants not in the reactogenicity subset (see presentation of unsolicited adverse events in a later section). Proportions of participants with serious adverse events, deaths, and withdrawals due to adverse events were balanced between treatment groups.

Table 14. Study C4591001 Safety Overview- Ages 16 years and older

Participants Experiencing at Least One:	BNT162b2 n/N (%)	Placebo n/N (%)
Immediate unsolicited AE Within 30 minutes after vaccination[a]		
Dose #1	78/18801 (0.4)	66/18785 (0.4)
Dose #2	52/18494 (0.3)	39/18470 (0.2)
Solicited injection site reaction within 7 days[b]		
Dose #1	3216/4093 (78.6)	525/4090 (12.8)
Dose #2	2748/3758 (73.1)	396/3749 (10.6)
Solicited systemic AE within 7 days[b]		
Dose #1	2421/4093 (59.1)	1922/4090 (47.0)
Dose #2	2627/3758 (69.9)	1267/3749 (33.8)
From Dose 1 through 1 month after Dose 2[a]		
Unsolicited non-serious AE	5071/18801 (27.0)	2356/18785 (12.5)
SAE	103/18801 (0.5)	81/18785 (0.4)
From Dose 1 through cutoff date (safety population)		
SAE	124/18801 (0.7)	101/18785 (0.5)
From Dose 1 through cutoff date (all-enrolled)[c]		
Withdrawal due AEs	37/21621 (0.6)	30/21631 (0.5)
SAE	126/21621 (0.6)	111/21631 (0.5)
Deaths	2/21621 (0.0)	4/21631 (0.0)

Source: c4591001-safety-tables-ae3.pdf pages 216,446,459,463; c4591001-safety-tables-cos-reacto.pdf, pages 113-114.
n= number of participants with the specified reaction or AE.
[a] N: number of participants in the phase 2/3 safety population.
[b] N: number of participants in the reactogenicity subset of the phase 2/3 safety population.
[b] N: number of participants in the all-enrolled population.
Data analysis cutoff date: November 14, 2020.

Solicited Local Reactions and Systemic Adverse Events

As of the cutoff date, solicited reactogenicity data in participants 16 and 17 years of age were not collected by e-diary and are not available. Symptoms consistent with solicited reactogenicity that were reported by these participants were collected and analyzed as unsolicited adverse events and are discussed with review of those data.

Solicited Local Reactions

For each age group in the reactogenicity subset (younger: 18 to 55 years, older: >55 years) and overall (18 years and older), the median onset of local reactions in the vaccine group was 0 (day of vaccination) to 2 days after either dose and lasted a median duration between 1 and 2 days.

For both age groups, injection site pain was the most frequent solicited local adverse reaction. After dose 2, the younger age group reported any pain more frequently than the older age group (77.8% vs 66.1%) and pain characterized as moderate (27.1% vs. 18.0%); a similar pattern was observed after Dose 1. Injection site redness and swelling after each dose were generally similar for both age groups.

Subgroup analyses by age

Table 15. Frequency of Solicited Local Reactions Within 7 Days After Each Vaccination, Reactogenicity Subset of the Phase 2/3 Safety Population*, 18 to 55 Years of Age

Local Reaction	BNT162b2 Dose 1 N=2238 n (%)	Placebo Dose 1 N=2248 n (%)	BNT162b2 Dose 2 N=2045 n (%)	Placebo Dose 2 N=2053 n (%)
Pain[a]				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Mild	1170 (51.1)	308 (13.4)	1039 (49.5)	225 (10.7)
Moderate	710 (31.0)	12 (0.5)	568 (27.1)	20 (1.0)
Severe	24 (1.0)	2 (0.1)	25 (1.2)	0 (0.0)
Redness[b]				
Any	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Mild	70 (3.1)	16 (0.7)	73 (3.5)	8 (0.4)
Moderate	28 (1.2)	6 (0.3)	40 (1.9)	6 (0.3)
Severe	6 (0.3)	4 (0.2)	10 (0.5)	0 (0.0)
Swelling[b]				
Any	132 (5.8)	11 (0.5)	132 (6.3)	5 (0.2)
Mild	88 (3.8)	3 (0.1)	80 (3.8)	3 (0.1)
Moderate	39 (1.7)	5 (0.2)	45 (2.1)	2 (0.1)
Severe	5 (0.2)	3 (0.1)	7 (0.3)	0 (0.0)

Source: adapted from EUA 27034, amendment 3, Table 17.
n = number of participants with the specified reaction.
N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.
[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Table 16. Frequency of Solicited Local Reactions Within 7 Days After Each Vaccination, Reactogenicity Subset of the Phase 2/3 Safety Population*, >55 Years of Age and Older

Local Reaction	BNT162b2 Dose 1 N=1802 n (%)	Placebo Dose 1 N=1792 n (%)	BNT162b2 Dose 2 N=1660 n (%)	Placebo Dose 2 N=1646 n (%)
Pain[a]				
Any	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Mild	1008 (55.9)	160 (8.9)	792 (47.7)	125 (7.6)
Moderate	270 (15.0)	6 (0.3)	298 (18.0)	2 (0.1)
Severe	4 (0.2)	0 (0.0)	8 (0.5)	0 (0.0)
Redness[b]				
Any	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Mild	55 (3.1)	12 (0.7)	59 (3.6)	8 (0.5)
Moderate	27 (1.5)	5 (0.3)	53 (3.2)	3 (0.2)
Severe	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Swelling[b]				
Any	118 (6.5)	21 (1.2)	124 (7.5)	11 (0.7)
Mild	71 (3.9)	10 (0.6)	68 (4.1)	5 (0.3)
Moderate	45 (2.5)	11 (0.6)	53 (3.2)	5 (0.3)
Severe	2 (0.1)	0 (0.0)	3 (0.2)	1 (0.1)

Source: EUA 27036, amendment 3, Table 21.
n = number of participants with the specified reaction.
N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.
[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Solicited Systemic AEs

For each age group in the reactogenicity subset (younger: 18 to 55 years, older: >55 years) and overall (18 years and older), the median onset of systemic AEs in the vaccine group in general was 1 to 2 days after either dose and lasted a median duration of 1 day.

The frequency and severity of systemic AEs were higher in the younger than the older age groups. Within each age group, the frequency and severity of systemic AEs was higher after Dose 2 than Dose 1, except for vomiting and diarrhea, which was generally similar regardless of dose. For both age groups, fatigue, headache and new/worsened muscle pain were most common.

Subgroup analyses by age

Table 17. Frequency of Solicited Systemic Adverse Events Within 7 Days After Each Vaccination-Reactogenicity Subset of the Phase 2/3 Safety Population*, 18 to 55 Years of Age

Adverse Event	BNT162b2 Dose 1 N=2238 n (%)	Placebo Dose 1 N=2248 n (%)	BNT162b2 Dose 2 N=2045 n (%)	Placebo Dose 2 N=2053 n (%)
Fever				
≥38.0℃	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
>38.0℃ to 38.4℃	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4℃ to 38.9℃	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9℃ to 40.0℃	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0℃	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)

Adverse Event	BNT162b2 Dose 1 N=2238 n (%)	Placebo Dose 1 N=2248 n (%)	BNT162b2 Dose 2 N=2045 n (%)	Placebo Dose 2 N=2053 n (%)
Fatigue[a]				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	46 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache[a]				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills[a]				
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)
Vomiting[b]				
Any	28 (1.2)	28 (1.2)	40 (1.9)	25 (1.2)
Mild	24 (1.0)	22 (1.0)	28 (1.3)	16 (0.8)
Moderate	4 (0.2)	5 (0.2)	8 (0.4)	9 (0.4)
Severe	0 (0.0)	1 (0.0)	4 (0.2)	0 (0.0)
Diarrhea[c]				
Any	255 (11.1)	270 (11.7)	219 (10.4)	177 (8.4)
Mild	206 (9.0)	217 (9.4)	179 (8.5)	144 (6.8)
Moderate	46 (2.0)	52 (2.3)	36 (1.7)	32 (1.5)
Severe	3 (0.1)	1 (0.0)	4 (0.2)	1 (0.0)
New or worsened muscle pain[a]				
Any	487 (21.3)	249 (10.8)	783 (37.3)	173 (8.2)
Mild	256 (11.2)	175 (7.6)	326 (15.5)	111 (5.3)
Moderate	218 (9.5)	72 (3.1)	410 (19.5)	59 (2.8)
Severe	13 (0.6)	2 (0.1)	47 (2.2)	3 (0.1)
New or worsened joint pain[a]				
Any	251 (11.0)	138 (6.0)	459 (21.9)	109 (5.2)
Mild	147 (6.4)	95 (4.1)	205 (9.8)	54 (2.6)
Moderate	99 (4.3)	43 (1.9)	234 (11.2)	51 (2.4)
Severe	5 (0.2)	0 (0.0)	20 (1.0)	4 (0.2)
Use of antipyretic or pain medication	638 (27.8)	332 (14.4)	945 (45.0)	266 (12.6)

Source: adapted from EUA 27036, amendment 3, Table 19.
n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Table 18. Frequency of Solicited Systemic Adverse Events Within 7 Days After Each Vaccination-Reactogenicity Subset of the Phase 2/3 Safety Population*, >55 Years of Age and Older

Adverse Event	BNT162b2 Dose 1 N=1802 n (%)	Placebo Dose 1 N=1792 n (%)	BNT162b2 Dose 2 N=1660 n (%)	Placebo Dose 2 N=1646 n (%)
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
>38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue[a]				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)
Headache[a]				
Any	454 (25.2)	325 (18.1)	647 (39.0)	229 (13.9)
Mild	348 (19.3)	242 (13.5)	422 (25.4)	165 (10.0)
Moderate	104 (5.8)	80 (4.5)	216 (13.0)	60 (3.6)
Severe	2 (0.1)	3 (0.2)	9 (0.5)	4 (0.2)
Chills[a]				
Any	113 (6.3)	57 (3.2)	377 (22.7)	46 (2.8)
Mild	87 (4.8)	40 (2.2)	199 (12.0)	35 (2.1)
Moderate	26 (1.4)	16 (0.9)	161 (9.7)	11 (0.7)
Severe	0 (0.0)	1 (0.1)	17 (1.0)	0 (0.0)
Vomiting[b]				
Any	9 (0.5)	9 (0.5)	11 (0.7)	5 (0.3)
Mild	8 (0.4)	9 (0.5)	9 (0.5)	5 (0.3)
Moderate	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Diarrhea[c]				
Any	147 (8.2)	118 (6.6)	137 (8.3)	99 (6.0)
Mild	118 (6.5)	100 (5.6)	114 (6.9)	73 (4.4)
Moderate	26 (1.4)	17 (0.9)	21 (1.3)	22 (1.3)
Severe	3 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain[a]				
Any	251 (13.9)	149 (8.3)	477 (28.7)	87 (5.3)
Mild	168 (9.3)	100 (5.6)	202 (12.2)	57 (3.5)
Moderate	82 (4.6)	46 (2.6)	259 (15.6)	29 (1.8)
Severe	1 (0.1)	3 (0.2)	16 (1.0)	1 (0.1)
New or worsened joint pain[a]				
Any	155 (8.6)	109 (6.1)	313 (18.9)	61 (3.7)
Mild	101 (5.6)	68 (3.8)	161 (9.7)	35 (2.1)
Moderate	52 (2.9)	40 (2.2)	145 (8.7)	25 (1.5)
Severe	2 (0.1)	1 (0.1)	7 (0.4)	1 (0.1)

Adverse Event	BNT162b2 Dose 1 N=1802 n (%)	Placebo Dose 1 N=1792 n (%)	BNT162b2 Dose 2 N=1660 n (%)	Placebo Dose 2 N=1646 n (%)
Use of antipyretic or pain medication	358 (19.9)	213 (11.9)	625 (37.7)	161 (9.8)

Source: EUA 27036, amendment 3, Table 23.
n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
* Participants in the reactogenicity subset of the safety population ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Unsolicited (non-serious) AEs

A higher frequency of unsolicited, non-serious adverse events was reported in the vaccine group compared to placebo group and was primarily attributed to local reactions and systemic adverse events in subjects not in the reactogenicity subset and are consistent with solicited reactions/events reported by reactogenicity subset participants during the first 7 days following vaccination. Table 19 below presents unsolicited adverse events reported by at least 1% of participants in any treatment group for the phase 2/3 safety population.

Reports of lymphadenopathy were imbalanced with notably more cases in the vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. Bell's palsy was reported by four vaccine participants and none in the placebo group. These cases occurred at 3, 9, 37, and 48 days after vaccination. One case (onset at 3 days postvaccination) was reported as resolved with sequelae within three days after onset, and the other three were reported as continuing or resolving as of the November 14, 2020 data cut-off with ongoing durations of 10, 15, and 21 days, respectively. The observed frequency of reported Bell's palsy in the vaccine group is consistent with the expected background rate in the general population, and there is no clear basis upon which to conclude a causal relationship at this time, but FDA will recommend surveillance for cases of Bell's palsy with deployment of the vaccine into larger populations. There were no other notable patterns or numerical imbalances between treatment groups for specific categories (system organ class or preferred term) of non-serious adverse events, including other neurologic, neuro-inflammatory, and thrombotic events, that would suggest a causal relationship to BNT162b2 vaccine.

Table 19. Frequency of Unsolicited AEs with Occurrence in ≥1% of Participants in any Treatment Group from Dose 1 to 1-month After Dose 2, Phase 2/3 Safety Population*, 16 Years of Age and Older

System Organ Class Preferred Term	BNT162b2 N=18801 n (%)	Placebo N=18785 n (%)	Total N=37586 n (%)
General disorders and administration site conditions	3521 (18.7)	737 (3.9)	4258 (11.3)
Injection site pain	2125 (11.3)	286 (1.5)	2411 (6.4)
Fatigue	1029 (5.5)	260 (1.4)	1289 (3.4)
Pyrexia	1146 (6.1)	61 (0.3)	1207 (3.2)
Chills	999 (5.3)	87 (0.5)	1086 (2.9)
Pain	455 (2.4)	36 (0.2)	491 (1.3)
Musculoskeletal and connective tissue disorders	1387 (7.4)	401 (2.1)	1788 (4.8)
Myalgia	909 (4.8)	126 (0.7)	1035 (2.8)
Arthralgia	212 (1.1)	82 (0.4)	294 (0.8)
Nervous system disorders	1158 (6.2)	460 (2.4)	1618 (4.3)
Headache	973 (5.2)	304 (1.6)	1277 (3.4)
Gastrointestinal disorders	565 (3.0)	368 (2.0)	933 (2.5)
Diarrhoea	194 (1.0)	149 (0.8)	343 (0.9)
Nausea	216 (1.1)	63 (0.3)	279 (0.7)

Source: FDA analysis.
Adverse events in any PT = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
%: n/N. n = number of participants reporting at least 1 occurrence of the specified event.
of any event. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
* Participants ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Subgroup analyses by age

16 and 17 years of age: the table below represents an FDA-generated summary of unsolicited AEs consistent with reactogenicity and AEs that occurred at ≥1% and higher in the BNT162b2 Vaccine Group, classified by MedDRA System Organ Class and Preferred Term.

Table 20. Frequency of Unsolicited AEs with Occurrence in ≥1% of Participants in any Treatment Group from Dose 1 to 1 Month After Dose 2, Phase 2/3 Safety Population*, 16 and 17 Years of Age

System Organ Class Preferred Term	BNT162b2 N=53 n (%)	Placebo N=50 n (%)	Total N=103 n (%)
General disorders and administration site conditions	7 (13.2)	3 (6.0)	10 (9.7)
Injection site pain	5 (9.4)	2 (4.0)	7 (6.8)
Pyrexia	5 (9.4)	0	5 (4.9)
Pain	2 (3.8)	0	2 (1.9)
Chills	1 (1.9)	0	1 (1.0)
Injury, poisoning and procedural complications	1 (1.9)	0	1 (1.0)
Concussion	1 (1.9)	0	1 (1.0)
Facial bones fracture	1 (1.9)	0	1 (1.0)
Road traffic accident	1 (1.9)	0	1 (1.0)
Investigations	1 (1.9)	0	1 (1.0)
Body temperature increased	1 (1.9)	0	1 (1.0)

Source: FDA analysis.
Adverse events in any PT = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
%: n/N. n = number of participants reporting at least 1 occurrence of the specified event.
of any event. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
* Participants ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

Table 21. Frequency of Unsolicited AEs with Occurrence in ≥1% of Participants in any Treatment Group from Dose 1 to 1 Month After Dose 2, Phase 2/3 Safety Population*, 65 Years and Older

System Organ Class Preferred Term	BNT162b2 (N=4058) n (%)	Placebo (N=4043) n (%)	Total (N=8101) n (%)
General disorders and administration site conditions	577 (14.2)	118 (2.9)	695 (8.6)
Injection site pain	361 (8.9)	39 (1.0)	400 (4.9)
Fatigue	175 (4.3)	44 (1.1)	219 (2.7)
Chills	143 (3.5)	19 (0.5)	162 (2.0)
Pyrexia	148 (3.6)	10 (0.2)	158 (2.0)
Pain	60 (1.5)	7 (0.2)	67 (0.8)
Musculoskeletal and connective tissue disorders	231 (5.7)	83 (2.1)	314 (3.9)
Myalgia	125 (3.1)	23 (0.6)	148 (1.8)
Arthralgia	42 (1.0)	21 (0.5)	63 (0.8)
Pain in extremity	33 (0.8)	10 (0.2)	43 (0.5)
Nervous system disorders	179 (4.4)	87 (2.2)	266 (3.3)
Headache	127 (3.1)	45 (1.1)	172 (2.1)
Gastrointestinal disorders	127 (3.1)	72 (1.8)	199 (2.5)
Diarrhea	49 (1.2)	26 (0.6)	75 (0.9)
Nausea	40 (1.0)	13 (0.3)	53 (0.7)

Source: FDA analysis.
Adverse events in any PT = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
%: n/N. n = number of participants reporting at least 1 occurrence of the specified event.
of any event. N = number of participants in the specified group. This value is the denominator for the percentage calculations.
* Participants ≥16 years of age enrolled by October 9, 2020 and received at least 1 dose of vaccine or placebo.
Data analysis cutoff date: November 14, 2020.

FDA independently conducted standard MedDRA queries (SMQs) using FDA-developed software (MAED) to evaluate for constellations of unsolicited adverse event preferred terms that could represent various diseases and conditions, including but not limited to allergic, neurologic, inflammatory, and autoimmune conditions. The SMQs, conducted on the phase 2/3 all-enrolled safety population, revealed a slight numerical imbalance of adverse events potentially representing allergic reactions, with more participants reporting hypersensitivity-related adverse events in the vaccine group (137 [0.63%]) compared with the placebo group (111 [0.51%]). No imbalances between treatment groups were evident for any of the other SMQs evaluated.

Immediate AEs (phase 2/3 safety population)
The frequency of immediate AEs reported in the vaccine group was 0.4% after Dose 1 and <0.3% after Dose 2 and were mainly consistent with solicited reactogenicity events. In both study groups, the most frequently reported immediate AE was injection site pain (BNT162b2 vaccine 0.3%, placebo 0.2%).

Study Withdrawals due to an AE (all-enrolled population)
Of 43,448 enrolled participants, 37 (0.2%) vaccine recipients and 30 (0.1%) placebo recipients (0.1%), and no adolescents 16 to <18 years of age, withdrew from the study due to an AE. AEs in the SOC of General Disorders and Administration Site Conditions (7 vaccine, 3 placebo) was common, with injection site pain the most frequent (2 vaccine, 0 placebo).

Serious Adverse Events

Deaths

A total of six (2 vaccine, 4 placebo) of 43,448 enrolled participants (0.01%) died during the reporting period from April 29, 2020 (first participant, first visit) to November 14, 2020 (cutoff date). Both vaccine recipients were >55 years of age; one experienced a cardiac arrest 62 days after vaccination #2 and died 3 days later, and the other died from arteriosclerosis 3 days after vaccination #1. The placebo recipients died from myocardial infarction (n=1), hemorrhagic stroke (n=1) or unknown causes (n=2); three of the four deaths occurred in the older group (>55 years of age). All deaths represent events that occur in the general population of the age groups where they occurred, at a similar rate.

Non-fatal SAEs

In the all-enrolled population of (total N=43,448), the proportions of participants who reported at least 1 SAE during the time period from Dose 1 to the data cutoff date (November 14, 2020) were 0.6% in the BNT162b2 vaccine group and 0.5% in the placebo group. The most common SAEs in the vaccine group which were numerically higher than in the placebo group were appendicitis (0.04%), acute myocardial infarction (0.02%), and cerebrovascular accident (0.02%), and in the placebo arm numerically higher than in the vaccine arm were pneumonia (0.03%), atrial fibrillation (0.02%), and syncope (0.02%). Occurrence of SAEs involving system organ classes and specific preferred terms were otherwise balanced between treatment groups, including no imbalance overall in cardiovascular serious adverse events.

Appendicitis was reported as a SAE for 12 participants, and numerically higher in the vaccine group: 8 vaccine participants ([appendicitis [n=7], appendicitis perforated [n=1]) and 4 placebo participants (appendicitis [n=2], appendicitis perforated [n=1], complicated appendicitis [n=1]). All of the vaccine participants (n=8) and 2 placebo participants were younger than 65 years of age. The cases were considered unrelated to vaccination by the study investigators and occurred no more frequently than expected in the given age groups. FDA agrees that there is no clear basis upon which to suspect that this imbalance represents a vaccine-related risk.

Three SAEs reported in the BNT162 group were considered by the investigator as related to vaccine or vaccine administration: shoulder injury, ventricular arrhythmia, and lymphadenopathy. The investigator and the sponsor thought that the shoulder injury was related to vaccine administration. Two SAEs in the BNT162b2 group and none in the placebo group were considered by the investigator, but not the Sponsor, as related to study vaccination: shoulder injury (n=1), ventricular arrhythmia in a participant with known cardiac conditions (n=1), and lymphadenopathy temporally following vaccination (n=1). In FDA's opinion following review of the adverse event narratives, two of these events were considered as possibly related to vaccine: shoulder injury possibly related to vaccine administration or to the vaccine itself, and lymphadenopathy involving the axilla contralateral to the vaccine injection site. For lymphadenopathy, the event was temporally associated and biologically plausible.

Among participants 16 to 17 years of age, there was 1 participant in the vaccine group who experienced an SAE of facial bones fracture, which was not considered related to study intervention by the investigator.

Suspected COVID-19 Cases

As specified in the protocol, suspected cases of symptomatic COVID-19 that were not PCR-confirmed were not recorded as adverse events unless they met regulatory criteria for seriousness. Two serious cases of suspected but unconfirmed COVID-19 were reported, both in the vaccine group, and narratives were reviewed. In one case, a 36-year-old male with no medical comorbidities experienced fever, malaise, nausea, headache and myalgias beginning on the day of Dose 2 and was hospitalized 3 days later for further evaluation of apparent infiltrates on chest radiograph and treatment of dehydration. A nasopharyngeal PCR test for SARS-CoV-2 was negative on the day of admission, and a chest CT was reported as normal. The participant was discharged from the hospital 2 days after admission. With chest imaging findings that are difficult to reconcile, it is possible that this event represented reactogenicity following the second vaccination, a COVID-19 case with false negative test that occurred less than 7 days after completion of the vaccination series, or an unrelated infectious process. In the other case, a 66-year-old male with no medical comorbidities experienced fever, myalgias, and shortness of breath beginning 28 days post-Dose 2 and was hospitalized one day later with abnormal chest CT showing a small left-sided consolidation. He was discharged from the hospital 2 days later, and multiple nasopharyngeal PCR tests collected over a 10-day period beginning 2 days after symptom onset were negative. It is possible, though highly unlikely, that this event represents a COVID-19 case with multiple false negative tests that occurred more than 7 days after completion of the vaccination regimen, and more likely that it represents an unrelated infectious process.

Among 3410 total cases of suspected but unconfirmed COVID-19 in the overall study population, 1594 occurred in the vaccine group vs. 1816 in the placebo group. Suspected COVID-19 cases that occurred within 7 days after any vaccination were 409 in the vaccine group vs. 287 in the placebo group. It is possible that the imbalance in suspected COVID-19 cases occurring in the 7 days postvaccination represents vaccine reactogenicity with symptoms that overlap with those of COVID-19. Overall though, these data do not raise a concern that protocol-specified reporting of suspected, but unconfirmed COVID-19 cases could have masked clinically significant adverse events that would not have otherwise been detected.

Subgroup Analyses

There were no specific safety concerns identified in subgroup analyses by age, race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection, and occurrence of solicited, unsolicited, and serious adverse events in these subgroups were generally consistent with the overall study population.

Pregnancies

Female study participants of childbearing potential were screened for pregnancy prior to each vaccination, with a positive test resulting in exclusion or discontinuation from study vaccination. The study is collecting outcomes for all reported pregnancies that occur after vaccination, or before vaccination and not detected by pre-vaccination screening tests. Twenty-three pregnancies were reported through the data cut-off date of November 14, 2020 (12 vaccine, 11 placebo). Study vaccination occurred prior to the last menstrual period (LMP) in 5 participants (4 vaccine, 2 placebo), within 30 days after LMP in 8 participants (4 vaccine, 6 placebo), >30 days after LMP in 1 participant (0 vaccine, 2 placebo), and date of LMP not known in 5 participants (4 vaccine, 1 placebo). Unsolicited AEs related to pregnancy include spontaneous abortion and retained products of conception, both in the placebo group. Pregnancy outcomes are otherwise

unknown at this time.

Clinical Laboratory Evaluations

Clinical laboratory tests (hematology, chemistries) were assessed in study BNT162-01 and C4591001 phase 1. The only common laboratory abnormality reported throughout the studies was transient decreases in lymphocytes 1-3 days after Dose 1, which increased in frequency with increasing dose, were mostly Grade 1-2, generally normalized at the next laboratory assessment 6-8 days after Dose 1 and did not occur after Dose 2. Among C4591001 phase 1 participants who received the 30 µg dose of BNT162b2, transient decreases in lymphocytes post-Dose 1 occurred in 5 of 12 participants 18-55 years of age and in 4 of 12 participants 65-85 years of age. These transient hematological changes were not associated with clinical symptoms.

Safety Summary

The information provided by the Sponsor was adequate for review and to make conclusions about the safety of BNT162b2 in the context of the proposed indication and population for intended use under EUA. The number of participants in the phase 2/3 safety population (N=37586; 18801 vaccine,18785 placebo) meets the expectations in FDA's Guidance on Development and Licensure of Vaccines to Prevent COVID-19 for efficacy, and the median duration of at least 2 months follow-up after completion of the 2-dose primary vaccination series meets the agency's expectations in FDA's Guidance on its Emergency Use Authorization for Vaccines to Prevent COVID-19. The all-enrolled population contained more participants >16 years of age, regardless of duration of follow-up (43448; 21720 vaccine, 21728 placebo). The demographic and baseline characteristics of the all-enrolled population and the safety population were similar. Although the overall median duration of follow-up in the all-enrolled population was less than 2 months, because the protocol was amended to include subpopulations such as individuals with HIV and adolescents, the data from both populations altogether provide a comprehensive summary of safety.

Local site reactions and systemic solicited events after vaccination were frequent and mostly mild to moderate. The most common solicited adverse reactions were injection site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%); severe adverse reactions occurred in 0.0% to 4.6% of participants, were more frequent after Dose 2 than after Dose 1, and were generally less frequent in adults ≥55 years of age (≤2.8%) as compared to younger participants (≤4.6%). Among adverse events of special interest, which could be possibly related to vaccine, lymphadenopathy was reported in 64 participants (0.3%): 54 (0.5%) in the younger (16 to 55 years) age group; 10 (0.1%) in the older (>55 years) age group; and 6 in the placebo group. The average duration of these events was approximately 10 days, with 11 events ongoing at the time of the data cutoff. Bell's palsy was reported by four vaccine participants. From Dose 1 through 1 month after Dose 2, there were three reports of Bell's palsy in the vaccine group and none in the placebo group. This observed frequency of reported Bell's palsy is consistent with the expected background rate in the general population. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to BNT162b2 vaccine.

A total of six deaths occurred in the reporting period (2 deaths in the vaccine group, 4 in placebo). In the vaccine group, one participant with baseline obesity and pre-existing atherosclerosis died 3 days after Dose 1, and the other participant experienced cardiac arrest

60 days after Dose 2 and died 3 days later. Of the four deaths in the placebo arm, the cause was unknown for two of them, and the other two participants died from hemorrhagic stroke (n=1) and myocardial infarction (n=1), respectively; three deaths occurred in the older group (>55 years of age). All deaths represent events that occur in the general population of the age groups where they occurred, at a similar rate.

The frequency of non-fatal serious adverse events was low (<0.5%), without meaningful imbalances between study arms. The most common SAEs in the vaccine arm which were numerically higher than in the placebo arm were appendicitis (0.04%), acute myocardial infarction (0.02%), and cerebrovascular accident (0.02%), and in the placebo arm numerically higher than in the vaccine arm were pneumonia (0.03%), atrial fibrillation (0.02%), atrial fibrillation (0.02%) and syncope (0.02%). Appendicitis was the most common SAE in the vaccine arm. There were 12 participants with SAEs of appendicitis; 8 in the BNT162b2 group. Of the 8 total appendicitis cases in the BNT162b2 group, 6 occurred in the younger (16 to 55 years) age group and 2 occurred in the older (>55 years) age group (one of the cases in the older age group was perforated). One of the 6 participants with appendicitis in the younger age group also had a peritoneal abscess. Cases of appendicitis in the vaccine group were not more frequent than expected in the general population.

6. Sponsor's Plans for Continuing Blinded, Placebo-Controlled Follow-Up

The Sponsor plans to offer vaccination to participants ⩾16 years of age who originally received placebo and who become eligible for receipt of BNT162b2 according to local or national recommendations. The Sponsor proposes that these participants will be unblinded upon request and will have the opportunity to receive BNT162b2 as part of the study. The Sponsor also proposes that all placebo recipients ⩾16 years of age will be offered BNT162b2 after completing 6 months of follow-up after Dose 2, if they did not request and receive vaccine previously. The participants will provide consent to receive vaccination and to continue follow-up. For these participants, the Sponsor plans a total follow up period of 18 months, with one visit 1-month postvaccination and subsequent phone contacts at 1, 6, and 18 months postvaccination. Safety and efficacy monitoring during this period will include collection of AEs, SAEs, and screening and diagnosing COVID-19 cases.

7. Pharmacovigilance Activities

Pfizer submitted a Pharmacovigilance Plan (PVP) to monitor safety concerns that could be associated with Pfizer-BioNTech COVID-19 Vaccine. The Sponsor identified vaccine-associated enhanced disease including vaccine-associated enhanced respiratory disease as an important potential risk. Use in pregnancy and lactation and vaccine effectiveness are areas the Sponsor identified as missing information. In addition to the safety concerns specified by the Sponsor, FDA requested that the Sponsor update their PVP to include missing information in pediatric participants less than 16 years of age.

The Sponsor will conduct both passive and active surveillance activities for continued vaccine safety monitoring. Passive surveillance activities will include submitting spontaneous reports of the following events to the Vaccine Adverse Event Reporting System (VAERS) within 15 days:

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome in children and adults
- Cases of COVID-19 that result in hospitalization or death

The Sponsor will also conduct periodic aggregate review of safety data and submit periodic safety reports at monthly intervals. Each periodic safety report is required to contain descriptive information which includes:

- A narrative summary and analysis of adverse events submitted during the reporting interval, including interval and cumulative counts by age groups, special populations (e.g., pregnant women), and adverse events of special interest
- Newly identified safety concerns in the interval
- Actions taken since the last report because of adverse experiences (e.g., changes made to Vaccination Provider fact sheets, changes made to studies or studies initiated)

Sponsor studies will include completion of long-term follow-up from ongoing clinical trials as well as the following three planned active surveillance studies. Of note, the Sponsor will submit plans for a clinical study to assess safety and immunogenicity in pregnant women and has proposed active surveillance studies designed to monitor vaccination during pregnancy within populations expected to receive the vaccine under EUA.

- Study Protocol Number C4591008. The Sponsor proposes to survey 20,000 U.S. health care workers enrolled in the COVID-19 HERO registry as well as health care workers in certain participating health care facilities about adverse events of special interest, and other clinically significant events of interest after vaccination with the Pfizer-BioNTech COVID-19 Vaccine. Incidence rates of these events in this cohort will be compared to expected rates. The respondents would receive follow-up surveys for a 30-month period.
- Study Protocol Number C4591011. This study is an active safety surveillance evaluation conducted within the Department of Defense Health System Databases using data derived from electronic health records and medical service claims among covered U.S. military and their families. Rates of safety events of interest in vaccinated participants will be compared to unvaccinated comparators. The study will be conducted for 30 months.
- Study Protocol Number C4591012. This study is an active surveillance study for adverse events of special interest and other clinically significant events associated with the Pfizer-BioNTech COVID-19 Vaccine using the Veteran's Health Administration electronic medical record database. Vaccinated participants will be compared to unvaccinated participants or to recipients of seasonal influenza vaccine. The study will be conducted for 30 months.

Currently, the primary objective of all three proposed studies above is descriptive, and the list of adverse events in the studies has not been finalized. FDA will provide feedback on these studies after further review.

Reporting to VAERS and Pfizer, Inc.

Providers administering the Pfizer-BioNTech COVID-19 Vaccine must report to VAERS (as required by the National Childhood Vaccine Injury Act) and to Pfizer the following information associated with the vaccine of which they become aware:

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events (irrespective of attribution to vaccination)
- Cases of Multisystem Inflammatory Syndrome in children and adults
- Cases of COVID-19 that result in hospitalization or death

Additional VAERS Reporting

An additional source of VAERS reports will be through a program administered by the CDC known as v-safe. V-safe is a new smartphone-based opt-in program that uses text messaging and web surveys from CDC to check in with vaccine recipients for health problems following COVID-19 vaccination. The system also will provide telephone follow-up to anyone who reports medically significant (important) adverse events. Responses indicating missed work, inability to do normal daily activities, or that the recipient received care from a doctor or other healthcare professional will trigger the VAERS Call Center to reach out to the participant and collect information for a VAERS report, if appropriate.

8. Benefit/Risk Assessment in the Context of Proposed Indication and Use Under EUA

8.1. Known Benefits

The known benefits among recipients of the proposed vaccine relative to placebo are:

- Reduction in the risk of confirmed COVID-19 occurring at least 7 days after Dose 2
- Reduction in the risk of confirmed COVID-19 after Dose 1 and before Dose 2
- Reduction in the risk of confirmed severe COVID-19 any time after Dose 1

The protocol-specified 2-dose vaccination regimen was highly effective in preventing PCR-confirmed COVID-19 occurring at least 7 days after completion of the vaccination regimen. Additional primary efficacy analyses in the all-available efficacy population, including participants who had protocol violations, showed consistency with outcomes in the primary analysis population. Efficacy findings were also consistent across various subgroups, including racial and ethnic minorities, participants aged 65 years and older, and those with one or more of the following conditions: obesity, diabetes, hypertension, and chronic cardiopulmonary diseases. While limited, available data suggest that individuals with previous SARS-CoV-2 infection can be at risk of COVID-19 (i.e., re-infection) and may benefit from vaccination.

Among participants with no evidence of COVID-19 prior to vaccination, the vaccine was effective in reducing the risk of COVID-19 and severe COVID-19 after Dose 1. Fewer severe cases were also observed in the vaccine recipients relative to recipients of placebo during the follow up period after Dose 1. The findings post Dose 1, from a post-hoc analysis, cannot be the basis to assess the potential efficacy of the vaccine when administered as a single dose because the period of observation is limited by the fact that most participants received a second dose three weeks after the first one.

8.2. Unknown Benefits/Data Gaps

Duration of protection

As the interim and final analyses have a limited length of follow-up, it is not possible to assess sustained efficacy over a period longer than 2 months.

Effectiveness in certain populations at high-risk of severe COVID-19

Although the proportion of participants at high risk of severe COVID-19 is adequate for the overall evaluation of safety in the available follow-up period, the subset of certain groups such as immunocompromised individuals (e.g., those with HIV/AIDS) is too small to evaluate efficacy outcomes.

Effectiveness in individuals previously infected with SARS-CoV-2

The primary endpoint was evaluated in individuals without prior evidence of COVID-19 disease, and very few cases of confirmed COVID-19 occurred among participants with evidence of infection prior to vaccination (although more cases occurred in the placebo group compared with the vaccine group). Therefore, available data are insufficient to make conclusions about benefit in individuals with prior SARS-CoV-2 infection. However, available data, while limited, do suggest that previously infected individuals can be at risk of COVID-19 (i.e., reinfection) and could benefit from vaccination.

Effectiveness in pediatric populations

The representation of pediatric participants in the study population is too limited to adequately evaluate efficacy in pediatric age groups younger than 16 years. No efficacy data are available from participants ages 15 years and younger. Although adolescents 16 to 17 years of age were included in the overall efficacy analysis, only one confirmed COVID-19 case was reported in this age group. However, it is biologically reasonable to extrapolate that effectiveness in ages 16 to 17 years would be similar to effectiveness in younger adults. Efficacy surveillance continued beyond November 14, 2020, and the Sponsor has represented that additional data will be provided in a BLA.

Future vaccine effectiveness as influenced by characteristics of the pandemic, changes in the virus, and/or potential effects of co-infections

The study enrollment and follow-up occurred during the period of July 27 to November 14, 2020, in various geographical locations. The evolution of the pandemic characteristics, such as increased attack rates, increased exposure of subpopulations, as well as potential changes in the virus infectivity, antigenically significant mutations to the S protein, and/or the effect of co-infections may potentially limit the generalizability of the efficacy conclusions over time. Continued evaluation of vaccine effectiveness following issuance of an EUA and/or licensure will be critical to address these uncertainties.

Vaccine effectiveness against asymptomatic infection

Data are limited to assess the effect of the vaccine against asymptomatic infection as measured by detection of the virus and/or detection of antibodies against non-vaccine antigens that would indicate infection rather than an immune response induced by the vaccine. Additional evaluations will be needed to assess the effect of the vaccine in preventing asymptomatic infection, including data from clinical trials and from the vaccine's use post-authorization.

Vaccine effectiveness against long-term effects of COVID-19 disease

COVID-19 disease may have long-term effects on certain organs, and at present it is not possible to assess whether the vaccine will have an impact on specific long-term sequelae of COVID-19 disease in individuals who are infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 should translate to overall prevention of COVID-19-related sequelae in vaccinated populations, though it is possible that asymptomatic infections may not be prevented as effectively as symptomatic infections and may be associated with sequelae that are either late-onset or undetected at the time of infection (e.g., myocarditis). Additional evaluations will be needed to assess the effect of the vaccine in preventing long-term effects of COVID-19, including data from clinical trials and from the vaccine's use post-authorization.

Vaccine effectiveness against mortality

A larger number of individuals at high risk of COVID-19 and higher attack rates would be needed to confirm efficacy of the vaccine against mortality. However, non-COVID vaccines (e.g., influenza) that are efficacious against disease have also been shown to prevent disease-associated death.[11-14] Benefits in preventing death should be evaluated in large observational studies following authorization.

Vaccine effectiveness against transmission of SARS-CoV-2

Data are limited to assess the effect of the vaccine against transmission of SARS-CoV-2 from individuals who are infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 may translate to overall prevention of transmission in populations with high enough vaccine uptake, though it is possible that if efficacy against asymptomatic infection were lower than efficacy against symptomatic infection, asymptomatic cases in combination with reduced mask-wearing and social distancing could result in significant continued transmission. Additional evaluations including data from clinical trials and from vaccine use post-authorization will be needed to assess the effect of the vaccine in preventing virus shedding and transmission, in particular in individuals with asymptomatic infection.

8.3. Known Risks

The vaccine has been shown to elicit increased local and systemic adverse reactions as compared to those in the placebo arm, usually lasting a few days. The most common solicited adverse reactions were injection site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%). Adverse reactions characterized as reactogenicity were generally mild to moderate. The number of subjects reporting hypersensitivity-related adverse events was numerically higher in the vaccine group compared with the placebo group (137 [0.63%] vs. 111 [0.51%]). Severe adverse reactions occurred in 0.0-4.6% of participants, were more frequent after Dose 2 than after Dose 1 and were generally less frequent in older adults (>55 years of age) ($\underline{\leq}$2.8%) as compared to younger participants (≤4.6%). Among reported unsolicited adverse events, lymphadenopathy occurred much more frequently in the vaccine group than the placebo group and is plausibly related to vaccination.

Serious adverse events, while uncommon (<1.0%), represented medical events that occur in the general population at similar frequency as observed in the study. Three SAEs in the BNT162b2 group were considered related by the investigator, but not the Sponsor, as related to study vaccination: shoulder injury (n=1), ventricular arrhythmia in a participant with known cardiac conditions (n=1), and lymphadenopathy temporally related following vaccination (n=1). We considered two of the events as possibly related to vaccine: the shoulder injury possibly due to vaccine administration or the vaccine itself and lymphadenopathy. Lymphadenopathy was temporally associated and biologically plausible.

No specific safety concerns were identified in subgroup analyses by age, race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection. Although participants 16 to 17 years of age were enrolled in the phase 3 trial, safety data for this age group is limited. However, available data are consistent with the safety profile in the adult population, and it is biologically reasonable to extrapolate the greater safety experience in adults, in particular younger adults, to the oldest pediatric age group of 16 to 17 years.

8.4. Unknown Risks/Data Gaps

Safety in certain subpopulations

There are currently insufficient data to make conclusions about the safety of the vaccine in subpopulations such as children less than 16 years of age, pregnant and lactating individuals, and immunocompromised individuals.

Adverse reactions that are very uncommon or that require longer follow-up to be detected

Following authorization of the vaccine, use in large numbers of individuals may reveal additional, potentially less frequent and/or more serious adverse events not detected in the trial safety population of nearly 44,000 participants over the period of follow up at this time. Active and passive safety surveillance will continue during the post authorization period to detect new safety signals.

A numerically greater number of appendicitis cases occurred in the vaccine group but occurred no more frequently than expected in the given age groups and do not raise a clear concern at this time for a causal relationship to study vaccination. Although the safety database revealed an imbalance of cases of Bell's palsy (4 in the vaccine group and none in the placebo group), causal relationship is less certain because the number of cases was small and not more frequent than expected in the general population. Further signal detection efforts for these adverse events will be informative with more widespread use of the vaccine.

Vaccine-enhanced disease

Available data do not indicate a risk of vaccine-enhanced disease, and conversely suggest effectiveness against severe disease within the available follow-up period. However, risk of vaccine-enhanced disease over time, potentially associated with waning immunity, remains unknown and needs to be evaluated further in ongoing clinical trials and in observational studies that could be conducted following authorization and/or licensure.

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10. Appendix A. Study BNT162-01

Design

Study BNT162-01 is an ongoing, first-in-human, phase 1 dose-level finding study conducted in Germany to evaluate the safety and immunogenicity of several different candidate vaccines, including BNT162b2. Twelve adults 18 to 55 years of age received 30ug BNT162b2.

Secondary and exploratory objectives were specified to describe the immune response, measured by functional antibody titer, antibody binding assay, and cell-mediated immune responses (cytokines associated with Th1 and Th2 responses to assess for the induction of a balanced versus Th1 or Th2 dominant immune response) at baseline and various time points after vaccination, specifically 7 days post Dose 2. Adverse event monitoring was the same as in study C4591001.

Results

No SAEs were reported in the BNT162-01 safety database included in the EUA submission, and the safety profile for BNT162b2 in this study was similar to that in the much larger study, C4591001.

Evaluable ELISPOT data were available from 39 participants across dose levels of BNT162b2 (data cutoff date was 17 September 2020). Evaluable intracellular cytokine staining and FACS data were available from 36 participants across dose levels of BNT162b2 (cutoff date was 04 September 2020). Data for serology results for serum neutralizing titers were available for 45 participants across dose levels of BNT162b2 (data cutoff date was 18 September 2020). Most participants who received both doses of BNT162b2 had evidence of SARS-CoV-2 S protein-specific CD4+ (39/39, 100%) and CD8+ (35/39, 89.7%) T cell responses. These T cell responses were directed against different parts of the antigen, including epitopes in the RBD, indicating the induction of multi-epitope responses by BNT162b2. Functionality and polarization of S-specific BNT162b2-induced SARS-CoV-2 T cells were assessed by intracellular accumulation of cytokines IFNγ, IL-2, and IL-4 measured after stimulation with overlapping peptide pools representing the full-length sequence of the whole SARS-CoV-2 S protein. For benchmarking, PBMC fractions from 15 convalescent patients with virologically confirmed COVID-19 were used. The Th1 polarization of the T helper response was characterized by the IFNγ and IL-2 production, and only minor IL-4, production upon antigen-specific (SARS-CoV-2 S protein peptide pools) re-stimulation. The SARS-CoV-2 neutralizing geometric mean titer (GMTs) increased over baseline after Dose 1, with a boost effect after Dose 2 that was most pronounced at the 30 µg dose level.

Thus, the immunogenicity results from Study BNT162-01 showed evidence of antibody-mediated SARS-CoV-2 neutralization and a Th1 polarization in the cell-mediated cellular immune responses in healthy adults 18 to 55 years of age, which supports the final dose selection and prospect of benefit for the enrollment of larger numbers of participants in Study C4591001.

11. Appendix B. Charlson Comorbidity Index

This index is based on a list of 19 conditions identified from diagnoses in hospital and physician data. Each condition is assigned a weight from 1 to 6. The index score is the sum of the weights for all identified conditions (Charlson et al., 1987). An index score of 0 indicates no comorbid conditions, while higher scores indicate a greater level of comorbidity.

Charlson Index Diagnoses: Cancer, Chronic Pulmonary Disease, Diabetes without Complications, Congestive Heart Failure, Cerebrovascular Disease, Dementia, Renal Disease, Peripheral Vascular Disease, Myocardial Infarction, Diabetes with Complications, Paraplegia and Hemiplegia, Connective Tissue Disease-Rheumatic Disease, Peptic Ulcer Disease, Mild Liver Disease, Metastatic Carcinoma, Moderate or Severe Liver Disease, HIV/AIDS.

Reference: Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373–383. [PubMed: 3558716]

12. Appendix C. Guidance for Industry: Emergency Use Authorization for Vaccines to Prevent COVID-19

Emergency Use Authorization for Vaccines to Prevent COVID-19

January 19, 2021

Representative Karen M. Rohr,
Chair, Human Services Committee
North Dakota Legislative Assembly
600 East Boulevard
Bismarck, ND 58505

Senator Judy Lee
Vice Chair, Human Services Committee
North Dakota Legislative Assembly
600 East Boulevard
Bismarck, ND 58505

Dear Chair Rohr, Vice Chair Lee, and Members of the Human Services Committee,

I am writing in support of bills HB 1306, HB 1307, and HB 1320. I have a BSN in nursing and a graduate doctoral degree in Chiropractic. I've worked in health RESTORATION for over of 12 years. I've worked in ICU work as an RN before continuing my Doctoral education. Because we take a different view of the human body (one that looks at triggers of dysfunction and why the body breaks down, as opposed to the end point-disease) I see protection from being injured is paramount in protecting people who choose to be responsible for their own health.

There are questions that need to be asked when considering coercion of health care choices.

"Are my health choices private? Will I eventually need to divulge what I eat, my exercise/fitness routine, Lab findings, Sexual orientation, and history? Will my health care choices determine my ability to access my bank accounts, To get on an airplane, or To fill gas?"

"Do vaccines do what you are taught to believe they do?"

"Who should make your health care decisions- you or your government?"

"If there are admitted, inherent dangers to a health care decision, should you be coerced into that health care decision?"

"What about people with known side effects to inoculation? Will they be treated as second rate citizens?"

For the record, I would like to enter in some important information, as coercion of health care choices is a very slippery slope. A year ago I was laughed at for saying we will be given vaccination ID's and will need to prove status for travel. Today, it has become a reality.

1. Vaccines are classified as biologics. This means that they are NOT subject to true placebo controlled studies. Rarely, if ever, are they studied against a true placebo. Almost every study uses other vaccines (example: the astrazeneca covid-19 study used the meningitis vaccine) [1] and/or the equally as risky ingredients (adjuvants like alumimum or mercury) in vaccines as a

"control" which allows them to hide expected adverse reactions with other reactions in the placebo group. Adjuvants have the capability of producing neuroinflammation which can lead to damage to the central and peripheral Nerve System.[2] Encephalopathy is a form of neuroinflammation. Encephalopathy can lead to autism and other neurologic and immune related disorders.

2. Vaccine injuries are severely underreported. Less than 1% of adverse events are ever reported. This has been researched and can be validated:[3]

> "Adverse events from drugs and vaccines are common but underreported. Although 25% of ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events and 1-13% of serious events are reported to the Food and Drug Administration (FDA). **Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of "problem" drugs and vaccines that endanger public health.** New surveillance methods for drug and vaccine adverse effects are needed. **Barriers to reporting include a lack of clinician awareness, uncertainty about when and what to report, as well as the burdens of reporting:** reporting is not part of clinicians' usual workflow, takes time, and is duplicative."[3]

This brings out the inconvenient truth that adverse events are 100 times more common than the mainstream media and medical doctors would like to admit.

I have personal experience with this, and a good example is the HPV inoculation. However as listed above, is prevalent in many more. Public marketing campaigns downplay risks and overestimate efficacy. They ignore the actual data (or lack thereof) to unduly influence the public. They will tell you that injuries are estimated to be "one in a million". However, since moving back to North Dakota 10 years ago, I have taken care of THREE teenagers in the Burleigh/Morton area alone whose severe symptomatology (diagnosed as POTS disease) began within 7 days of their HPV inoculation. Based on basic math and how many teenaged people there are in the Bismarck-Mandan area alone, along with how many I see, these numbers are massively higher than publicized. Then put into the equation that I came across these people randomly, for other reasons like sports injuries. This means the I am likely to have seen an extremely small minority of these people effected. So you have to ask, how does this happen? When questioned, the parents and patients had no idea to even ponder a link or to share with their doctor. Furthermore, not a single medical doctor had questioned them about inoculation history prior to onset of their problems. It was not until I asked the question about inoculation history that the family began to put the pieces together, and when they then inquired to their medical doctor, there was no testing or validation, nor was it reported to VAERS (the Vaccine Adverse Event Reporting System), a government entity responsible for diverting tax dollars to pay out damages caused by vaccines.

3. Drug companies are all exempt from paying out damages for vaccine damage, even though many of the biggest vaccine production companies are convicted felons for fraud and marketing—Pfizer,[4] Johnson & Johnson,[5] Astrazeneca,[6,7] and Merck all have some of the largest fines ever given out in court due to fraud, false marketing, kickbacks and bribery, false claims act related, and drug or medical equipment safety violation. (but hey, they "Pledged" transparency

in their studies, so we can trust them, right?)[8] Many, including Pfizer, Glaxo, and Sanofi are convicted felons. They have no impetus to improve vaccine safety or improve studies. Therefore, those who question safety have valid concerns.

4. Vaccines to not create health. Until recently, the US government has not bothered to study vaccinated and non-vaccinated populations. However, recently, Dr. Paul Thomas published research in his own practice in regards chronic disease prevalence in children fully vaccinated, partially vaccinated, and nonvaccinated. Because of the published findings, politically he is facing a "witchhunt" and is being targeted by the powers that be (note who is the largest lobbying company in the world—the pharmaceutical industry). Nonvaccinated children had significantly less chronic disease than the other two groups.[9] If vaccines create health, then why is the vaccinated group much sicker than the nonvaccinated group?

5. My health care choices are MY health care choices. To even INQUIRE about inoculations is an intrusion of my HIPAA privacy laws. Furthermore, where does the intrusion stop? Once the vaccine tracking digitalized system comes out, will it lead to medical martial law?

6. We also know that the covid injection has caused a large number of anaphylactic reactions. We have ZERO long term safety data, regardless of what self-appointed experts' postulate. Without vigorous, accurate tracking (which, as referenced above, has never happened) how can this even be performed? The "placebo groups" (again, many are not even a real placebo) are being given the Covid vaccine themselves. I have anaphylactic food allergies (16 of 38 foods tested via IgE blood response testing). Many people have food allergies that they are unaware of. I CANNOT take the chance of injecting myself with these dangerous chemicals. People are dying from this intervention. Whether the mainstream media, social media sites, and the medical profession and want to censor it or not, it is happening. It saddens me that we even have to have a bill protecting my RIGHT to health and health choices, and to weight my OWN risks and benefits of a procedure.

7. To coerce someone into a forced medical procedure, based on false premises is not only wrong, but it can also be considered fraudulent. First, we must delineate the difference between SARS covid-2 and "Covid-19". SARS covid-2 is the infection. Covid-19 are the symptoms of infection (like influenza vs "the flu"). The marketing of "90%-95% efficacy has NOTHING to do with ability to infect/transmit SARS-CoV-2. It refers to decreasing symptoms in a small subset of individuals. **It is unlawful under the FTC Act, 15 U.S.C. § 41 et seq., to advertise that a product or service can prevent, treat, or cure human disease unless you possess competent and reliable scientific evidence,** including, when appropriate, well-controlled human clinical studies, substantiating that the claims are true at the time they are made.

   Definitions Per the CDC: Immunity: Protection from an infectious disease. If you are immune to a disease, **you can be exposed to it without becoming infected**.
   Vaccine: A product that stimulates a person's immune system to produce immunity to a specific disease, **protecting the person from that disease**. Vaccines are usually

administered through needle injections but can also be administered by mouth or sprayed into the nose.
This is taken directly from the Pfizer phased 3 study:

8.2. Unknown Benefits/Data Gaps

Duration of protection

As the interim and final analyses have a limited length of follow-up, it is not possible to assess sustained efficacy over a period longer than 2 months.

Effectiveness in certain populations at high-risk of severe COVID-19

Although the proportion of participants at high risk of severe COVID-19 is adequate for the overall evaluation of safety in the available follow-up period, the subset of certain groups such as immunocompromised individuals (e.g., those with HIV/AIDS) is too small to evaluate efficacy outcomes.

Effectiveness in individuals previously infected with SARS-CoV-2

The primary endpoint was evaluated in individuals without prior evidence of COVID-19 disease, and very few cases of confirmed COVID-19 occurred among participants with evidence of infection prior to vaccination (although more cases occurred in the placebo group compared with the vaccine group). Therefore, available data are insufficient to make conclusions about benefit in individuals with prior SARS-CoV-2 infection. However, available data, while limited, do suggest that previously infected individuals can be at risk of COVID-19 (i.e., reinfection) and could benefit from vaccination.

Vaccine effectiveness against asymptomatic infection

Data are limited to assess the effect of the vaccine against asymptomatic infection as measured by detection of the virus and/or detection of antibodies against non-vaccine antigens that would indicate infection rather than an immune response induced by the vaccine. Additional evaluations will be needed to assess the effect of the vaccine in preventing asymptomatic infection, including data from clinical trials and from the vaccine's use post-authorization.

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COVID-19 disease may have long-term effects on certain organs, and at present it is not possible to assess whether the vaccine will have an impact on specific long-term sequelae of COVID-19 disease in individuals who are infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 should translate to overall prevention of COVID-19-related sequelae in vaccinated populations, though it is possible that asymptomatic infections may not be prevented as effectively as symptomatic infections and may be associated with sequelae that are either late-onset or undetected at the time of infection (e.g., myocarditis). Additional evaluations will be needed to assess the effect of the vaccine in preventing long-term effects of COVID-19, including data from clinical trials and from the vaccine's use post-authorization.

Vaccine effectiveness against mortality

A larger number of individuals at high risk of COVID-19 and higher attack rates would be needed to confirm efficacy of the vaccine against mortality. However, non-COVID vaccines (e.g., influenza) that are efficacious against disease have also been shown to prevent disease-associated death.[11-14] Benefits in preventing death should be evaluated in large observational studies following authorization.

Vaccine effectiveness against transmission of SARS-CoV-2

Data are limited to assess the effect of the vaccine against transmission of SARS-CoV-2 from individuals who are infected despite vaccination. Demonstrated high efficacy against symptomatic COVID-19 may translate to overall prevention of transmission in populations with high enough vaccine uptake, though it is possible that if efficacy against asymptomatic infection were lower than efficacy against symptomatic infection, asymptomatic cases in combination with reduced mask-wearing and social distancing could result in significant continued transmission. Additional evaluations including data from clinical trials and from vaccine use post-authorization will be needed to assess the effect of the vaccine in preventing virus shedding and transmission, in particular in individuals with asymptomatic infection.

8. Where there is clear risk, there needs to be freedom of choice. Coercion by public pressure is unethical. And we know that there will be pressure through lobbyists to coerce businesses and other entities to enforce these expectations just like they have the masking and shutdown practices.

Finally, I would like to bring up a glaring problem in society today, particularly with these HEALTH and LIFE MANDATES/COERCIONS. If this is truly about health, why is it that it always comes to drugs/injections? What about building and supporting a strong, robust, balanced immune response? What about addressing the triggers that lead to a damaged, incompetent immune response?

The cold hard fact is that there are ALWAYS going to be new viruses. Are we now setting precedence that every new virus needs an inoculation? In less than a year we are being told that there are additional strains of Coronavirus and more inoculations being developed. Guess what, they are not going anywhere. Will they just tell us we need to stay inside forever and keep giving more and more injections? The solution is not in more drugs. The solution lies in restoring normal immune function and addressing the reasons why people's immune response fails them. This is one thing that Sars Covid-2 has brought to light. 94% of people have comorbidities, the largest number being obesity and type 2 diabetes, which most have similar underlying mechanisms. Are we going to start mandating certain waist sizes as well? I have a novel idea. How about we admit that the United States is one of the most chronically ill countries and the the prescription drug culture we live in is not working. If you are truly healthy, your body handles these dis-eases as it should. Why should I as someone who studies these things daily need to follow the same path as the rest of the country, who is CLEARLY on the wrong path. If you want me to be responsible for other people's health, then let me mandate what foods people eat, how much exercise people get, what testing they do, what nutrients they consume… I hope that sounds preposterous, because this is what it sounds like to me.

Food and lifestyle factors play a MAJOR role in whether someone gets sick or stays well. IT is crucial for a balance, normal t-cell response and overall health. Why has this been all-but ignored and ridiculed for the last 10 years, especially the last 10 months. We have the burleigh-morton task force ridiculing the courageous people that have brought this up and taken a stand. Medical doctors threatening me for telling people that they need to be responsible for their own health. I've been saying that for 12 years. Covid didn't change that. It has always been a problem but now we are seeing the downstream effects and we either need to change course or sleep in the bed we make. I don't have to be part of the sick care cycle. And I should have the freedom to opt out for whatever means I feel necessary.

Thank you for your time. I would be happy to answer any of your questions.

Dr. Steve Nagel, DC

180 Health Solutions

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6. https://www.justice.gov/opa/pr/pharmaceutical-giant-astrazeneca-pay-520-million-label-drug-marketing
7. https://www.nytimes.com/2003/06/21/business/astrazeneca-pleads-guilty-in-cancer-medicine-scheme.html
8. https://violationtracker.goodjobsfirst.org/prog.php?parent=glaxosmithkline
9. https://www.mdpi.com/1660-4601/17/22/8674/htm

Good Afternoon, Chairman Weisz and members of the Human Services Committee. My name is Tracie Newman and I am a pediatrician, have a Master's Degree in Public Health, am a member of the Fargo Public School's Board of Education, and mother of three. I am here today testify in opposition to House Bill 1320.

Vaccines are arguably the 20th century's most successful public health achievement. Vaccines prevent disease in those who receive them and protect those most vulnerable who cannot be vaccinated (infants, immunocompromised). The American Academy of Pediatricians supports laws and regulatory measures that require certification of immunization to attend child care and school as a sound means of providing a safe environment for attendees and employees of these settings.

All 50 states in our country have legislation requiring specific vaccines for students and most allow exemptions. As you know, ND allows exemptions for medical, religious, and philosophical reasons. School Vaccination laws have played a key role in the prevention and control of vaccine preventable illness in North Dakota and The United States. Research has shown that school immunization mandates are the main driving factor leading to higher immunization rates. I certainly can attest to this, in my clinical duties, when children come in every Fall for their shots. This time allows for valuable screening and parental education as well.

Children who are not immunized, are more than 35 times more likely to contract measles and nearly 6 times more likely to contract pertussis compared to immunized children. Both illnesses I have diagnosed and managed in children. My own daughter contracted Chicken Pox at the age of 9 months from exposure to an older, unvaccinated child. Too young to be vaccinated herself, we had to watch her suffer needlessly and almost require hospitalization. As vaccines have become a victim of their own success, it is worth remembering that all of the diseases we currently vaccinate for still circulate in the world. In 2019, 1282 cases of confirmed measles occurred in 31 states, the most since 1992 and most cases were unvaccinated children.

Years of medical research have proven and reproved the safety and efficacy of vaccinations and the US long-standing vaccine safety program carefully monitors immunization safety. While most states are working to enhance their immunization laws, HB 1320 would be a major step backward to public health and the wellbeing of North Dakotans.

As North Dakota leaders, our priority should be putting children first. Children in our community often don't have a voice. As a School Board member of one of our state's largest districts and pediatrician, I have made it my life's work to be that voice. I believe strongly we must provide children with a safe learning environment in which to thrive, particularly for medically vulnerable children or those with special needs. Fargo Public Schools strongly opposes this Bill. Superintendent Rupak Gandhi stated: "I have had the fortune of working for three school districts in three different states during my career, which has allowed me to learn from a wide variety of experiences. I have always appreciated the importance of immunizations supported by the ND Legislature as it promotes a safe environment for all students and staff. During the past year, we have learned that students and staff have a safety responsibility to themselves and to their community. School immunization requirements help fulfill that obligation."

House Bill 1320 would put children and others across North Dakota at risk for preventable disease and death. Vaccines work and are safe – please oppose House Bill 1320. Thank you for your time and service.

NORTH Dakota | Health
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House Bill 1320
Human Services
January 19, 2021, 2:30 p.m.

Good afternoon, Chairman Weisz and members of the Human Services Committee. My name is Molly Howell, and I am the Immunization Director at the North Dakota Department of Health (NDDoH). I am here to provide testimony in opposition to HB1320.

Before immunizations were available, diseases like diphtheria, measles, whooping cough, polio, *Haemophilus influenzae* type B and rubella caused severe illness, hospitalization and death in the United States. More than 15,000 Americans died of diphtheria in 1921, before there was a vaccine. Because of the successes of vaccines, many people have forgotten these diseases.

Most vaccine-preventable diseases are spread from person-to-person. Vaccines not only protect the individual receiving the vaccine, but they also protect others around them, including children and adults who are unable to be vaccinated for medical reasons or who have weakened immune systems. The more people who are vaccinated, then the fewer opportunities there are to spread disease.

In addition to preventing disease, hospitalization and death, vaccination reduces costs. For every $1 spent on vaccines, the United States saves $10.90.[1] The vaccination of children born between 1994 and 2018 has saved the U.S. nearly $406 billion in direct medical costs and $1.88 trillion in total societal costs. Vaccination of one birth cohort (children born in 2009) will prevent ~42,000 early deaths, 20 million cases of disease, save $13.5 billion in direct costs and $68.8 billion in total societal costs.[2] In 2017, the Minnesota Department of Health spent $2.3 million in five months responding to an outbreak of 79 cases of measles.[3]

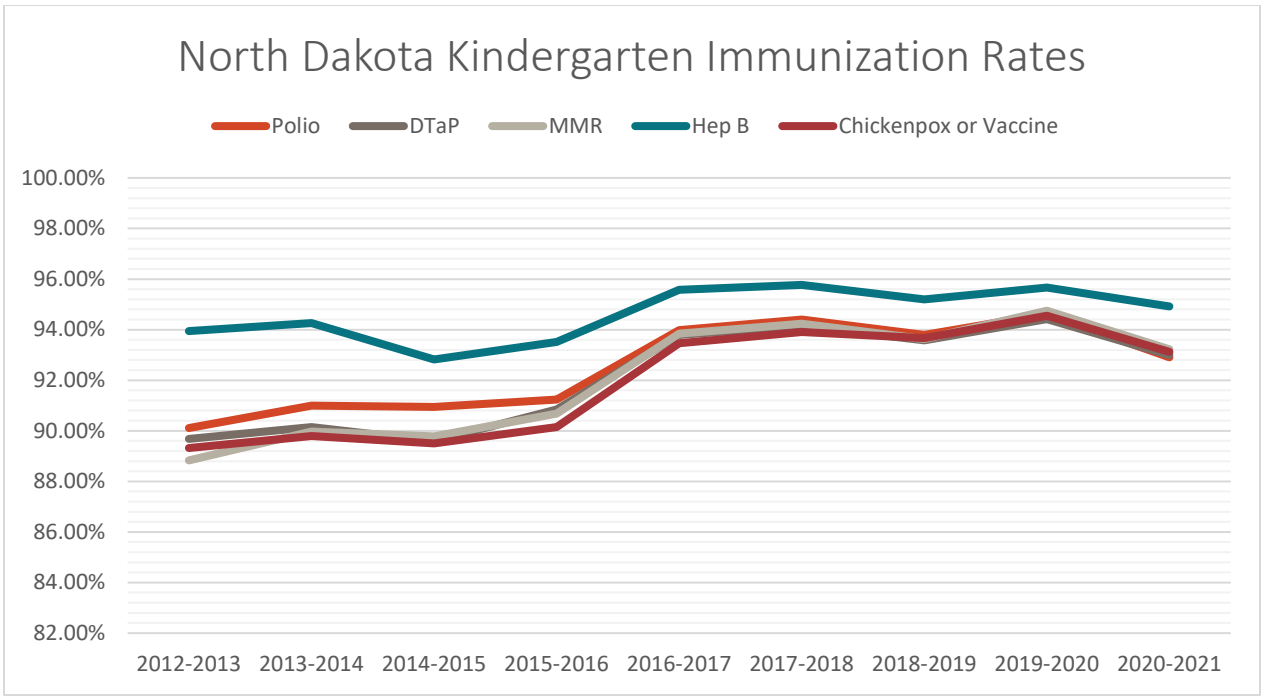
Childcare, school and university immunization requirements play an important role in increasing immunization rates and ensuring environments where children congregate are safe. North Dakota has one of the most relaxed

[1] https://doi.org/10.1542/peds.2013-0698
[2] Vaccines Are Cost Saving | Vaccinate Your Family
[3] MN Health Dept. Spent $2.3M During 5-Month Measles Outbreak – WCCO | CBS Minnesota (cbslocal.com)

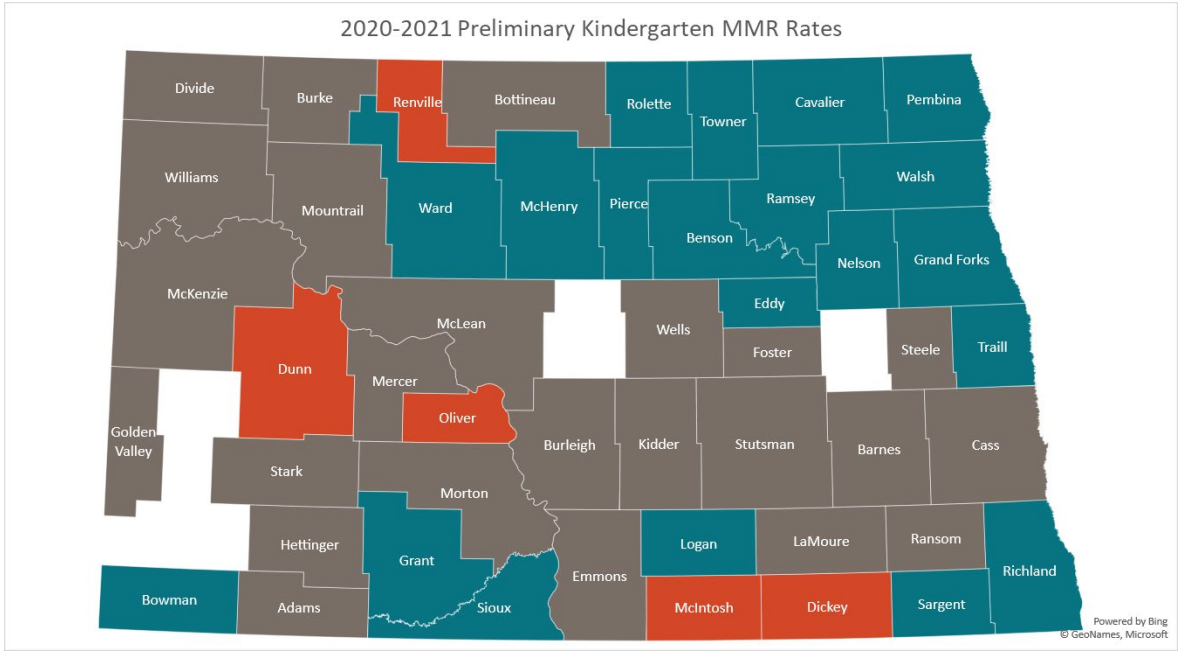
childcare and school immunization policies in the United States. North Dakota allows medical, religious, and moral/philosophical exemptions. Parents simply have to sign a document prior to school entry to claim a religious, moral/philosophical exemption. North Dakota is only one of 15 states that still allow moral/philosophical exemptions; many of the other states that allow philosophical exemptions require a notary signature or education from a healthcare provider prior to claiming an exemption. Five states only allow medical exemptions and don't offer religious or philosophical exemptions.[4] States that have easily-obtained personal belief exemptions have higher rates of pertussis and measles.[5],[6] If HB1320 were to pass, North Dakota would be the only state in the United States without childcare and school immunization requirements, putting North Dakota children at even greater risk for vaccine preventable diseases due to decreased immunization rates.

Preliminary school immunization entry rates from this past school year, show that 93.22% of kindergarten students were up-to-date for measles, mumps and rubella (MMR) vaccine. This is a decline from the previous school year, where the rate was 94.75%. Likely due to the COVID-19 pandemic, fewer schools (missing 48) reported school immunization rates and struggled with enforcement. Please see the chart below for historical kindergarten immunization rates in North Dakota. To achieve community (herd) immunity to measles, which is highly contagious, experts recommend a 95% vaccination rate. According to the Centers for Disease Control and Prevention, North Dakota ranked 29th in the nation for school MMR rates for the 2018-2019 school year.[7]

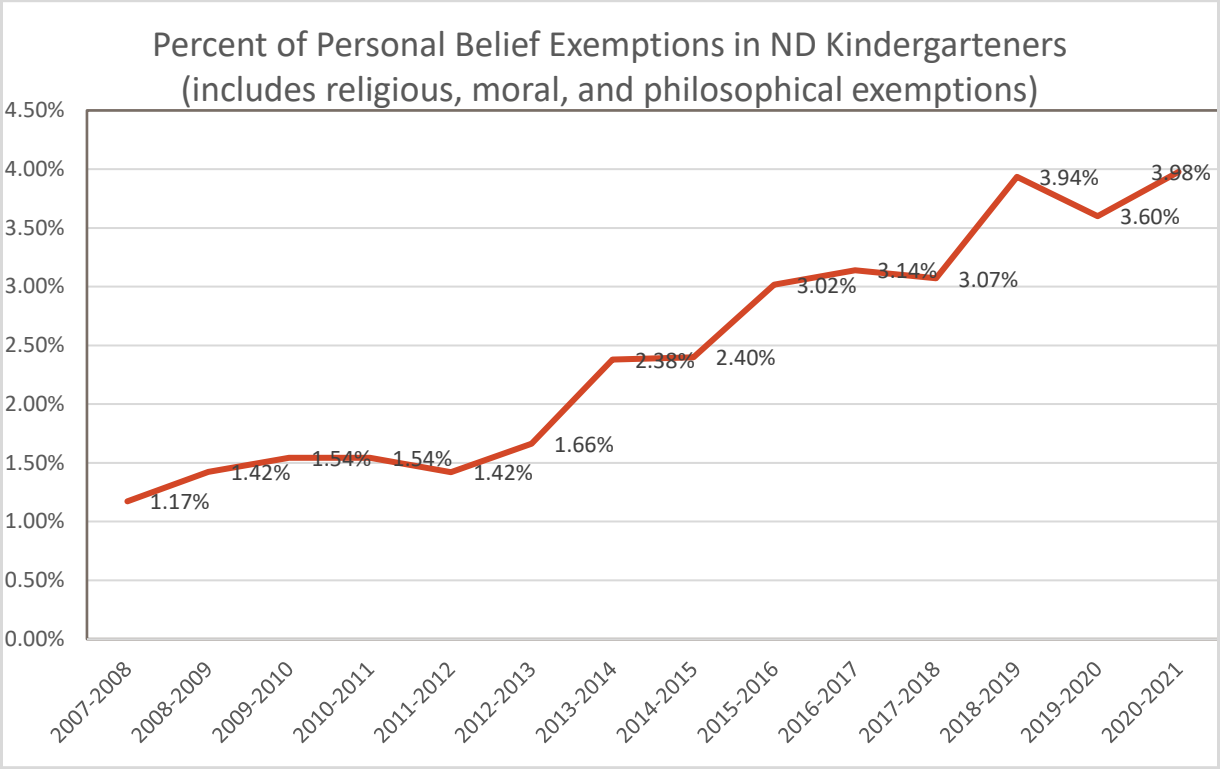
[4] States With Religious and Philosophical Exemptions From School Immunization Requirements (ncsl.org)
[5] Nonmedical Exemptions to School Immunization Requirements: Secular Trends and Association of State Policies With Pertussis Incidence | Infectious Diseases | JAMA | JAMA Network
[6] Individual and community risks of measles and pertussis associated with personal exemptions to immunization - PubMed (nih.gov)
[7] SchoolVaxView School Vaccination Coverage | CDC



Immunization coverage rates cannot be looked at just at a statewide level, but also must be monitored at the county and school levels. County MMR coverage rates range from 75% to 100%. School-level MMR rates range from 0% to 100%. This makes risks of outbreaks greater in pockets of un- or underimmunized children. Without immunization requirements, it is likely that immunization rates would decline, creating a greater risk for outbreaks.



North Dakota kindergarten exemption rates have increased most years. This past school year, personal belief (philosophical, religious) exemption rates were 3.91% (395 children). Up from 3.60% the previous year. Since the 2007-2008 school year, a 240 percent increase in exemptions has been reported in North Dakota. Please see the graph below for historical exemption rates. Because exemptions are so easy to claim in North Dakota, many schools and local public health are reporting that some of these exemptions are not truly exemptions, but just parents signing the form, so their child won't be excluded from school. Why eliminate NDCC 23-01-17.1, which already allows parents decline immunization for their children?



Eliminating NDCC 23-01-17.1 would also eliminate powers of the state health officer to respond to vaccine preventable outbreaks in childcares and schools, including excluding children who are not immunized when an outbreak is ongoing.

Section 3, number 2 prohibits employers from mandating vaccines. This would mean that healthcare facilities and long-term care facilities would no longer be

able to require influenza vaccination of employees, putting staff, patients and residents at risk.

It also appears that section 3, number 3 of this bill would prohibit state and local authorities from implementing immunization requirements in emergency situations by limiting authority in NDCC 23-01-05, NDCC 23-07-06, and NDCC 37-17.1. This would mean if an ebola outbreak were to occur in North Dakota, the NDDoH or local authorities could not implement potential immunization measures necessary to prevent the spread of disease.

Due to the COVID-19 pandemic, routine immunization coverage rates in North Dakota have already declined, with 8% less doses administered last year compared to 2019. Rates of vaccination have declined worldwide, increasing the risk for vaccine preventable disease outbreaks. A yes vote on this bill would cause immunization rates to decline further. For the reasons I have outlined today, the NDDoH asks you to oppose HB1320. This concludes my testimony. I am happy to answer any questions you may have.

One unvaccinated person affects those around them. Many people are unable to get vaccines, because of medical issues. Allowing healthy people to opt out of vaccines would put others at risk. If this bill passes it will likely result in deaths. Note the measles outbreaks that have been happening in recent years. The real tragedy of this idea is that it is more likely to be a person with a health condition who is negatively impacted by this than the likely healthy person refusing the vaccine. No one has a right to endanger someone else's life.

Voting for his law would indicate that you do not value human life. Our constitution says we should have the right to "Life, Liberty, and the Pursuit of Happiness," and this law would threaten the first of those.

Cara Halgren

3378 Primrose Court

Grand Forks, ND 58201

651.210.3356

Biotechnology Innovation Organization

January 19, 2021

Representative Karen M. Rohr
Chair, Human Services Committee
North Dakota Legislative Assembly
600 East Boulevard
Bismarck, ND 58505

Senator Judy Lee
Vice Chair, Human Services Committee
North Dakota Legislative Assembly
600 East Boulevard
Bismarck, ND 58505

Dear Chair Rohr, Vice Chair Lee, and Members of the Human Services Committee,

I am writing today on behalf of the Biotechnology Innovation Organization (BIO), a national trade association for the biotechnology industry, representing over 900 companies and academic institutions involved in the research and development of innovative healthcare, agriculture, industrial, and environmental biotechnology products. BIO membership includes vaccine developers and manufacturers who have worked closely with the public health community to support policies that help ensure access to innovation and life-saving vaccines for all individuals.

BIO and our member companies would like to express our **opposition to HB 1306, HB 1307, and HB 1320**, as these bills put North Dakotans at risk of preventable diseases.

Legislative efforts related to vaccines should focus on continuing to extend protection from these diseases and their side effects to all North Dakotans. The Legislature serves a critical function in passing laws to protect the people of North Dakota. Decisions to change the immunization laws should be held to high standards of evidence-based scientific deliberation. Prohibiting the State, employers, and schools from implementing any immunization requirements will have a detrimental effect on public health in North Dakota, particularly in the middle of a pandemic. North Dakota has experienced a high toll from the COVID-19 pandemic, particularly when cases spiked to a 16% positivity rate in November and December.[1] As COVID-19 vaccination begins and there is hopefully an end to the pandemic coming soon, we must remain vigilant against other infectious diseases. Removal of vaccine requirements risks outbreaks of measles,

[1] https://www.health.nd.gov/diseases-conditions/coronavirus/north-dakota-coronavirus-cases

1201 Maryland Avenue SW
Suite 900
Washington DC 20024

202.962.9200 P
202.488.6301 F
bio.org

pertussis, and influenza. Such outbreaks put lives at risk and are accompanied by great economic costs to the State[2] and society.[3]

HB 1305 is based upon false claims that vaccines are linked to sudden infant death syndrome (SIDS) and autism spectrum disorder (ASD). Potential links between vaccines and these conditions have been extensively studied, with no association found. In fact, studies have found that immunization may have a *protective* impact against SIDS. A metanalysis of existing research in 2007 found that immunizations were associated with *halving* the risk of SIDS.[4] Similarly, a 2001 study in the United Kingdom found immunization lowered the odds of SIDS[5] and a 1995 study in New Zealand found unimmunized infants had a higher risk of SIDS[6]. Additionally, more than nine studies have been conducted to investigate any possible connection between vaccines and ASD, all finding no association.[7] Thimerosal, the vaccine preservative alleged to cause autism was removed from all pediatric vaccines between 1999 and 2001, yet autism rates continue to rise.[8] Rather than continuing to look for a connection to vaccines, research should be done investigating the actual causes of these conditions.

HB 1307 and HB 1320 would restrict the ability of employers and schools to implement vaccination requirements. North Dakota's school entry requirements allow for freedom of choice by offering exemptions based upon personal beliefs. However, the choice to delay or reject some vaccines entirely is not just a personal decision. When we choose to not receive vaccines or vaccinate our children, we put ourselves and others in our community at risk for serious disease. Putting others, such as those who are immunocompromised or too young to receive vaccines, at risk for vaccine-preventable disease arguably presents a challenge to their personal freedom to go to the store, to school, or anywhere else they come into contact with their community without the possibility of contracting a dangerous, preventable illness. All North Dakotans deserve the right to freedom from preventable infectious diseases.

Individuals understandably have concerns about the unprecedented pace of development of COVID-19 vaccines. Time has been saved through prioritization of resources toward COVID-19, novel technologies that have been more efficient, public-private collaboration, and clinical trial phases happening in parallel rather than in sequence. These vaccines enrolled the same number of individuals in clinical trials as trials for other vaccines and the FDA and CDC have maintained their high standards. Therefore, individuals should be confident that there have not been shortcuts in testing

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[2] https://www.cdc.gov/mmwr/volumes/66/wr/mm6646a3.htm
[3] https://www.worldbank.org/en/news/feature/2020/06/08/the-global-economic-outlook-during-the-covid-19-pandemic-a-changed-world#:~:text=Businesses%20might%20find%20it%20hard,by%20almost%208%25%20in%202020
[4] https://www.ncbi.nlm.nih.gov/pubmed/17400342
[5] https://www.bmj.com/content/322/7290/822.short
[6] https://adc.bmj.com/content/73/6/498
[7] https://www.cdc.gov/vaccinesafety/pdf/cdcstudiesonvaccinesandautism.pdf
[8] https://www.cdc.gov/vaccinesafety/concerns/autism.html

the safety and efficacy of these vaccines and such concerns should not lead to overreaching policies that impact the use of all vaccines.

Vaccinations have led to steep decreases and eradication of many significant infectious diseases such as polio, measles, mumps, pertussis, and haemophilus influenza type B (Hib). Immunizations are our best protection against preventable disease and can help North Dakotans live longer, healthier lives.

BIO and our member companies urge the Committee to oppose HB 1306, HB 1307, and HB 1320. We stand ready to help in any discussion of legislation to strengthen immunizations and to share our knowledge of activities and initiatives from around the country.

Sincerely,

/s/

John Gregory Hoke

Director, State Government Affairs

cc: Rep. Jeff A. Hoverson
Rep. Dwight Kiefert
Rep. Lisa Meier
Rep. Matthew Ruby
Rep. Mary Schneider
Rep. Kathy Skroch
Rep. Bill Tveit
Rep. Greg Westlind
Sen. JoNell A. Bakke
Sen. Dick Dever
Sen. Kathy Hogan
Sen. Tim Mathern
Sen. Jessica Unruh-Bell

2021 HB 1320

House Human Services Committee

Representative Robin Weisz, Chairman

January 19, 2021

Chairman Weisz and members of the House Human Services Committee, I am Tim Blasl, President of the North Dakota Hospital Association (NDHA). I am here to testify in opposition to House Bill 1320. I ask that you give this bill a **Do Not Pass** recommendation.

I am here on behalf of hospitals in opposition to the bill because it would prohibit a state or local elected official, the state, or a political subdivision from mandating an individual receive a vaccination. It also provides that this provision "…prohibits making receipt of a vaccine a condition for entry, education, employment, or services." It is unclear if this later language prohibits private employers and schools from mandating vaccines, or if it only applies to employees of the governmental entities listed in the first subsection. In any case, we are concerned with the outright prohibition on mandatory vaccinations.

Immunizations have rightfully been acknowledged as one of the 10 greatest public health achievements of the 20th century. School vaccination laws, for example, have played a key role in the prevention and control of vaccine preventable disease. Currently, all states have immunization requirements for school children, and these requirements have helped our country achieve high vaccination rates.

In the healthcare setting, immunizations don't just protect vulnerable patients, they also protect employees. Healthcare workers are at risk for exposure to serious, and sometimes deadly, diseases. If they work directly with patients or handle material that could spread infection, they should get appropriate vaccines to reduce the chance that they will get or spread vaccine-preventable diseases. Even those workers not directly involved in patient care can potentially be exposed to infectious agents that can be transmitted to and from patients.

Patients who require hospitalization are often the most vulnerable and need more protection. Hospitals and health care workers have a shared responsibility to prevent occupationally acquired infections and avoid causing harm to patients by taking reasonable precautions to prevent transmission of vaccine-preventable diseases. We are concerned that the bill would prohibit any healthcare provider from being able to require a vaccine as a condition of employment. It would mean that vaccination programs would no longer be an essential part of hospital infection prevention and control. Vulnerable patients would not be as protected as they could and should be.

North Dakota should implement policies that are aimed at increasing immunization rates, not policies that undermine vaccination efforts. Mandating vaccination is akin to legally requiring that young children be secured in an appropriate car seat. The state is acting to prevent parents from making decisions on behalf of their children that unnecessarily expose them to the risk of infectious disease. Failure to vaccinate not only puts the unvaccinated individual at risk, but also anyone they come into contact with — including those too young to be immunized and people who, for medical reasons, cannot be vaccinated. It is imperative that North Dakota continues to allow healthcare providers the ability to determine which immunizations are necessary to keep patients and employees safe, just as we should continue to require vaccinations for school entry.

Since 1980, all 50 states have formally linked vaccination to school entry. That action was backed by nationwide surveys in the 1970s showing that the incidence of measles was higher in states without mandates, and lowest in states where mandates were strictly enforced. If this bill passed, North Dakota would become the only state in the country that doesn't require immunizations for school. It is worth pointing out that our current policy does not force anyone to be vaccinated - it is a foundational principle of medical ethics that consent must be given for any procedure. The decision to make vaccination mandatory is therefore a decision to impose some form of penalty on those who do not follow the law. A common penalty is to exclude unvaccinated children from school, or to allow a healthcare provider to decide not to employ those who refuse to be vaccinated.

Especially as the COVID-19 pandemic continues, we are reminded of the importance of vaccines and their ability to stop the spread of disease and save lives. Rather than telling employers and schools what they cannot do, we see a need for greater engagement. The small (albeit vocal) minority of people who refuse vaccines outright rarely change their minds. The much larger hesitant population, however, does respond to information campaigns. Therefore, rather than prohibiting vaccination mandates outright, we would prefer to see greater investment in education and more efforts to facilitate meaningful conversations between concerned people and health-care professionals. For these reasons, we urge you to oppose House Bill 1320.

I would be happy to respond to any questions you may have. Thank you.

Respectfully Submitted,

Tim Blasl, President
North Dakota Hospital Association

Every morning and every night for the past 40 plus years have begun and ended with simple task. I put in or remove my hearing aids. I have been doing this since I was 18, when my progressive hearing loss made this imperative. What is not so common?

I was deafened by the mumps.

My entire family had the mumps in 1965, just two years before the vaccination for the mumps became common place. It's a rare side effect, but I estimate my family and then myself and my husband have spent well over $100,000 in the purchase of hearing aids, adaptive equipment (phones, alarms, amplifiers) over the course of my lifetime. So I am alarmed at HB 1320 and HB 1306 which seeks to undermine the requirements of vaccines and useless study of those vaccines.

Anyone who is a student of history knows that many deadly diseases were stopped by vaccines. Smallpox, polio, measles, tetanus, the flu, and yes, mumps. Why on earth would any civilized state seek to stop this? There are procedures in place for medical exemptions. If religious exemptions are requested, I would ask that the requester seek a Biblical lifestyle, free from medical interventions.

I would challenge the current state legislators to stop wasting tax payer monies on studies that are useless and legislation that is dangerous to public health. Perhaps they would like to speak with the 1,373 North Dakotans who have died of COVID 19 since last year? How many of those families would taken a shot with the current COVID 19 vaccine that is becoming available?

I will be.

Perhaps who refuse to believe in the efficacy of vaccinations can begin saving for medical care, adaptive equipment and/or funeral expenses of those who do NOT receive vaccines.

Jan Macdonald Russell

HB 1320 Testimony
Human Services Committee
January 19, 2021 2:30 p.m.

Good afternoon, Chairman Weisz and members of the Human Services Committee. My name is Kylie Hall, and I am here to testify in opposition to this bill. I have a Master's Degree in Public Health and have worked at the North Dakota State University Center for Immunization Research and Education for the past 5 and 1/2 years. I would like to make clear that my comments today are not on behalf of NDSU. I am also a parent to two young children who are both fully vaccinated.

I feel uniquely qualified to testify on this bill. In 2015 and 2016, I led a study in North Dakota that produced recommendations for how to improve immunization rates. The study engaged nearly 200 immunization stakeholders in North Dakota, including healthcare providers, school administrators and staff, public health staff, legislators, and parents.

If passed, House Bill 1320 would make North Dakota the only state in the country that does not require immunizations for school entry. This is concerning, as school vaccination requirements for school and daycare entry have played a key role in the prevention and control of vaccine-preventable diseases in the United States since 1827. In North Dakota, immunizations were first required for school entry at the start of the 1975-1976 school year. Today, all states have immunization requirements for school children, and school requirements have helped the United States achieve high vaccination rates.

Now, you might be thinking, do school mandates make an impact on immunization rates and rates of vaccine-preventable diseases? The answer is yes. Olshen et al found that school immunization mandates were the main factor leading to higher immunization rates, highlighting the importance of school immunization requirements.

I can also tell you that our study confirmed that school requirements help assure a fully vaccinated population. During our study, we conducted focus groups to learn more about school immunization requirements and enforcement. Time and time again, we heard from schools that the MAJORITY of children are immunized. However, at the start of school, there are many children who still haven't received their vaccine booster doses required for kindergarten or junior high. Some parents didn't know their kids needed extra vaccines for schools. These doses are important to boost immunity and prevent outbreaks. Because schools mandate vaccines, a number of parents bring their kids in to be immunized. We heard from a number of pediatricians during the fall of 2015 that some schools had clearly changed their immunization policies, because they had a ton of children come in to receive vaccine booster doses. These children were partially immunized, but just needed some of those 5-year-old shots or 7th grade shots. The school requirements brought them in to be vaccinated. Without school requirements, how long might their parents have waited to get those vaccines? We will never know, because school mandates help assure that ND students are protected from vaccine-preventable diseases.

Why are schools tasked with enforcing immunization requirements? The enforcement of immunization requirements is a responsibility given to schools across the United States because schools are a point of contact for the majority of children. Even if a child doesn't see a healthcare

provider, nearly all children attend school. As recently as 2015, over 97% of children in North Dakota attended school in-person. No other entity can reasonably enforce immunization requirements while also holding parents accountable. Additionally, schools would be directly impacted by an outbreak of a vaccine-preventable disease. Schools also have a large potential for the spread of diseases among children closely quartered for long periods of time, and in the event of a disease outbreak, learning could be disrupted for long periods of time.

Through our project, we were able to visit with a group of school staff that were impacted by a tuberculosis outbreak in 2012. While tuberculosis is not a disease we regularly vaccinate against in the United States, they were able to see how a case of a vaccine-preventable disease in their schools would be similar to what they experienced. In reliving their experiences with this outbreak, one school administrator said "There's nothing like an experience like that to get you on board with immunizations." Another administrator called dealing with the tuberculosis outbreak a nightmare, with another saying the outbreak was so disruptive to the school process that regular learning almost went out the window for those weeks or months. Vaccines prevent situations like this from being commonplace. High immunization rates keep vaccine-preventable diseases from spreading in schools. And in our schools, we have some students who are not able to be vaccinated. As a society, it is our duty to get vaccinated for them. As one administrator in our study said, "I think we are charged with providing a safe environment for our students, and that includes students who are medically fragile or vulnerable. We have an obligation to provide a safe environment for them, so it starts with the doorstep. We have to make sure our kids are healthy and immunized before they can get into our school setting." Another administrator added, "I do think our priority is to educate kids, and [immunizations] is certainly part of it. And it's our state law. If we don't have that feeling in our school that every child is safe, they can't learn."

Another reason why school immunization requirements are so important is that in the event of an outbreak, school officials need to know immediately who is and isn't immunized so they can remove susceptible individuals from the school setting. During an outbreak, many states have determined that it is in the best interest of children who are not immunized if they are removed from school until the threat of the outbreak has passed. As of 2015, 27 states had the authority to exclude unimmunized children during an outbreak. North Dakota is one of them.

In North Dakota, we should be focused on protecting children and implementing policies that will increase childhood immunization rates. We know that immunizations are safe and immunizations are effective. They protect not only the person being vaccinated, but those who cannot be vaccinated. I want to end with a personal story.

In 2019, I was pregnant with my second child. During routine blood work, I found that I no longer was considered "immune" to rubella. Rubella is viral illness that usually causes mild symptoms or even no symptoms in most people. However, it can cause serious problems for unborn babies whose mothers become infected during pregnancy. Rubella was eliminated from the United States in 2004, but there are a handful of cases reported each year in women who have traveled outside of the country. Rubella, like many infectious diseases, is only a plane ride away. As a pregnant mother, I was potentially susceptible to rubella, and I relied on herd immunity to protect me and my unborn child. I relied on school immunization mandates to make

sure kindergartners received their second dose of MMR to boost their immunity to measles, mumps, and rubella.

As you've heard, school immunization mandates help boost immunization rates and assure a vaccinated population, and I hope you can understand that the effects are far-reaching. In 2019, a highly immunized population protected me and my now one-year-old son Graham from rubella.

Please vote no on House Bill 1320. Please keep school and daycare immunization requirements in North Dakota. It benefits all of us.

Good Afternoon, Chairman Weisz and members of the Human Services Committee. My name is Dr. Liann Hanson and I am a principal at Centennial Elementary with Fargo Public Schools. I taught for 5 years and have been a school administrator for 16 years. I have been a principal in the state of Colorado, Minnesota, and North Dakota. I have seen different vaccine regulations in different states and districts. I am here today testify in opposition to House Bill 1320.

The COVID-19 Pandemic has put the spotlight on schools and the importance they have in keeping our community safe and healthy. All schools and districts have done an admirable job in implementing safety measures to keep our students and staff safe. I believe we have played an important role with the mitigation of COVID 19 in our communities and our state.

We have adjusted learning models (from distance learning to hybrid, to 4 or 5 day in person). Teachers, staff, and students have tackled online learning. We have put podding of students into place. We have adjusted where and how students eat lunch. We have limited the number of students that are outside at recess at a time. We have taken extensive time to contact trace, communicate with parents, and send students home to quarantine. We have required face masks and we have social distanced to the best of our ability. All these measures were important to make sure we could stay as safe as possible.

We are finally seeing the light at the end of this COVID 19 tunnel. We are seeing progress in getting all students back to a normal school day. We are meeting the needs of students academically, socially, and emotionally. It would be a detriment to have to worry about other preventable diseases. If we did not require vaccines, there is potential that these diseases could infiltrate our community and we would need to put into place mitigation strategies (again) in our schools. This is a disruption to the education of our students.

It is important for the school districts in the state of North Dakota to continue to provide a safe and healthy learning environment for all students. One way we can do that is to oppose House Bill 1320 and to continue to require the appropriate vaccines for our students.

We need to have in place requirements for vaccines for preventable diseases such as pertussis and measles. If we don't, we could potentially have another outbreak that affects our schools and community.

We need to keep kids safe and in school. Vaccines and proper regulations of vaccines is the appropriate way to mitigate risk and keep kids healthy.

I appreciate you taking the time to listen to my testimony. Thank you for serving kids and serving the state of North Dakota.

Testimony to the House Human Services Committee on HB 1320
Testimony by Barbara Frydenlund
Rolette County Public Health District Administrator

Good afternoon, Chairman Weisz and members of the House Human Services Committee. My name is Barbara Frydenlund, and I am the Nurse Administrator for Rolette County Public Health District. I am offering this testimony today in opposition of HB 1320.

Vaccinations are a critical part of preventative health care and are the backbone of public health. It is always better to prevent a disease than to treat it after it occurs. As you are aware, there are several vaccine preventable diseases. Many of these diseases have never been seen by today's healthcare providers and parents, in part because we have been actively vaccinating our infants and children for several years. Science and data confirm that vaccinations work to curb infection rates. Vaccinations are the most effective medical treatment in the prevention of infectious diseases around the world. North Dakota law sets minimum requirements for children attending early childhood facilities, head start programs, preschool education, kindergarten through 12th grade. Age-appropriate vaccinations are designed to be a simple, safe, and effective way of protecting children from serious and potentially life-threatening diseases. Vaccinations not only help protect children, but also protect the broader community by minimizing the spread of disease. It is the responsibility of parents, guardians, and the healthcare providers to protect the health and safety of children. **ALL CHILDREN in public daycare facilities and schools have the right to be protected from vaccine preventable disease.**

Unfortunately, COVID 19 has shown us how a disease can overtake and paralyze the world that we live in and answers the question of **"why vaccines are important".**

Thank you for allowing me to share my expertise in this field. I urge a **DO NOT PASS recommendation on HB 1320.**

January 19, 2021

Testimony by: Malinda Weninger
Bismarck, ND 58504

Dear Members of the Human Services Committee:

I am writing regarding HB1307, HB1320 and HB1306.

HB1320 – would prohibit state and local government from mandating vaccination and would prohibit making the receipt of a vaccine a condition for entry, education, employment or services.

- **I support this bill. Restricting individuals into buildings, education, employment or obtaining services for not having a vaccine is taking away individuals FREEDOM of choice and limiting their choices for living and earning an education.**
-
- I am the mother of a vaccine injured child. My daughter was injured in 2006 by the Gardasil vaccination (HPV vaccine) which came out in 2006. My daughter was one of the first inoculated for this vaccine. As time went on, many reports of injuries started coming out. This allowed me to make the connection to a mysterious sudden autoimmune illness that came upon my daughter after her 2nd and 3rd required injections. We went to many doctors and finally went to Mayo Clinic to try and figure out why my daughter's body turned into a horrific ill body with many many life altering symptoms.

- Everyone's body is made up differently and we don't know how each individual body will react. Each individual knows their bodies and their limits to chemical exposures and issues they may have from these injections, they should not be FORCED to be immunized and they need their FREEDOM of choice. ALL vaccines carry the risk of injury or death so there has to be informed consent and the right to refuse any vaccine without penalty.

- There is a reason there is a National Vaccine Injury Compensation Program that has paid out over $ 4.5 billion in damages.

- Individuals need to be allowed to make their own decisions when it involves THEIR body – the only thing they truly own in this world.

North Dakota needs to be a LEADER not a FOLLOWER.

To: Legislative Assembly of North Dakota

From: Heather Miller,
Mandan, ND

Date: January 18, 2021

RE: Testimony in favor of HB 1320

Ladies and gentlemen, my name is Heather Miller and I am a resident of Mandan, North Dakota. I hereby give testimony about House Bill 1320 which would prohibit state and local government from mandating vaccination and would prohibit making the receipt of a vaccine a condition for entry, education, employment, or services. I support this bill.

As a mother of a vaccine-injured child, this bill is important to me because I have not vaccinated any of my children since my second-born was vaccine injured. I am proud to live in a state where I have the freedom to choose Exemption to Immunization Law. My third-born child has never been vaccinated and has been the healthiest of my three children. The difference is remarkable. Vaccines carry the risk of injury or death. I propose it should be up to the individual to assess the risks of taking a vaccine and to have the right to refuse any vaccine without penalty. House Bill 1320 needs to be passed to prevent law abiding citizens from losing their jobs, losing access to education, losing access to enter into businesses or obtaining services for refusing to take a vaccine.

House Bill 1320 helps my family because it protects our right to choose what we put in our body. Every body is unique. The varied symptoms of COVID-19 underscores the uniqueness of an individual's immune response. At the height of my son's vaccine injury he lost the ability to speak. He was lethargic. His smile and shining 18-month-old eyes were replaced by a blank stare. So devastating. But it was a choice I made to vaccinate. And I fought the battle to restore healing to my child. I prayed. I researched. I took him to various doctors. We changed our diet. It was a long journey. Now I choose to not vaccinate. Would North Dakota take away my ability to choose? Does North Dakota know what is best for my body and would North Dakota fight to restore healing to my vaccine-injured body?

Please pass House Bill 1320 and protect my right to choose what I put in my body. Let the individual decide. Let parents and caregivers decide what is best for their charges. Please protect my family's right to refuse vaccines while preserving access to employment, education, and services.

HB 1320

House Human Services Committee

January 19, 2021

Jessica Doty, RN, Director of Student Health Services

701.777.0500 | jessica.doty@und.edu

Chair Weisz and Committee Members:

My name is Jessica Doty, and I am a Registered Nurse and the Director of Student Health Services at the University of North Dakota. I have worked in collaboration with Laura Oster-Aaland, Vice Provost for Student Affairs and Enrollment Management from North Dakota State University to oppose HB1320. The bill would challenge the ability to identify student immunization status, which is critical to achieve herd immunity on college campuses due to the close nature of student interactions in living, working, and learning environments. Furthermore, this bill directly contradicts CDC recommendations to increase vaccine uptake and reduce vaccine-preventable disease.

UND and NDSU together bring over 26,400 students from across the state, nation and world together to create diverse learning experiences. Currently, measles, mumps, rubella, and meningococcal vaccines and documentation is required to attend North Dakota colleges and universities per NDUS policy 506.1.

Vaccine requirements help protect our campuses from highly contagious vaccine-preventable disease occurrences, as well as promote a quick public health response to protect other community members in case of an infection through the tracking of students' immunization status. Exemptions to the vaccine requirement are available to students with medical, religious, or philosophical objections to the vaccine requirement per each individual campus policy.

To highlight the rapid transmission that could occur on a campus consider this example. Measles is spread through the air and 9 out of 10 non-immune people in contact with someone infected with measles can become ill. Measles hangs in the air for up to 2 hours (cdc.gov/measles). Imagine how quickly measles could spread in a dorm, college classroom, or sporting event. Being able to identify vulnerable students who may be exposed to vaccine-preventable disease is an important reason to require vaccination records be submitted on college campuses.

As we work to fight a worldwide pandemic, opening the threat for preventable outbreaks is not advisable. The elimination of immunization requirements would impact the learning and living of university students and adversely affect the mission of our college and university populations.

I respectfully request a Do Not Pass on HB1320 and am available to answer your questions.

Thank you.

References

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This written testimony is in support of HB 1320: A BILL for an Act to create and enact a new section to chapter 23-07 of the North Dakota Century Code, relating to limitations on vaccinations requirements; to amend and reenact subsection 2 of section 15.1-23-02 and section 23-01-05.3 of the North Dakota Century Code, relating to immunization records and data; and to repeal section 23-07-17.1 of the North Dakota Century Code, relating to immunizations required for entry to school or day care.

Imposing limitations on vaccination requirements is something I fully support.

Sean Thorenson

January 18, 2021

Re: Support for HB 1320

To Representative Weisz and the House Human Services Committee,

I am writing to express my support to North Dakota House Bill 1320.

I am a healthcare provider in the state of North Dakota and have been a ND resident my entire life. I have worked in the healthcare field since 1994 and have two children. I have always been an advocate of vaccinations. I, however, have serious reservations about mandating individuals in regards to their healthcare. I believe that all individuals should have the right to choose what they feel is best for the care of themselves and their children. This is especially true for any treatment that has the potential to cause harm. This should be a choice for parents with input from their healthcare provider. As a healthcare provider it is my responsibility to educate my patients on the importance of vaccinations. It is also my responsibility to look at each patient's individual health and take this into account in that discussion. I am a vaccine advocate, but I do not support the mandating of any form of healthcare. House Bill 1320 helps our state prevent the slippery slope of mandated healthcare.

I also happen to be someone living with a chronic autoimmune disease and have a child with a rare genetic condition. I require treatments every six weeks that lower my immunity. I am unable to take live vaccinations. My son's condition also puts him at higher risk for illness. I have to safeguard myself and my son when it comes to illnesses. I was educated about these precautions by my own healthcare provider. And I take the precautions for my own health and my child's, this includes vaccinations. I do not believe **others** should be mandated to take a vaccination to protect me or my son, as I know that **no vaccination is 100% effective**. Someone who cannot take vaccinations should be taking precautions to protect their health at all times, not just in school. Do we then require all public places to monitor vaccination records to protect those that cannot vaccinate?

I am very fearful of a society that judges individuals on their ability to take a vaccination. I am fearful of a society that limits an individual's ability to attend school or daycare based on the opinions of others. There will always be new illnesses. There may be another pandemic on the horizon. We cannot use the fear associated with COVID-19 to cloud our judgment on constitutional rights.

In summary, individuals worried about illness have the right to choose to vaccinate themselves and their children for their own protection. They also have the responsibility to protect themselves in regards to their health. Individuals who are unable to vaccinate should already be taking precautions to protect themselves as vaccinations are never 100% effective. For the above stated reasons I urge you to support House Bill 1320.

Sincerely,

Cori Randall, APRN FNP-C

I support HB1320.

Respectfully,

Dr. Allen Rudolph

January 19th, 2021

Dear ND House Human Services Committee Members,

I am writing this morning to urge you to support and pass:

HB 1307 that would enact a law that prohibits places of public accommodation from refusing services, goods, or access to facilities to individuals who refuse vaccination.

HB 1320 that would prohibit state and local government from mandating vaccination and would prohibit making the receipt of a vaccine a condition for entry, education, employment, or services.

HB 1306 that would establish an interim committee to study the interrelationship between sudden infant death syndrome, vaccines, and autism spectrum disorder in children.

I am a retired pharmacist having worked 32 years in hospital, community, and compounding pharmacies. Having done so, I have been eyewitness to vaccine injury over the years and have grave concerns over the SARS-COV2 vaccine. New pharmaceutical drugs commonly take 7-8 years to come on the market because of extensive animal and human trials done first to ensure safety of the drug and thereby ensure the pharmaceutical manufacturer will not face exorbitant damage liability. However, as you likely know, vaccine manufacturers are exempt from damage liability. Though it is amazing that this vaccine has been formulated in a short amount of time, it has not passed the test of time and trials to determine safety. I also oppose this vaccine because it is a mRNA vaccine with the possibility of being incorporated into one's genetic code. Also, the use of cell lines from aborted babies is highly problematic for religious reasons.

Last September, I was sick with what appeared to be COVID and recovered without incident. I have had numerous bouts of influenza in my lifetime which were worse. My observation has been that people with symptoms have not been treated adequately in the early stages of the disease, especially when complaining of shortness of breath. I know of MD's who successfully treat people with Vitamin C, D, and Zn, Quercetin, HCQ or Ivermectin, and Budesonide for inhalation. These treatments were vilified by the powers that be who likely stood to benefit from the emergency authorization of the vaccines. Herd immunity will happen without vaccines. The number of deaths due to COVID is dropping weekly. I would encourage you to keep that statistic before you, and not the number of cases which is determined by a test with dubious false positives. Also, the study of the 30 million people in Wuhan showed that there is not asymptomatic spread of the virus.

Finally, I believe that implementation of a laws to prevent people without the vaccine from enjoying their rights as citizens of the United States of America is unconstitutional. For most, this disease is not worse than the common flu and draconian measures to attempt to vaccinate everyone with an untested vaccine is reckless and suspect. Thank you so much for your time and consideration of my concerns.
Regards,

Maureen Bratten
827 19th St E
Dickinson, ND

Althouse and Scarpino *BMC Medicine*
DOI 10.1186/s12916-015-0382-8

BMC Medicine

RESEARCH ARTICLE Open Access

Asymptomatic transmission and the resurgence of *Bordetella pertussis*

Benjamin M. Althouse* and Samuel V. Scarpino

Abstract

Background: The recent increase in whooping cough incidence (primarily caused by *Bordetella pertussis*) presents a challenge to both public health practitioners and scientists trying to understand the mechanisms behind its resurgence. Three main hypotheses have been proposed to explain the resurgence: 1) waning of protective immunity from vaccination or natural infection over time, 2) evolution of *B. pertussis* to escape protective immunity, and 3) low vaccine coverage. Recent studies have suggested a fourth mechanism: asymptomatic transmission from individuals vaccinated with the currently used acellular *B. pertussis* vaccines.

Methods: Using wavelet analyses of *B. pertussis* incidence in the United States (US) and United Kingdom (UK) and a phylodynamic analysis of 36 clinical *B. pertussis* isolates from the US, we find evidence in support of asymptomatic transmission of *B. pertussis*. Next, we examine the clinical, public health, and epidemiological consequences of asymptomatic *B. pertussis* transmission using a mathematical model.

Results: We find that: 1) the timing of changes in age-specific attack rates observed in the US and UK are consistent with asymptomatic transmission; 2) the phylodynamic analysis of the US sequences indicates more genetic diversity in the overall bacterial population than would be suggested by the observed number of infections, a pattern expected with asymptomatic transmission; 3) asymptomatic infections can bias assessments of vaccine efficacy based on observations of *B. pertussis*-free weeks; 4) asymptomatic transmission can account for the observed increase in *B. pertussis* incidence; and 5) vaccinating individuals in close contact with infants too young to receive the vaccine ("cocooning" unvaccinated children) may be ineffective.

Conclusions: Although a clear role for the previously suggested mechanisms still exists, asymptomatic transmission is the most parsimonious explanation for many of the observations surrounding the resurgence of *B. pertussis* in the US and UK. These results have important implications for *B. pertussis* vaccination policy and present a complicated scenario for achieving herd immunity and *B. pertussis* eradication.

Keywords: *Bordetella pertussis*, Whooping cough, Asymptomatic infection, Phylodynamic analysis, Stochastic disease dynamical modeling, Vaccination policy

Background

Many countries have seen a startling increase in the incidence of *Bordetella pertussis*, an important causative agent of whooping cough, over the past 20 years [1]. In the United States (US), 2012 saw more diagnosed *B. pertussis* cases than in any year since 1955 (Fig. 1 and [2], accessed 20 January 2015). The United Kingdom (UK) has seen a similarly startling rise, with more cases occurring in 2013 than since the vaccine refusal era of the 1970s and 1980s (data available here: [3], accessed 20 January 2015). Two general hypotheses have been proposed to explain the rise in *B. pertussis* incidence: either vaccination coverage is too low, where individuals remain unvaccinated or unvaccinated susceptible individuals move into populations; or vaccinated individuals can still become infected [1, 4]. While vaccination coverage has likely played a role in increasing incidence, coverage has historically been high [1, 5], raising the likelihood that the resurgence is — at least in part — due to low vaccine effectiveness [6].

To date, three primary mechanisms have been proposed to explain why vaccinated individuals can become

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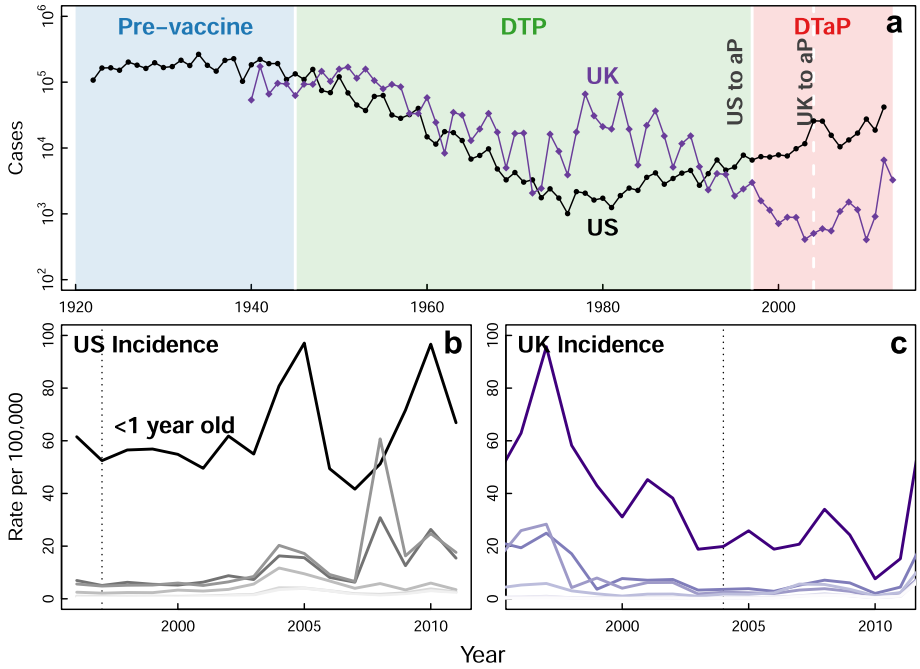

Fig. 1 Increase in *B. pertussis* incidence over time. Panel **a** shows *B. pertussis* cases in the United States from 1922 through 2012 and in the United Kingdom from 1940 through 2013 (from: [17] and [70]). Shaded regions correspond to the pre-vaccine era, the DTP era, and the DTaP era, respectively. Panels **b** and **c** show the incidence of *B. pertussis* by age group with darker color indicating younger ages in the US and UK, respectively. Infants less than 1 year old are labeled in darkest colors

infected with *B. pertussis*: 1) the vaccine mounted a sterilizing immune response that waned over time [7], 2) the pathogen evolved to escape sterilizing immunity induced by the vaccine [8], or 3) the vaccine failed to induce sterilizing immunity to the pathogen [9]. While the first two mechanisms have received considerable attention, the third was only recently proposed by Warfel, Zimmerman, and Merkel (2014) [9]. In their study, Warfel et al. used non-human primates as a model for *B. pertussis* infection, and found evidence that individuals vaccinated with current acellular *B. pertussis* vaccines (aP) can become asymptomatically infected, and can then transmit infection to susceptible individuals. The potential for this type of vaccine failure has been observed in humans where reanalyses of aP vaccine studies revealed that individuals vaccinated with components of the aP vaccine were protected against disease, but not bacterial colonization [10, 11]. This is in addition to the extant, but limited, evidence for natural asymptomatic infection [12–14].

Warfel et al. point out that asymptomatic infection in aP vaccinated individuals, and subsequent transmission, may partially account for the increase in observed *B. pertussis* incidence. However, from a public health perspective, the presence of vaccine-induced or naturally infected asymptomatic individuals who transmit disease could have consequences beyond facilitating an increase in incidence. In response to Warfel et al., Domenech de Cellès et al. (2014) [15] argue that a reduction in incidence among unvaccinated individuals in a population with high aP coverage shows that aP must reduce *B. pertussis* transmission to some extent. It may be that aP vaccinated infected people are less efficient at transmitting *B. pertussis* compared with unvaccinated infected people, though it is not clear to what extent [16].

Here, we examine incidence and genetic data to provide empirical support for asymptomatic transmission and then construct mathematical models of *B. pertussis* transmission to explore the public health consequences of asymptomatic transmission. Our results suggest that: 1) there is strong empirical support for asymptomatic transmission from both the epidemiological and genomic data; 2) the presence of asymptomatic transmitters will bias estimates of vaccine efficacy derived from observations of stochastic fadeouts across cities; and 3) asymptomatic transmission provides the most parsimonious explanation for many of the observed patterns associated with current *B. pertussis* dynamics in the US and UK (that is, the resurgence of cases, the changes in age-specific attack rates, the observed level of bacterial genetic variation, and the failure of

ring-vaccinating, or "cocooning", unvaccinated infants). The results on vaccination have important public health and clinical implications, especially related to recommendations for isolating unvaccinated or partially vaccinated infants.

Methods

Empirical data

All reported *B. pertussis* cases in the United States from 1922 through 2012 were obtained from the US Centers for Disease Control (CDC) [17], and all reported *B. pertussis* cases for the United Kingdom from 1940 through 2013 were obtained from Public Health England (PHE, data available here: [18], accessed 8 October 2014). Age-specific *B. pertussis* incidence was obtained from the CDC and the PHE. Population sizes for the denominators were obtained from the US Census through the CDC, and for the UK from the UK Office for National Statistics (data available here: [19], accessed 8 October 2014). Historic US incidence data come from the CDC's Public Health Reports and Morbidity and Mortality Weekly Reports (MMWR), digitized and downloaded from Project Tycho [20, 21].

The model

We formulate deterministic and stochastic Susceptible, Infected, Removed (SIR) models of *B. pertussis* transmission [22–24]. Briefly, susceptible individuals are born at rate μ, where they are vaccinated with either the whole-cell (wP) or acellular (aP) *B. pertussis* vaccine, depending on which vaccine is currently in use. Our model includes three vaccine epochs: one without vaccination, one with only wP vaccination, and one with only aP vaccination. These epochs are non-overlapping, similar to the advent of wP and its replacement by aP [25]. We assume those vaccinated with wP are completely immune to infection (see Discussion). Those vaccinated with aP move into a vaccinated class where they can become asymptomatically infected (that is, they incur a direct benefit from vaccination because they will not develop symptomatic disease [26, 27]). Unvaccinated individuals become infected with *B. pertussis* at rate β and become symptomatic with probability σ (sensitivity to which is explored in the supplementary information Additional file 1), and aP vaccinated individuals become asymptomatically infected at rate β. We assume no difference in transmissibility between symptomatic and asymptomatic individuals (see Discussion and Additional file 1). Individuals recover from symptomatic and asymptomatic infection at rates γ_s and γ_a. Individuals die at rate ν, which we set equal to μ to keep the population size constant. Individuals can wane from protective immunity at rate ω. The equations governing transmission dynamics are:

$$\begin{aligned} S'(t) &= \mu \cdot (1 - wP - aP) - \beta[I_s(t) + I_a(t)]\, S(t) \\ &\quad + \omega R(t) - \nu S(t) && (1) \\ I_s'(t) &= \beta\sigma[I_s(t) + I_a(t)]\, S(t) - \gamma_s I_s(t) - \nu I_s(t) && (2) \\ I_a'(t) &= \beta(1-\sigma)[I_s(t) + I_a(t)]\, S(t) + \beta[I_s(t) + I_a(t)] \\ &\quad V(t) - \gamma_a I_a(t) - \nu I_a(t) && (3) \\ V'(t) &= \mu \cdot aP - \beta[I_s(t) + I_a(t)]\, V(t) - \nu V(t) && (4) \\ R'(t) &= \mu \cdot wP + \gamma_s I_s(t) + \gamma_a I_a(t) - \omega R(t) - \nu R(t) && (5) \end{aligned}$$

We assume that the aP vaccine has 100 % efficacy in preventing disease; however, this is a conservative assumption with respect to our conclusions. We formulate both deterministic and stochastic (Gillespie stochastic simulation algorithm [28] with the binomial tau-leap approximation [29]) versions of the model. Analytical expressions for the basic reproduction number (R_0) and model equilibria are given in Additional file 1.

Phylodynamic analysis

We fit a series of phylodynamic models to concatenated single nucleotide polymorphisms (SNPs) identified from whole *B. pertussis* genome sequences isolated from patients infected in the US between 1935 and 2005 [30]. The resulting data set contained 36 isolates: 2 from the pre-vaccine era, 8 from the wP vaccine era, and 26 from the aP vaccine era, each with a nucleotide length of 5,414 bases. Sequencing, alignment, and variant calling were all performed by Bart et al. (2014) [30].

Using this data set, we inferred the parameters of a phylodynamic model using Bayesian Markov chain Monte Carlo (MCMC) methods implemented in BEAST 2.1 [31] with a Hasegawa-Kishino-Yano (HKY) substitution model, as suggested by jModelTest 2.1 [32], and a birth-death skyline tree model with serial sampling [33]. The underlying model is a stochastic birth-death process, which is the same underlying stochastic process for models such as SI, SIR, and SEIR. We are interested in two parameters: the birth rate, which is the rate at which new cases enter the population through transmission; and the sampling rate, which is the rate at which cases leave the population because they are sampled. We make the assumption that sampling a case, that is, collecting *B. pertussis* bacteria and sequencing the genome, removes that infected individual from the population. This is an assumption, but it appears logical: once an individual is diagnosed with whooping cough, and *B. pertussis* isolated, the individual is no longer transmitting due to having cleared the infection, or being socially removed from susceptible individuals. Convergence of the model was obtained with two independent MCMC runs of more than 75 million generations and confirmed with effective sample size (ESS) values above 200 calculated with TRACER v1.6. Similar results were obtained using both a relaxed lognormal and relaxed exponential molecular clock [34].

Results

Empirical evidence of asymptomatic transmission

Despite its perceived importance, ascertaining evidence for asymptomatic transmission for any disease remains a challenge. This has been especially true with *B. pertussis*, where identifying individuals asymptomatically infected has historically been difficult [12–14]. Perhaps the most compelling piece of evidence for asymptomatic transmission is the documented failure of cocooning to protect newborns [35, 36], which can only be parsimoniously explained by asymptomatic transmission [9]. Other empirical patterns are expected — in both incidence and genetic data — if asymptomatic transmission is occurring as a result of the aP vaccine preventing symptomatic disease, but failing to block transmission. Here we provide empirical observations, which are both consistent with and in total most parsimoniously accounted for by asymptomatic transmission.

Figure 2 shows a wavelet analysis of *B. pertussis* incidence in the UK in unvaccinated and under-vaccinated infants (< 1 year old), both considered indicators of overall *B. pertussis* transmission in a population [37]. As wP vaccine coverage increases to greater than 90 % (from the early 1980s to the early 1990s) we see a disruption of the natural approximately 4-year periodicity of *B. pertussis* cases driven by susceptible turnover [38, 39]. However, the switch from wP to aP in the UK coincides with the return of cyclic patterns, which are similar to the approximately 4-year periodicity seen in the pre-vaccine era.

A second line of evidence comes from changes in age-specific attack rates in the US and UK. Both countries switched to the aP vaccine; however, the US switch occurred seven years before the UK switch. Changes in age-specific attack rates are observed in both countries after switching to the aP vaccine, and appear similar when viewed as time since the switch to aP (Fig. 3). Another important facet of these data is that within both countries the rise in attack rates is synchronous across age groups. These two observations would be an expected consequence of asymptomatic transmission from aP vaccinated individuals as fully aP vaccinated individuals become old enough to attend school and become infected. These observations are challenging to explain with either waning immunity or pathogen evolution alone; for example, waning immunity should most often induce asynchrony in age-specific attack rates [22]. Increases in incidence could be explained by heterogeneous vaccine coverage or

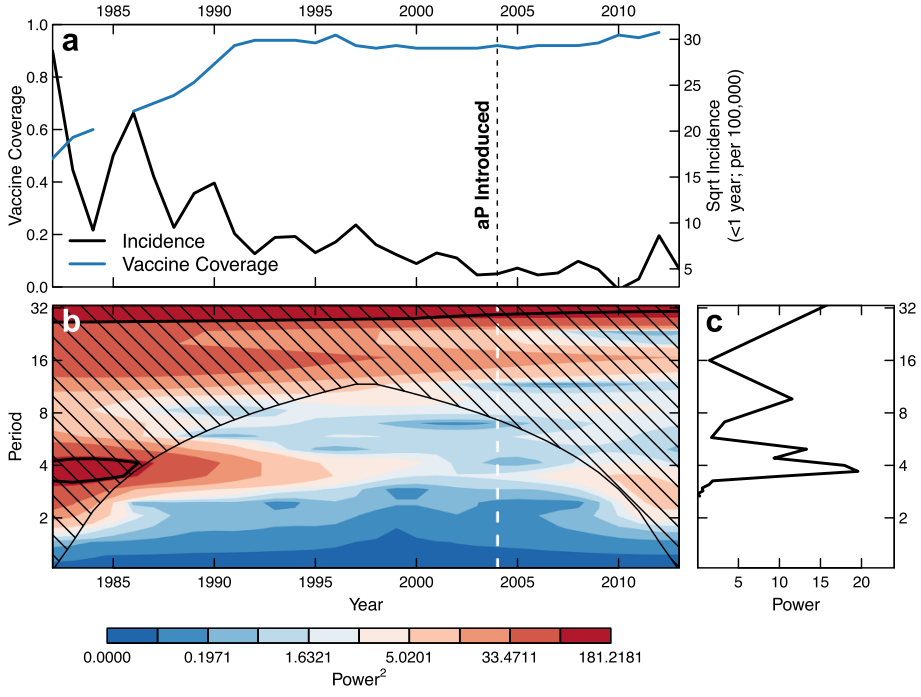

Fig. 2 Disruption of *B. pertussis* cycles by vaccination. Panel **a** shows the square root of *B. pertussis* cases in infants less than 1 year old in the United Kingdom from 1982 through 2013 (in black) and the percentage vaccine coverage over the same period (in blue). Vertical dashed line indicates the switch to an aP vaccination schedule. Panel **b** shows the standard wavelet spectrum of the incidence in panel **a**; panel **c** shows the Fourier spectrum of the incidence. As vaccination coverage increases (1985 through about 1991) we see a decrease in the power of cycles of approximately 4 years. We begin to see an increase in this power after the introduction of aP vaccination in 2004, suggesting transmission patterns similar to those observed in the pre-transmission-blocking vaccine era

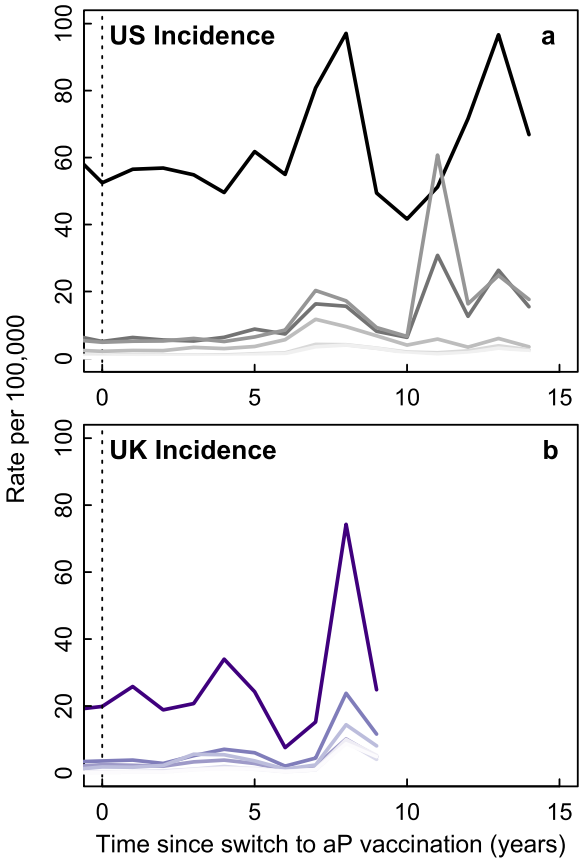

Fig. 3 Increase in *B. pertussis* incidence after switch to aP vaccination. Figure compares the incidence of *B. pertussis* after the switch to aP vaccination in the US (panel **a**) and the UK (panel **b**). Time since the switch is presented on the x-axis. Note the similarities in the timing of spikes in incidence after the switch to aP vaccination

changing vaccine effectiveness, which we are assuming in switching from the wP to aP vaccine.

Lastly, we find evidence consistent with asymptomatic transmission using the results of a transmission-oriented phylodynamic model [31] fit to 36 US *B. pertussis* genomes [30]. Asymptomatic transmission is expected to cause a mismatch between incidence estimated from case data and incidence reconstructed from genetic data. Intuitively, this happens because the population genetic variation of the bacteria is a function of the entire infected population size, while case data can only come from symptomatic individuals. This is true even if bacterial sequences are only collected from symptomatic individuals, assuming asymptomatic and symptomatic individuals are mixing with each other. The observed pattern can only be accounted for by asymptomatic transmission or underreporting. Because whooping cough reporting has increased in recent years [40, 41], asymptomatic transmission remains the only plausible explanation for the observed population genomic pattern.

Figure 4 shows the changes in sampling and rates since the mid-1960s for the US. We see an increase in the birth rate after the switch to aP, as expected given the rise in incidence; however, we see a decrease in the sampling rate after the switch to aP. This mismatch between the birth rate and sampling rate indicates that, despite increasing numbers of new *B. pertussis* cases, the fraction of cases identified decreases. Importantly, the estimated decrease in the sampling rate coincides with the time-window containing the largest number of sampled bacteria and in an era with the greatest accuracy in the laboratory methods used in diagnosing *B. pertussis* cases [42]. This finding is indicative of an increase in the overall genetic diversity of *B. pertussis* in the population after the US switched from the wP to the aP vaccine. Natural selection favoring a vaccine escape variant would be expected to reduce the genetic variation and increase the estimated sampling rate, as seen in Australia by Bart et al. [30]. Additionally, waning immunity could result in an increase in the genetic diversity of the bacterial population; however, without systematic underreporting it would not result

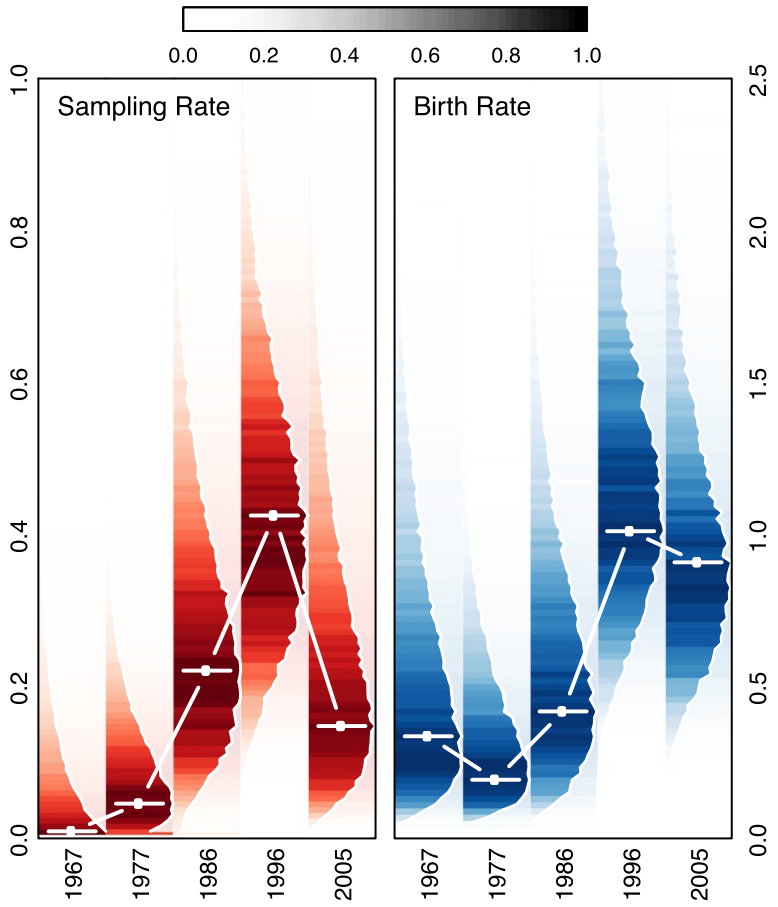

Fig. 4 Phylodynamic analyses. Figure shows the sampling rate and birth rate derived from the BEAST analysis for the 36 US *B. pertussis* genomes. Solid white lines with square boxes indicate the posterior median, with the shaded region indicating the 95 % highest posterior density. Darker colors are associated with regions of higher posterior density, with the shape representing the actual posterior density. Despite the birth rate remaining higher after the switch to aP, the sampling rate declines. This pattern would be expected with an increasing rate of asymptomatic transmission

in a lower estimated sampling rate. Again, we conclude that asymptomatic transmission remains the only parsimonious explanation for the observed phylodynamic patterns.

Consequences of asymptomatic transmission: biased estimates of vaccine effectiveness

Historically, a key indicator of success for vaccination programs is a reduction in pathogen transmission in populations, as measured by the mean proportion of disease-free weeks [24, 43, 44]. Figure 5 presents the proportion of reported *B. pertussis*-free weeks (fade-outs, panel **a**) and mean duration of fade-outs (panel **b**) for the 50 US states in pre-vaccine (1920–1945) and post-vaccine (2006–2013) epochs. The pre-vaccine epoch clearly has fewer weeks with no reported *B. pertussis* cases than does the modern vaccine epoch. This has been widely interpreted as evidence for decreasing levels of *B. pertussis* transmission and some degree of herd immunity afforded by the vaccine [7, 15, 44]. However, if situational awareness is impaired by a vaccine that protects against symptomatic disease but does not block transmission, interpreting reported *B. pertussis*-free weeks can be misleading.

Figure 6 presents the results of stochastic simulations of the model across various population sizes. Comparing the observed symptomatic cases in the no vaccine and aP vaccine eras, we see results qualitatively similar to empirical data [44]: introduction of aP vaccine leads to a higher proportion of *B. pertussis*-free weeks across population sizes (Kolmogorov-Smirnov [KS] test, $D = 0.46$, $p = 1.2 \cdot 10^{-9}$; panel **a**). However, examination of the asymptomatic population (the true burden) reveals many fewer weeks with no cases of *B. pertussis* (KS test, $D = 0.53$, $p = 1.2 \cdot 10^{-12}$; panel **b**), which is in fact not different from the pre-vaccine era (KS test, $D = 0.07$, $p = 0.97$; panel **c**).

Figure 7 demonstrates the percentage of the true infections observed at steady state ([Observed Incidence/Total

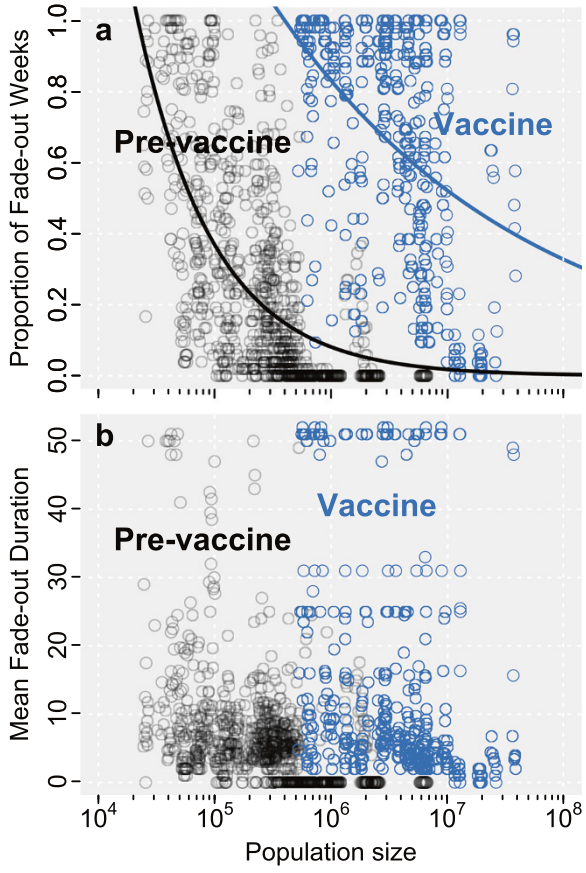

Fig. 5 Comparing disease-free weeks in pre- and post-vaccination scenarios. Panel **a** shows the proportion of disease-free weeks (fade-outs) per year for the 50 US states in the pre-vaccine (1920–1945, black points and line) and post-vaccine (2006–2013, blue points and line) eras. Lines indicate best-fit exponential curves. Panel **b** shows the mean duration of consecutive disease-free weeks in both eras

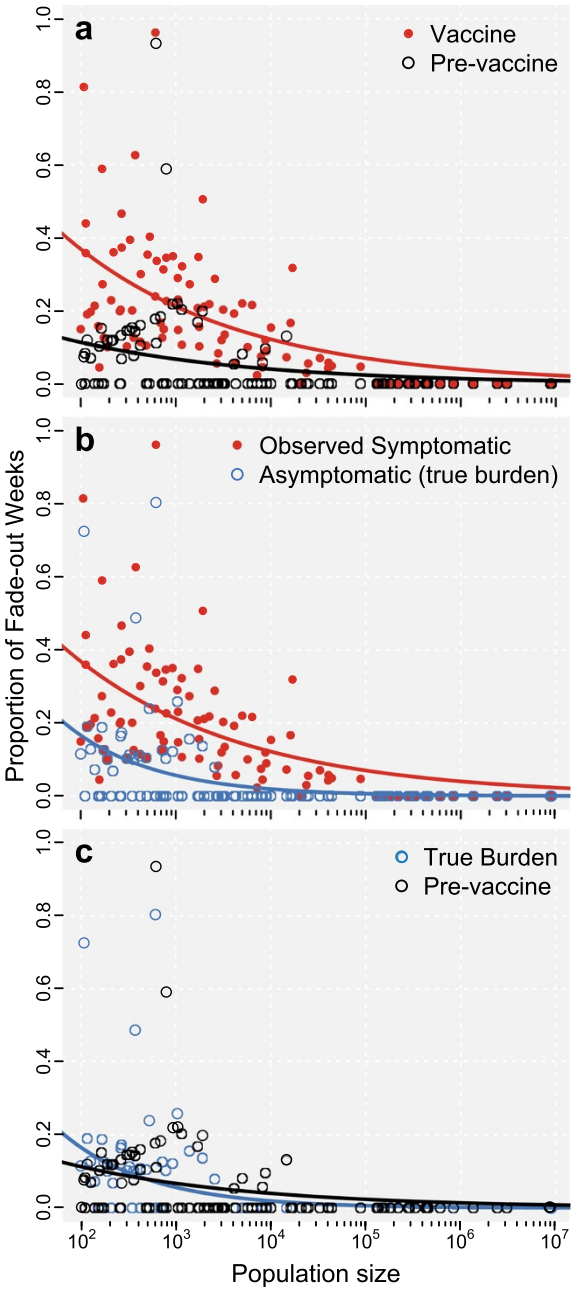

Fig. 6 Changes in transmission in pre- and post-vaccination scenarios? Figure shows the proportion of disease-free weeks (fade-outs) for various population sizes from the stochastic formulation of the model. Panel **a** compares the symptomatic cases in the aP vaccination era with those in the pre-vaccine era; panel **b** compares the symptomatic to asymptomatic cases in the vaccine era; panel **c** compares the asymptomatic cases in the post-vaccine era with those in the pre-vaccine era. These results demonstrate no changes in transmission due to vaccination. Parameters: birth rate (μ) = death rate (ν) = 1/75 years^{-1}; recovery rates for symptomatic (γ_s) and asymptomatic (γ_a) = 14 days^{-1}; probability of symptomatic infection (σ) = 0.25; transmissibility (β) is calculated per value of R_0

Incidence-1]*100) as aP vaccination rate increases and the probability of symptomatic infection (σ) increases. We find that for realistic aP coverage rates (between 85 % and 95 %), the percentage of total cases expected to be observed is low (< 15 %), and is highly dependent on the probability of an infection becoming symptomatic (a parameter that is generally not known). These results are likely to be conservative given the low, but unknown, diagnosis rate of asymptomatic infections and known underreporting of symptomatic infections in adults [45].

Consequences of asymptomatic transmission: increased *B. pertussis* incidence

Figure 8 illustrates the fold increase in observed symptomatic and unobserved asymptomatic infections after transitioning from a wP to an aP vaccine at equilibrium. This is calculated by dividing the number of symptomatic or asymptomatic cases with various levels of aP coverage

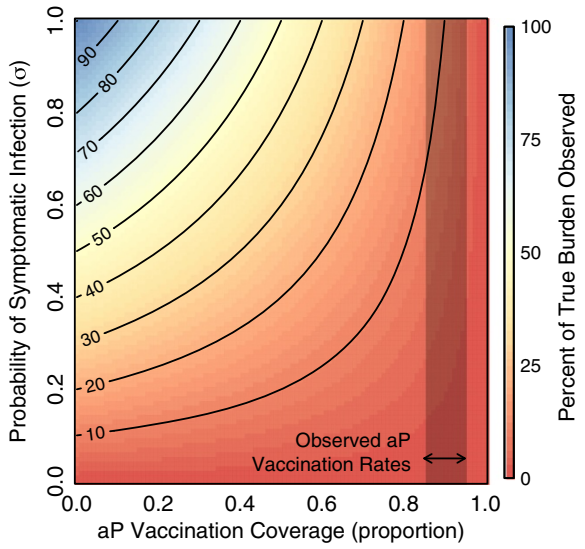

Fig. 7 How does an inefficient vaccine affect situational awareness? Figure shows the percent difference in observed infections (symptomatic) from true infections (symptomatic + asymptomatic) at steady state as aP vaccination rate increases and the probability of symptomatic infection increases. Shaded area indicates a range of reasonable aP vaccination rates. At current aP vaccination coverage levels, the majority of cases are asymptomatic and therefore undetected. See Additional file 1 for model details. Parameters: birth rate (μ) = death rate (ν) = 1/75 years^{-1}; recovery rates for symptomatic (γ_s) and asymptomatic (γ_a) = 14 days^{-1}; baseline *wP* vaccination rate = 0.9; transmissibility (β) is calculated such that $R_0 = 18$. Note that previously published values of R_0 for pertussis range from 16–20 [71] to closer to 5 in some populations [72]

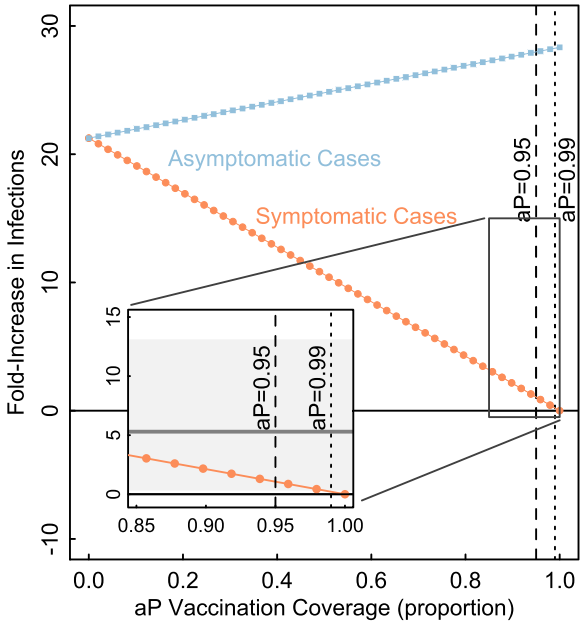

Fig. 8 Can an inefficient vaccine lead to increased transmission? Figure demonstrates the fold increase in observed symptomatic and unobserved asymptomatic infections after transitioning from a wP to an aP vaccine. This is calculated by dividing the number of symptomatic or asymptomatic cases with various levels of aP coverage (reported on the x-axis) and 0 % wP coverage by the number of cases with 90 % wP coverage and 0 % aP coverage. This was designed to simulate the switch from wP to aP in the US and UK (going from high wP coverage to coverage with aP). We see an increase in symptomatic cases across a large range of aP vaccination coverage levels. See Additional file 1 for model details. The gray band indicates the empirical 5.4-fold (95 % bootstrap confidence interval: 0.4–13.3) increase in cases in the US comparing 2012 to the years 1985 through 1995. The model recreates the observed increase in cases. Parameters: birth rate (μ) = death rate (ν) = 1/75 years^{-1}; recovery rates for symptomatic (γ_s) and asymptomatic (γ_a) = 14 days^{-1}; probability of symptomatic infection (σ) = 0.25; baseline *wP* vaccination rate = 0.9; transmissibility (β) is calculated such that $R_0 = 18$

(reported on the x-axis) and 0 % wP coverage by the number of cases with 90 % wP coverage and 0 % aP coverage. This is done to simulate the switch from wP to aP in the US and UK (going from high wP coverage to coverage with aP), and indicates that a change in vaccine could partially account for the rise in cases.

As aP vaccination coverage increases, asymptomatic infections increase up to nearly 30-fold. We see a substantial increase in the observed numbers of symptomatic cases after wP vaccination is replaced by aP vaccination. At low to moderate levels of aP vaccination, there is a 5- to 15-fold increase in symptomatic cases. Only at extremely high levels of aP vaccination (> 99 %) is there no change in symptomatic infections. This is in line with the observed rise in *B. pertussis* incidence: cases in 2012 were 5.4-fold (95 % bootstrap confidence interval: 0.4–13.3) higher than cases in years 1985 through 1995 ([46]). This result is similar to previous findings by van Boven et al. (2005) [47], who found that as wP vaccination coverage increased, primary infections (symptomatic) decreased, while secondary infections (subclinical, or asymptomatic) increased.

Effects of waning immunity to *B. pertussis*

It is clear that waning immunity plays a role in the epidemiology of *B. pertussis*, though estimates of the duration of protection to *B. pertussis* are highly varied [7, 15, 48]. Because the exclusion of waning immunity was a conservative modeling assumption, we focused our analysis on a model where immunity due to vaccination was lifelong. However, as Fig. 9 demonstrates, the inclusion of waning immunity increases symptomatic infections up to 12 % and asymptomatic infections up to 8 %. Importantly, waning immunity would not explain the failure of infant cocooning strategies, the synchrony in age-specific attack rates after the switch to the aP vaccine as presented above, or the observed *B. pertussis* genomic patterns.

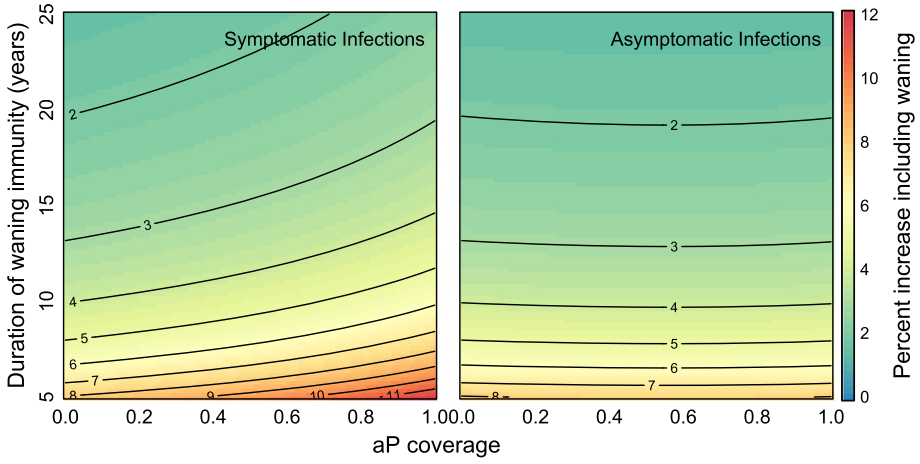

Fig. 9 Effects of including waning immunity on symptomatic and asymptomatic infections. Figure shows percent increases in symptomatic and asymptomatic cases at equilibrium after the switch to aP vaccination with inclusion of waning immunity. Parameters: birth rate (μ) = death rate (ν) = 1/75 years^{-1}; recovery rates for symptomatic (γ_s) and asymptomatic (γ_a) = 14 days^{-1}; probability of symptomatic infection (σ) = 0.25; baseline *wP* vaccination rate = 0.9; transmissibility (β) is calculated such that $R_0 = 18$

Discussion

In this paper, we have presented empirical evidence — from both case and genomic data — for asymptomatic *B. pertussis* transmission following the switch from the wP to the aP vaccine in the US and UK. Then, using mathematical and computational transmission models, we have demonstrated that an aP vaccine which blocks symptomatic disease but not asymptomatic transmission is able to account for the observed increase in *B. pertussis* incidence; complicates situational awareness surrounding levels of current *B. pertussis* transmission; and potentially biases estimates of vaccine efficacy obtained from case data. When coupled with the laboratory results on asymptomatic transmission in non-human primates from Warfel et al. (2014) and evidence from cross-sectional, human studies in China by Zhang et al. (2014) [12], we conclude that asymptomatic transmission from aP vaccinated individuals to fully susceptible individuals provides the most parsimonious explanation for the observed resurgence of *B. pertussis* in the US and UK, the changes in age-specific attack rates, the observed increase in *B. pertussis* genetic variation, and the multiply demonstrated failure of cocooning unvaccinated infants [35, 36].

Our observation of increased cases due to asymptomatic or subclinical infections has been noted in previous studies of wP vaccination [47–49], as well as examinations of the effects of natural and vaccine-induced protection on the duration of immunity [4, 50]. While these previous studies suggest that asymptomatic infections may account for an increase in whooping cough incidence, they do not provide strong evidence of asymptomatic transmission and do not discuss the failure of infant cocooning. Also, these studies were focused on cases occurring during the wP vaccine era.

There are several limitations to the data presented in this study. First and foremost is a lack of publicly available data to more fully explore the hypotheses suggested. This lack of available data is well known among researchers studying *B. pertussis* [51]. Longer time series of age-stratified data (specifically in infants too young to be vaccinated) would be required to fully explore how the natural periodicity of *B. pertussis* incidence shifted as wP coverage changed. However, these data either do not exist or are unavailable to researchers. A second issue is that clearly not enough time has elapsed since the switch to aP to draw definitive conclusions about the resumption of cycles of *B. pertussis* incidence. While the data appear most consistent with asymptomatic transmission from aP vaccinated individuals, it may be many years before enough time has elapsed to be able to rule out this hypothesis.

In this study we focused on the United States and the United Kingdom where *B. pertussis* incidence has increased in the past 20 years. We acknowledge that this resurgence is not universal and that countries vary greatly in reporting rates, vaccine composition or schedule, historical and current vaccination coverage levels, and the genetic diversity of *B. pertussis* strains [1]. The initial increase in US *B. pertussis* cases also began before the aP switch. However, the empirical evidence we presented, specifically the phylodynamic results, wavelet analysis, changing attack rates, and failure of cocooning, all occurred after the aP switch. It may also be the case that a large factor in the observed resurgence is the improvement in *B. pertussis* diagnostics; however, this

would not explain the bulk of the empirical evidence presented here. Disentangling the effects of this variation, in order to evaluate hypotheses to explain the resurgence, will require high resolution case and genetic data. The US and UK have the largest, publicly available, sufficiently granular data, but only the US had a sufficient number of *B. pertussis* genomes available to conduct phylodynamic analyses.

Although the phylodynamic results from the US provide support for an increase in the asymptomatic population size after the switch to the aP vaccine, that analysis has a number of important caveats. First, genomic data were only available through 2005, leaving nearly the last decade without samples. Second, although the posterior median estimate of the sampling rate decreases drastically after the switch to the aP vaccine, the 95 % highest posterior densities overlap. As a result, we are unable to statistically conclude that sampling rates are lower. Third, an increase in underreporting could also explain a decrease in the estimated sampling rate; however, due to changes in *B. pertussis* diagnostics [1, 42] it is unlikely that there has been a substantial *decrease* in underreporting coinciding with the aP switch. Nevertheless, the well-documented issues associated with underreporting of *B. pertussis* cases in adults remains an important area for future phylodynamic studies [52]. Lastly, data availability prevented us from performing phylodynamic analyses in different countries. For example, predictions could be tested for those countries where: a resurgence is also occurring (such as the UK) [1], case counts remain fairly constant and low (such as Italy) [1], molecular evidence highlights the importance of vaccine escape (such as Australia) [30, 53], and where the wP vaccine is still in use (such as Kenya) [54].

As is the case with all models, the one used in this study makes a number of simplifying assumptions. However, most of these assumptions render our conclusions conservative. We assume that wP vaccination is 100 % effective, which is not the case [55]. Relaxing this assumption is analogous to having lower coverage overall, and thus our estimates of fold increase after the aP switch are conservative. Our model does not explicitly account for evolution of the *B. pertussis* bacterium [7, 56] — a factor which may play a large role in the epidemiological dynamics of *B. pertussis*. For example, it has been posited that *B. pertussis* has adapted to vaccination in several European countries. Mooi et al. (2001) identified genetic changes between pre- and post-vaccination strains of *B. pertussis* [8]. Despite this evidence, including evolution would merely increase the number of individuals susceptible to both symptomatic and asymptomatic infection and would yield exactly the opposite pattern of population genomic variation than seen empirically.

Our model also assumes that symptomatic and asymptomatic infections have the same basic reproduction number. Asymptomatic or subclinical/misdiagnosed individuals may spread *B. pertussis* through direct contact, breathing, or coughing [57]. Although coughing may increase transmission, the total bacterial load in the nasopharynx of *B. pertussis*-infected non-human primates is similar between symptomatic and asymptomatic individuals (see Figure one, panel a in [9]). The same study suggested that the duration of higher bacterial loads may be longer in asymptomatic individuals, and that there may not be differences in routes of transmission between asymptomatic and symptomatic individuals. However, and perhaps more importantly, being asymptomatic suggests that individuals may not alter their behavior and thus contact more individuals than a symptomatic individual [58]. Therefore, it seems equally plausible to conclude that the R_0 for aP vaccinated individuals is higher [47]. Future studies should make estimating the distribution of effective reproductive numbers for symptomatic and asymptomatic individuals a priority.

It is important to note that distinguishing true asymptomatic infections from attenuated, symptomatic infections, especially in older age groups, is challenging. If infections were truly asymptomatic, interventions based on teaching clinicians about the potential range of clinical presentations of *B. pertussis* infection would not work, while proper identification of attenuated symptomatic infections could allow for proper increased use of prophylactic measures. Finally, our study assumes a constant probability of symptomatic infection, whereas previous work has shown the probability of becoming symptomatic may depend on the history of exposures of an individual [59]. Future work should explore the probability of symptomatic infection and its potential changes over the life of an individual.

Conclusions

That there has been a rise in whooping cough incidence in many countries around the globe is irrefutable. The findings presented in Warfel et al., in conjunction with ours, have profound implications for the understanding of *B. pertussis* transmission dynamics and for vaccination policy. Specifically, our results would explain the negative outcomes found in recent studies of postnatal cocooning [35, 36] and would further complicate efforts to achieve herd immunity and possible eradication [60]. Long-term solutions to *B. pertussis* vaccination are necessary, and new vaccines are in development [61, 62]. In the years before a new vaccine is ready for clinical use, other options are necessary for reducing incidence, including vaccination of pregnant women [63, 64] or potentially a switch back to wP vaccination as a priming dose [65–67].

Clearly, more research is necessary, but if our results hold, public health authorities may be facing a situation similar to that of polio, where vaccinated individuals can still transmit infection [68]. This suggests further modifications of recommendations to clinicians for protecting unvaccinated children [69] and ensuring that aP coverage remains high. Our results on the potential surveillance bias associated with *B. pertussis* incidence highlight a critical need for population-wide serological surveys to detect recent infection, studies to examine the genetic diversity of the *B. pertussis* bacterium, more detailed studies of the incidence rate in unvaccinated individuals, and increased active surveillance of attenuated symptomatic *B. pertussis* infections. In light of current evidence and our results, we cannot dismiss the potential far-reaching epidemiological consequences of asymptomatic transmission of *B. pertussis* and an ineffective *B. pertussis* vaccine.

Additional file

Additional file 1: Supplementary Information. Supplementary Information includes model equation and further details, as well as analytical calculations of the steady-state equilibria and R_0. It also includes sensitivity analyses for the force of infection (β) and the fraction of symptomatic infection (σ).

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
BMA and SVS conceived all models and phylodynamic analyses. BMA executed the models, and SVS executed the phylodynamic analyses. BMA and SVS wrote the manuscript. Both authors read and approved the final manuscript.

Acknowledgements
The authors thank David Dowdy, Damien Caillaud, and Laurent Hébert-Dufresne for helpful discussions, Nick Generous for providing MMWR *B. pertussis* data for the post-vaccine era used in Fig. 5. This work was supported by the Omidyar Group and the Santa Fe Institute.

Received: 18 February 2015 Accepted: 22 May 2015
Published online: 24 June 2015

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Members of the Committee,

Again, I am Melyssa Howry, from New Town. I am going to address this from a different angle, as I have already submitted other testimony regarding vaccine safety and efficacy for the other two bills being heard today. Please know that I consider both of those testimonies to be relevant to all of the bills in this hearing today. I am in support of HB1320, however I would like to suggest language in addition to what has already been adjusted. My suggestion is in regards to homeschoolers. Currently in the state of North Dakota, homeschoolers are required to submit immunization records and/or exemption forms along with letters of intent to homeschool. As other written testimony has stated, immunizations are required for attendance in a public school setting, because of gathering daily with a large group of other children and adults. However, homeschoolers are almost never in the public school setting. The state that I am previously from, New Hampshire, does not require any medical information to be provided for homeschoolers. This information is private and irrelevant, as I previously stated. I believe it's unnecessary and therefore, further amendments should be made to exempt homeschoolers from needing to provide this information to public schools.

Another point I would like to make is that requiring immunization records does not prevent the spread of disease. Children might be up to date on certain vaccines, but there is still a possibility of outbreaks in school settings. In fact, there are several instances throughout the country of pertussis and measles outbreaks, in mostly or even fully vaccinated groups. This is due to the fact that the measles vaccine does not provide lasting immunity, as I can personally attest to. I was tested for immunity when I was pregnant with my first child, and was found to have none, even though I am fully vaccinated. My mother also was informed that she is no longer immune to the measles, either. I have heard this same information from many other adults who have had their bloodwork done to test for measles immunity.

Something similar is true of the pertussis vaccine. While it is advertised as being important for adults to get a pertussis shot in order to be around newborns and young children who cannot yet receive the shot, this is misleading. Research in the past few years has discovered that the pertussis vaccine, similar to what has been discovered with the Covid-19 vaccine, only masks symptoms for the person who received the shot, but will not prevent them from contracting and spreading pertussis. In fact, it makes them more likely to spread the illness to someone who is vulnerable, because they will not have the tell-tale symptoms, such as a cough or fever, that would lead them to avoid leaving the house. Instead, they will freely move about, believing they are "protected", when in fact they could truly spread a dangerous illness to an infant or other immune-compromised individual.

Here is an article highlighting one such incidence in our country within the past two years. This is a key quote:

"Forty-six students have been diagnosed with pertussis at Harvard-Westlake, where enrollment is about 1,600. Eighteen students there have not been

vaccinated against pertussis, but none of them has caught the illness, school spokesman Ari Engelberg said."
https://www.latimes.com/local/california/la-me-ln-whooping-cough-vaccine-20190316-story.html

Those who did not receive the vaccine did not contract pertussis at all. While we don't know the reason for this, it does present the possibility that unvaccinated individuals are not necessarily the drivers of the spread of illness. There are other factors, which need to be studied further. If people contract natural pertussis, they are immune for life, and therefore provide true protection. If they are vaccinated, they can possibly be protected from the severe symptoms for a few years, but can still spread the infection to others.

The next document I will submit as written testimony is the study on how pertussis can still be spread after vaccination.

In conclusion, I believe that these discussions should happen. Whether or not this bill passes, the conversation is an important one. Please hear the public, those who have experienced these things first hand. Many experts will weigh in, almost always in opposition to any bill regarding medical freedom. Please ask yourselves, why is that? What do they have to gain from giving people the freedom to make their own choices in regards to their own bodies? How do you personally feel about people being forced to put something into their bodies with which they have medical, philosophical, and/or religious objections? Speak with your constituents before dismissing these bills, I plead with you. Ask us what we think. You will find that these issues are important to many of us. Please do your own research before you make a decision. I am happy to chat with any of you further on this subject or on any of the other bills I submitted testimony for. Thank you for your time and consideration!

I am in support of this bill due to the incomplete science of the long term health effects of vaccinations. Where there is inherent risk, there should also be choice.

NDMA
Est.1887 NORTH DAKOTA MEDICAL ASSOCIATION

House Human Services Committee
HB 1320
January 19, 2021

Chair Weisz and Committee Members, I am Courtney Koebele, the executive director of the ND Medical Association. The North Dakota Medical Association is the professional membership organization for North Dakota physicians, residents, and medical students.

NDMA stands in opposition to HB 1320.

Childhood vaccinations have proven to be one of the most effective public health strategies to control and prevent disease. Reductions in childhood morbidity and mortality of many communicable diseases have significantly decreased in Western countries largely because of national immunization strategies aimed at infants and children.

According to a study in the National Center for Biotechnology (NCBI), it is estimated that for each U.S. birth cohort receiving recommended childhood immunizations, around 20 million illnesses and more than 40,000 deaths are prevented, resulting in $70 billion in savings.

The potential for vaccines to prevent morbidity and to save lives has never been greater, but this potential can only manifest if there is compliance with the recommendations for childhood and adolescent immunization.

Efforts by health care providers, as well as community- and government-based interventions to increase vaccine coverage, must continue in order to reduce morbidity and mortality in children due to vaccine-preventable diseases.

Thank you for the opportunity to testify today. I would be happy to answer any questions.

These bills regarding personal health freedoms have been brought to our attention. We would hope that you would support these bills to prevent discrimination against those who choose, for many different reasons not to vaccinate.

We have a voting-age son who has a documented reaction to a childhood vaccine and currently has a medical exemption for several vaccines. Knowing the things that can be triggered in a persons body by an immunization has caused us to be quite leery of many vaccines. We are certainly not “anti-vaxxers”, as our son and other family members have received certain other vaccines since his reaction. This term and the

negative attitude that go along with it are proof of the discrimination, shaming and bullying that already is happening to those choose to not vaccinate.
If doctors would not be so afraid to learn the truth about vaccine-triggered illnesses and be honest about them, people would have far more trust.
Ourselves and many, many people we have talked to are choosing to wait on receiving any covid vaccine until short & long term effects are known. Part of the problem is that we have already seen the denial by doctors of injuries/ negative reactions. Obviously resulting in lack of trust.
The thought of mandatory vaccines and the refusing of services/

discrimination to those who refuse is absolutely appalling and I would have never believed it could happen here in the United States of America, certainly not here in North Dakota. This should not be a partisan issue in any way. All you need to do is imagine yourselves or a loved one being forced to receive any sort of medical treatment that you don't want. The idea of taking away personal rights is a dangerous path to go down. We would ask that you support these bills and stand up for the personal health freedom of North Dakota residents!

Sincerely,

Patricia and Tyrone Unruh

Sykeston, ND

House Human Services
Robin Weisz, Chairman
January 19, 2021

Testimony by April Heinz
RE: HOUSE BILL NO. 1320

My name is April Heinz and I am in favor of HB 1320. As stated in my written testimony for House Bill No. 1307, immunizations are not for everyone. Each individual has a choice to get immunizations or not. It is the individual's choice as an adult and for minor's it is the parents' choice, not anyone else's, nor is it anyone else's business to know if someone has the vaccine or not!

I am proud to live in a state where I have the freedom to choose whether or not to immunize myself or my child with the facts I know. It should stay up to the individual to assess the risks of the vaccine and have the right to deny that vaccine, without consequences. My son is in daycare and will be in the school system in the future, please leave it up to ME to decide whether or not, I get or allow my child to get certain vaccines.

Please pass house bill 1320 and protect my rights to choose or refuse, while preserving access to employment, education, and services.

Thank you for your attention to this matter.

April Heinz

Lisa Pulkrabek
4795 Co Rd 82
Mandan, ND 58554
701-595-4264
wadenlisa@aol.com
Jan 19, 2021

Members of the House Human Services,

I am writing to you today in support of HB 1320 relating to immunizations required to enter daycare or school. I am very much in support of the new SECTION 3.

A new section to chapter 23-07 of the North Dakota Century Code is created and enacted as follows:
Limitations on immunizations. 1. A state or local elected official, the state, or a political subdivision of the state may not mandate an individual in this state receive a vaccination.
2. Subsection 1 prohibits making receipt of a vaccine a condition for entry, education, employment, or services.
3. Subsection 1 applies, notwithstanding authority granted under other provisions of law, including section 23 - 01 - 05, section 23 - 07 - 06, and chapter 37 - 17.1.
4. If a state or local elected official, the state, or a political subdivision of the state recommends an individual in this state receive a vaccination, the official or entity shall provide notice the recommendation is not mandatory.

I kindly urge a DO PASS on this.

Thanks for your time.
Lisa Pulkrabek

1-19-21

To whom it may concern,

One of my children received two vaccinations at the same time in his left arm, as was recommended by our pediatrician. He received the vaccinations and within hours his arm swelled up to 3-4 times its normal size, was red, hot, and he was in severe pain. We brought him back in to the clinic and they indicated he was having an allergic reaction to one of the vaccinations but were unable to differentiate which one it to was to as he had received 2 in the same arm. They also informed us "that there is no way to know for certain that it was a result of his vaccination." We brought him in to the clinic 4 times over the next 2 weeks from his symptoms not improving. They were only able to state, "There is nothing we can do." The response to us choosing to put something in our son's body, at a recommendation from our pediatrician, was our son being at risk of losing his arm. Thankfully, he did not, but the realty existed if his allergic response did not improve. We have since stopped vaccinating our children. I believe It should be a parent's right to decide if their child should or should not be vaccinated as we are the ones that assume the "risk of or death" as it states in the medical data sheets when getting the vaccinations. Along with our son having this allergic reaction to the vaccination, out of our 7 children, we have 1 that has severe allergies, it happens to be this same child. Up until the time he was vaccinated as an infant he tolerated eating all the foods we ate. Once vaccinated he has around 20+ allergies, some of them to the point of needing to have an epi-pen to protect his life. Is this a coincidence or is it a result of his vaccinations? We will never truly know the answer to that question and again were told, There is not way to know for certain that it is a result of his vaccination." We are the ones that have to sign a document stating we will not hold pharmaceuticals accountable for our choice. So, shouldn't it be our choice to vaccinate or not? I support HB 1320 as no individual should be forced to get vaccinated against their wishes. I support HB1306 as more research should be done to see if there is a relationship between vaccinations and injury to children. I believe my child was injured and there is nothing that was ever done to study the possibility of a link in his body. Recently through testing we discovered he has severely high levels of aluminum in his hair follicles, is this a coincidence or could it be related to his vaccinations from about 10 years ago? I urge our government to step up to doing more research and to put a stop to forcing parents to possibly cause harm to our own children through possible vaccine mandates.

Sincerely,

Erica Hanson

1-19-21
To whom it may concern,

This is a letter submitted to my employer regarding my application being denied to have an exemption from the flu vaccination this winter. I was denied an exemption 2 times, as I appealed their decision. Following my third attempt at filing for an exemption (see letter below), based on having adequate personal protective equipment being worn from covid-19 precautions, I was granted the exemption but not indefinitely. I was scheduled to work on a Saturday and Sunday, December 12-13, and was told if I had not received the exemption, I would not be able to return to work. They informed me on Friday, December 11, 2020 that I would be able to continue to work. I continue to work at Altru Health System and feel that I should not be mandated to have any vaccination in my workplace that has possible risk of "serious injury or death."

Sincerely,

Erica Hanson

November 23, 2020

To whom it may concern,

This does not make any sense to me. In the command center update I received on Friday it states,

"The COVID-19 vaccine will not be mandatory for employees. We have educational resources available for employees to read covering how a vaccine is developed, approved and manufactured."

Why is the flu vaccine mandatory with no exception for my personal views but not the covid virus vaccine? I don't understand why I can't have a reasonable accommodation made for me to still do my job. Why can't I have a reasonable accommodation, like the accommodation of wearing a facemask, while working with patients? If this is a method of preventing transmission of viruses, why can I utilize this method to prevent the spread of flu instead of getting a vaccination?

I ask Altru Health System to again reconsider their decision and make a reasonable accommodation to allow me to continue to work for this healthcare system.

Sincerely,

Erica Hanson

November 20 Denial letter
Erica:

I just wanted to inform you that after review of your flu shot exempt request by the review board, your exempt from the flu shot was not approved.

xxxx

This was my 2nd appeal letter

November 2, 2020

To whom it may concern,

I received notification that Altru health System has denied my request for an exemption from the flu shot this year. This email is an appeal to your decision. In Altru's email it states, "A determination has been made that those articles do not present evidence strong enough to make a change in policy. Your exemption has been denied at this time." I did not request a change in Altru's flu shot policy, I asked for a personal exemption from the flu shot. I should have a right to decide what I put in my body. In the list of side effects on the flu vaccination information sheet (VIS) from the CDC it states, "As with any medicine, there is a very remote chance of a vaccine causing a severe allergic reaction, other serious injury, or death." I have a right to decide if I accept the "very remote chance of death." I have a right to decide if I accept "Other serious injury" to my body. There are so many unknowns in the corona virus world we are in today that have me greatly concerned for what I choose to put in my body. I have attached additional research to provide additional evidence why I should be allowed to have an exemption from the flu vaccination.

(1) JAMA found 106,000 deaths in the US related to adverse effects of medication and it is likely that many others were not reported accurately as stated by my personal beliefs with medical error in the next link below: https://www.jhsph.edu/research/centers-and-institutes/johns-hopkins-primary-care-policy-center/Publications_PDFs/A154.pdf

(2) Medical error-the third leading cause of death in the US. If a person develops a life-threatening side effect from a vaccination would it get reported as such? I have personal testimony to one of my children having a severe allergic reaction to vaccinations and

yet Altru Health systems doctors stated to me and my husband, "There is no way to know for certain this is a result of his vaccination." Again, the VIS states, "Remote chance...death." : https://www.bmj.com/content/353/bmj.i2139

(3) "Seasonal influenza vaccines provide limited protection against divergent influenza strains. Therefore, the development of a universal influenza vaccine is a top priority for the NIH." https://pubmed.ncbi.nlm.nih.gov/33092070/

(4) https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm 9-60% flu vaccination efficacy "yet I should assume remote risk of death"

(5)"forms of immunity may lessen disease severity but are insufficient to prevent epidemic spread " https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-065X.2010.00974.x?fbclid=IwAR02J76-7RhsXhRSu6Uk7miCTqOiCjNXI9xZ8Cir96QtmB6sp5OCJZByyMQ

(6) What price is my health being bought for? I previously provided an article about money controlling decision making that may affect my health. Here is another article to support my concerns. "$4 billion global influenza vaccine market" https://www.genengnews.com/topics/translational-medicine/novartis-selling-flu-vaccine-business-to-csl-for-275m/#:~:text=Novartis%20is%20selling%20its%20influenza,set%20to%20close%20next%20year.
https://www.cnbc.com/2015/10/19/the-16-billion-business-of-flu.html
I should question if WHO is making decisions in my best interest when the 2 greatest financial contributors are Warren Buffet and Bill Gates. https://www.politico.eu/article/bill-gates-who-most-powerful-doctor/

(7)This article found a "Positive association between COVID-19 deaths and influenza vaccination rates in elderly people worldwide." While there are other research articles that state the opposite, it should cause all of us to question if we actually know how COVID-19 and the flu shot are working together. If I have concerns with having a flu shot possibly causing or correlating to decrease tolerance to COVID-19 why would I get the flu shot this year? https://peerj.com/articles/10112/

(8)Throughout the history of vaccines, there have been ingredients in them that have been found to be harmful to our health. One of my own children has toxic levels of aluminum in his hair follicles that our medical doctor believes to have come from vaccinations. https://www.fda.gov/vaccines-blood-biologics/safety-availability-

biologics/thimerosal-and-vaccines?fbclid=IwAR3QsL9ZqDjPnGPeiN0s0hgVqE2pGq23w3lTgDRq9Zn8X0wy0EhDUlc3WvU

(9) Influenza vaccination was associated with an increased risk of developing influenza-like illnesses (ILI)- what does this look like with our current pandemic? I don't want to put something in my body that has even a small chance of making covid-19 worse than it may be. This article also addresses antiviral resistance. We have a virus running rampant in our world, is antiviral resistance something to be concerned with? This article also addresses the live virus risks (mist) to the population that does not vaccinate versus the use of harmful chemicals that are not even listed in the vaccination ingredients (more studies to follow regarding this statement). The influenza virus strains change and according to the CDC they determined that immunization with the 2003-2004 influenza vaccine offered negligible population protection. Again, I ask, "Should I assume a remote chance of death" for something that "offers negligible population protection" since we won't know until after the flu season is over is our vaccination was for the correct strain? https://www.jpands.org/vol11no3/geier.pdf?fbclid=IwAR34zk-bfM2czYPE6Vts9X2uP3RaUtyyAc0GGyKdr4UMnuk8g1pafLmXf_U

(10) This is an article where ingredients in vaccinations were studies and what was not listed in the ingredient lists that was actually in the vaccinations. This study was published 3years ago, if pharmaceutical companies were not disclosing their entire ingredient list 3 years ago, why would I trust them today? https://medcraveonline.com/IJVV/IJVV-04-00072.pdf

This is a list of ingredients in vaccines as of Feb 2020 per the CDC: https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf

(11) Vaccine insert states numerous reasons to question safety and efficacy with vaccine: https://www.fda.gov/media/83072/download

(12) This article states reduced effectiveness with recurrent vaccinations as well as more aerosol shedding compared to those that were unvaccinated. https://www.pnas.org/content/115/5/1081

(13) Flu shot may blunt effectiveness of vaccine through antibody interference. http://www.cmaj.ca/content/187/6/E180

(14) Facts about Vaccine injuries reported https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6500451/

(15)This study found that only 1% of vaccine injuries are actually reported. https://drive.google.com/file/d/1pAyZOnPgcd0ZcrMwUi8cNcZovftfK_YN/view?fbclid=IwAR2QaRoD08bAZhNmlfxCi8O1oXSkytFy15RypospNTqRa3mARLZNFUK-8qw

(16) The national vaccine compensation injury link: Why is there an organization that even has to exist like this. If there is risk in vaccinations shouldn't I have a right to not take them? When my child had a huge side effect from having a vaccination, I signed a paper authorizing Altru to give him the vaccination so they would not be held accountable if something happened to him. Did I understand there was risk? Yes. Did I let him get the vaccination? Yes. On my shoulders as his parent. This year, I say NO to the flu vaccine as I fear the risk of complications from covid 19 as well as not trusting the ingredients fully being disclosed to me. Will a medical organization test the covid vaccine on me without my consent? If so, my Altru Employee health wouldn't protect me, help me because I signed a paper saying I assume the risk of injury. The vaccine compensation organization wouldn't help me either because I signed a paper saying I assume the risk of injury. Therefore, it is my right to request and be honored an exemption from the flu vaccination. https://www.hrsa.gov/vaccine-compensation/index.html.

(17) A few years ago, when I was pregnant with one of my children, I filed for an exemption from the flu shot as I had one but could not find the paperwork indicating I had it. Employee health stated that I had to get a second shot or would not be able to work until after delivery and therefore complying with Altru's policy. I elected to take a leave of absence in order to protect my baby with the unknown possibility of causing harm from having 2 shots. Again, Altru did not consider my or my babies best interest, only if I was following your policy. This article states there are reported cases of miscarriage that are connected to flu shots. https://www.jeremyrhammond.com/2019/05/14/the-cdcs-criminal-recommendation-for-a-flu-shot-during-pregnancy/?utm_source=ActiveCampaign&utm_medium=email&utm_content=The%20Ignorance%20of%20Doctors%20(Part%20II)&utm_campaign=The%20Ignorance%20of%20Doctor

(18) This article indicates there are many unknowns to vaccinations, again with the current state of health concerns I feel my concerns should be respected. https://childrenshealthdefense.org/news/most-of-you-think-we-know-what-our-vaccines-are-doing-we-dont/?fbclid=IwAR1vKLaeIBqa07RTOcVv2IMT7BHTAnkcPfKfLD-hBxjJcGjtl6cYNU1PT2E

(19)Sleep problems have began to occur in my life. Is this a result of hormonal changes or is the a possibility that it could be related to annual compliance with Altru's Influenza virus policy? These studies address my sleep concerns. https://www.ncbi.nlm.nih.gov/pubmed/24485154 https://n.neurology.org/content/80/14/1276

(20) This article address concerns with increased risk of non-influenza respiratory viral infections associated with receipts of the inactivated influenza vaccine. So, we have covid-19 a non-influenza respiratory viral infection present in our society, shouldn't I be concerned? https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/

(21) Unvaccinated children are the healthiest according to this doctor and his research. If that applies to children, does that apply to adults as well? https://thestaracademy.co.za/former-vaccine-bully-board-certified-pediatrician-now-claims-unvaccinated-children-are-healthiest/

https://www.youtube.com/watch?v=8RwoGibCKhc

(22) Do health care organizations or insurance companies profit from vaccinations? Why push vaccinations? Does Altru get a kickback of some sort for their percentage of compliance to the influenza vaccination?
"Systems of Care and Contracted Groups are eligible to receive an additional 10% of their Medicare Advantage base payment based on individual providers' performance. To receive this bonus, 50% of the providers affiliated to the SOCs or contracted groups must achieve an overall aggregated Star rating of 4.5 Stars or above for their Medicare Advantage performance. " Is Altru being bought by incentives? https://www.bcbsri.com/sites/default/files/portal_files/providers/2020-PCP-Quality-Incentive-Program-FINAL.pdf

https://nursesagainstmandatoryvaccines.wordpress.com/2014/11/17/employee-vaccination-rates-are-tied-to-government-funding-and-reimbursement/

(23) This article address antibiotic overuse. Many vaccinations have antibiotics in them (neomycin, kanamycin, polymyxin B, and gentamicin) further contributing to the antibiotic resistance problems we have in our society. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378521/

Here is the link from above from the CDC with vaccine ingredients that you can look up to verify my statement as well as the article

above: https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf

(24) Evidence for "consistent high-level protection is elusive," the researchers concluded. Although vaccination was found to provide modest protection from infection in young healthy adults who rarely have complications of flu, the authors found that "evidence for protection in adults 65 years of age and older [who represent over 90% of deaths from flu] . . . is lacking."
https://www.bmj.com/content/345/bmj.e7856.full

(25) Vaccines for preventing influenza in healthy adults: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001269.pub4/epdf

I fear that this will not change your decision. As stated previously, I have worked for Altru for 15 years, much of that time in a flex position. I value my position and feel I am of benefit to my fellow therapy team both at the hospital and rehab. I am dependable, reliable, and good at what I do. I bring fresh eyes and hands to the patients I serve and am therefore very valuable to all the patients that I have served over the 15 years I have worked here. I have seen people with illness work through physical impairments, family issues, addiction problems, etc. and be able to live a life they didn't know they could have again. I remember them and value their lives, their choices, their decisions, even when I don't agree. Isn't that what we are taught in our sensitivity training, we need to value each person's differences? I am different, I am unique, I have choices that should be respected. I have concern with the covid-19 pandemic and what risks I may have to endure from me having the influenza vaccination put into my body. If Altru Health System does not choose to respect my decision to have an exemption from the flu vaccination, you will have to terminate my position, as I don't feel I am doing anything wrong. I hope that through my research above and through your sensitivity training that you can find a way to respect my decision.

Sincerely,

Erica Hanson, PT
Physical Therapist

Thanks for your time. My name is Dustin Amundson, I am from Bismarck. I am not anti-vaccine, I just don't trust government. In the 20th century, people of all colors and persuasions were sterilized against their will or without their knowledge by their government. Compulsory sterilization was practiced by many countries, including America and is still taking place in some countries today.

Some will say there is no way that could happen today, and that our culture has evolved far enough to make it impossible in America today. That's not true. Culture is capable of both progressing and regressing. If you don't believe me, just compare Iran of the 1970's to Iran today.

Some will say "there is no way North Dakota legislators would authorize any sterilization programs or misuse the power to coerce immunizations." I agree that our current legislators would not authorize any deceptive programs, but our current legislators will not be in office forever. We do not know the character of the people who will comprise our legislature in the future.

Tyrannically minded people tend towards positions of power, and will eventually be in a position where they can do damage. Let's make it clear that they do not have the power to inject anything into the bodies of North Dakotans' against our will, even if they declare a state of emergency. (If governments could give themselves additional powers when in a state of emergency, what would stop them from declaring a state of emergency when they yearn for additional powers?)

Governments were created to protect our rights and they derive just powers from our consent. I do not consent to coerced vaccinations. I want to trust my government again. Help me.

Below are links where you can read about sterilization movements from 20th century.

African American Sterilization

https://ihpi.umich.edu/news/forced-sterilization-policies-us-targeted-minorities-and-those-disabilities-and-lasted-21st

Native American Sterilization

https://digitalworks.union.edu/cgi/viewcontent.cgi?article=1795&context=theses

German Sterilization Laws

https://www.fed.cuhk.edu.hk/history/history2005/q1_s7_01.pdf

We need to keep health freedom. The choice to vaccinate should be left 100% up to the parents. Forcing vaccinations is overreach by government.

I 100% Support 1320 – and strongly urge a do pass.

Dear Chairman Weisz and Members of the Human Services Committee,

Dear Chairman Weisz and Members of the Human Services Committee,

My name is Paul Carson. I am a physician who specializes in the area of infectious diseases, and am a Professor at North Dakota State University in the Dept. of Public Health, where I am the Medical Director of the Center for Immunization Research and Education. However, my comments today are not on behalf of NDSU.

I am testifying today in opposition to HB 1320, which seeks to eliminate school mandates for vaccination prior to school entry.

I am a physician who is old enough to well remember one vaccine-preventable disease, namely Haemophilus influenzae meningitis. This used to be the most common cause of childhood meningitis, and caused deafness, brain damage, and death in 10s of thousands of children every year. In addition, it could cause a life-threatening condition called epiglottitis that could suffocate a child in minutes. We had one or more such children in the hospital most of the time when you rounded on a pediatric ward. This was a terribly frightening and devastating disease. Amazingly, my younger pediatric colleagues universally tell me they have never seen a case. They only know if it historically from medical books. It is virtually gone from North America. Thankfully, I am not old enough to remember even more devastating diseases that plagued our children in even greater numbers, like measles, diphtheria, and polio. All of these have faded from our collective memory, due to vaccination. And they are all poised to easily return when our vaccination rates decline. You don't have to take my word for this, but just look at NY, OR, CA, and our neighboring state of MN, all who have had serious measles outbreaks costing them millions of dollars to control in the last few years when their immunization rates fell below the herd-immunity threshold of around 90-95%.

Vaccines have been rightly acknowledged as one of the crowning achievements of modern health care and public health. To achieve their greatest benefit, namely herd immunity, where enough of the population is immune that a contagious pathogen cannot get a foothold and spread, we need immunization rates typically in the 90% -plus range. Children who cannot receive vaccines due to medical contraindications, or children who do not respond to a particular vaccine, rely on those children around them to be immune so as not be exposed to these illnesses.

One way our country has achieved this safe school environment and herd-level immunity is through daycare and school-immunization requirements. These requirements make sense, since these diseases most often affect children, who can easily spread these pathogens to one another in the confined spaces of a school classroom or daycare center. Our country has left the regulation of these school-vaccination mandates up to the individual states, and all states have implemented these mandates in one form or another. The Supreme Court has upheld the constitutionality of these laws not once, but twice. If ND were to pass HB 1320, we would become the only state in the union not to require a safer school and daycare environment through the entry requirement of vaccinations.

This bill is unnecessary for those individuals who are staunchly opposed to vaccination. North Dakota is one of only 16 states in the country that allows parents to request an exemption to their child's vaccination requirement, either on the basis of religious objection, or just personal belief. Furthermore, we are one of the easiest states in the country to get such an exemption. All they need to do is sign a

form stating they have a religious or personal belief objection to the vaccine, turn it in to the school secretary, and their child is free to attend school unvaccinated. And, parents are increasingly using these exemptions, which partially explains why ND kindergartners have ranked in the bottom half of the U.S. for vaccinations since 2011.

Please do not compromise our children's safety by further weakening our vaccination laws, which will surely lead to even lower vaccination rates than we already have, and vote no on HB-1320.

Dear House Human Services Committee Members,

Thank you for your important service and dedication to the state of North Dakota.

I am a mother of nine children whom I homeschooled kindergarten thru high school for 32years.

I graduated from UND with a BS in Education, hold a ND teaching certificate, have my Masters in Public Health from the University of Michigan, and recently became a Certified Nursing Assistant.

After extensive careful study of vaccines, I stand in full support of the following three Bills…HB1307, HB1320, HB1306.

2020 was wrought by many albeit good intended but heavy-handed broad sweeping Public Health regulations that cancelled out so much additional effective scientific information, procedures, and practices in hasty political and financial overriding of the Truth and to personal freedom. Our Government, you, must allow us the right to choose whether to vaccinate or not without fear of losing our right to education and work! And, to continue to study the effects of vaccines is very important also.

Thank you for your consideration on this matter.

Please Vote in support of HB1307, HB1320, HB1306

Sincerely,

Julie Liffrig

District 33

2021 HOUSE STANDING COMMITTEE MINUTES

Human Services Committee
Pioneer Room, State Capitol

HB 1320
1/20/2021

Relating to immunizations required for entry to school or day car

Chairman Weisz opened the committee meeitng at 3:05 p.m.

Representatives	Attendance
Representative Robin Weisz	P
Representative Karen M. Rohr	P
Representative Mike Beltz	P
Representative Chuck Damschen	P
Representative Bill Devlin	P
Representative Gretchen Dobervich	P
Representative Clayton Fegley	P
Representative Dwight Kiefert	P
Representative Todd Porter	P
Representative Matthew Ruby	P
Representative Mary Schneider	P
Representative Kathy Skroch	P
Representative Bill Tveit	P
Representative Greg Westlind	P

Discussion Topics:

- Vaccine debate
- Loosened restrictions
- Vaccination objections
- Personal belief exemptions
- Religious belief exemptions

Rep. Matthew Ruby made a motion for **Do Not Pass**.

Rep. Gretchen Dobervich seconded the motion.

Representatives	Vote
Representative Robin Weisz	Y
Representative Karen M. Rohr	Y
Representative Mike Beltz	Y
Representative Chuck Damschen	Y
Representative Bill Devlin	Y
Representative Gretchen Dobervich	Y
Representative Clayton Fegley	Y
Representative Dwight Kiefert	Y
Representative Todd Porter	Y
Representative Matthew Ruby	Y

Representative Mary Schneider	Y
Representative Kathy Skroch	Y
Representative Bill Tveit	N
Representative Greg Westlind	Y

Motion passed 13-1-0

Bill Carrier: Rep. Todd Porter

Chairman Weisz adjourned at 3:24 p.m.

Tamara Krause, Committee Clerk

REPORT OF STANDING COMMITTEE

HB 1320: Human Services Committee (Rep. Weisz, Chairman) recommends **DO NOT PASS** (13 YEAS, 1 NAY, 0 ABSENT AND NOT VOTING). HB 1320 was placed on the Eleventh order on the calendar.