SECTION: PIL

IN THE SUPREME COURT OF INDIA
(CIVIL ORIGINAL JURISDICTION)
I.A. NO. _____ OF 2022
IN
WRIT PETITION (CIVIL) NO. 607 OF 2021

IN THE MATTER OF:

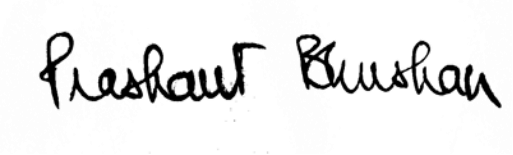
JACOB PULIYEL ....PETITIONER

VERSUS

UNION OF INDIA & ORS. ....RESPONDENTS

FILING INDEX

S.NO.	PARTICULARS	COPIES	C.FEE
1.	APPLICATION FOR DIRECTION WITH AFFIDAVIT	1	120/-
2.	ANNEXURE A1 TO ANNEXURE A 26	1	NIL



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PAPER BOOK

(FOR INDEX KINDLY SEE INSIDE)

COUNSEL FOR THE PETITIONER: **PRASHANT BHUSHAN**

INDEX

9.	**Annexure: A8:** A copy of the Indian Express report dated 28th October 2021 titled "Delhi: 97% people have Covid -19 antibodies, shows sero survey", and available at: https://indianexpress.com/article/cities/delhi/people-in-delhi-have-covid-19-antibodies-shows-sero-survey-7595390/	48-49
10.	**Annexure: A9:** The interview is available at https://timesofindia.indiatimes.com/videos/news/covid-vaccines-are-disease-modifying-dont-prevent-infection-icmr/videoshow/88597995.cms	50
11.	**Annexure: A10:** A copy of the article in The Guardian titled "Spain, Belgium and Italy restrict Astra Zeneca Covid vaccine to older people" dated 8th April 2021	51-53
12.	**Annexure: A11:** A copy of the paper titled "Risk of Myocarditis from COVID 19 infection in people under age of 20: A population-Based Analysis	54-60
13.	**Annexure: A12:** A copy of the paper in the New England Journal of Medicine titled "Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel	61-70
14.	**Annexure: A13:** A copy of an article in the New York Post titled "NIH orders $1.67M study on how COVID-19 vaccine impacts menstrual cycle" dated 7th September 2021	71-73
15.	**Annexure: A14:** A copy of the British Medical Journal paper titled "Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis, dated 26th February 2013	74-75
16.	**Annexure: A15:** A copy of the paper "Why are we vaccinating children against COVID-19?" published in Toxicology Reports	76-95

17.	**Annexure: A16:** A copy of the paper published in the Lancet titled 'COVID-19 herd immunity by immunisation: are children in the herd?' dated 19.04.2021	96-97
18.	**Annexure: A17:** A copy of the paper in the New England Journal of Medicine titled "Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel	98-107
19.	**Annexure: A18:** A copy of the paper titled 'The Ethics of Drug Research in Children by T. F. Ackerman' (2001) available on doi:10.2165/00128072-200103010-00003	108-120
20.	**Annexure: A19:** A copy of the order dated 15.01.2019 judgement in Master Hridaan Kumar Minor v. Union of India W.P.(C) 343/2019 & CM No. 1604/2019 & 1605/2019	121-128
21.	**Annexure: A20:** A copy of the Charter of Patient's Rights" as issued by the Ministry of Health and Family Affairs	129-155
22.	**Annexure: A21:** A copy of the order no. DMC-SPO-2020/14198 dated 1st January 2022 by the Haryana State Disaster Management Authority, Government of Haryana	156-158
23.	**Annexure: A22:** A copy of the letter dated 1st January 2022 by the District Educational Officer, YSR District, Kadapa, Andhra Pradesh	159
24.	**Annexure: A23:** A copy of the Deccan Herald article dated 04.01.2022 and titled 'Parents fume after some Karnataka schools make Covid-19 vaccinations mandatory	160-162
25.	**Annexure: A24:** A copy of the notice letter dated 4th January 2022 addressed to the 'The Principal	136-164

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VERSUS

THE UNION OF INDIA & ORS. .....RESPONDENTS

APPLICATION FOR DIRECTION ON BEHALF OF THE PETITIONER

1. That the petitioner has filed the instant writ petition under Article 32 of the Constitution of India for the enforcement of fundamental rights under Article 14 and 21 of the Constitution of India, seeking a writ directing the respondents to make public the segregated data of the clinical trials for the COVID-19 vaccines that are being administered to the population in India under Emergency Use Authorization and declare that the coercive mandates for use of these inadequately tested vaccines are repugnant to the right of humans to autonomy.

2. Through the instant application the petitioner seeks to bring on record and seek a stay on the coercive COVID-19 vaccine mandates that are

introduced in various states and by private establishments for children in the age group 15-18 years. These mandates have started surfacing after the Ministry to Health and Family welfare on the 27th of December issued guidelines for COVID-19 Vaccination of Children between 15 to 18years from 3rd January 2022 onwards. The petitioner also seeks disclosure of clinical trial data for the vaccines that are being administered to children in India.

(A copy of the guidelines issued by the Ministry of Health and Family Welfare are annexed as **Annexure A1 (Page 29 to 32).**

3. It is pertinent to note that that these guidelines were issued only a few days after the announcement through a presser on the 24th of December 2021, by the vaccination drive Chief Vinod K Paul, Indian Council of Medical Research Chief, Balram Bhargava and Union health secretary Rajesh Bhushan that their decisions are guided by science and that there isn't any scientific basis yet to necessitate paediatric vaccination. In a complete u-turn therefore the scientific basis seems to have altered and within three days guidelines were issued by the Ministry of Health and Family Welfare for vaccinating 15-18 year olds.

(A copy of The Wire report dated 26th December 2021, titled "10 Questions the Indian Government Must Answer About Vaccines for Minors and Boosters" is annexed as **Annexure A2 (Page 33 to 36)**

The data and scientific studies clearly show that children are hardly at any risk of serious illness due to COVID

4. No medical intervention should be introduced on a 'one size fits all' basis, but instead should be fully assessed for suitability according to the characteristics of the age cohort and of the individuals concerned, weighing up the risk versus benefit profile for each cohort and the individuals within a group. It has been established through published research that healthy children are at almost no risk from COVID-19. Previously healthy children dying of COVID or requiring admissions to hospital or intensive care are exceedingly rare, with most children having no or very mild symptoms. All medical interventions carry a risk of harm, so we have a duty to act with caution and proportionality. This is particularly the case when considering mass intervention in a healthy population, in which situation there must be firm evidence of benefits far greater than harms. The current, available evidence clearly shows that the risk versus benefit calculation does not support administering rushed and experimental COVID-19 vaccines to children, who have virtually no risk from COVID-19, yet face known and unknown risks from the vaccines. The Declaration of the Rights of the Child states that, "the child, by reason of his physical and mental immaturity, needs special safeguards and care, including appropriate legal protection".

5. An article in Nature.com tilted "Deaths from COVID incredibly rare among children" states that studies find that the overall risk of death or severe disease from COVID-19 is very low in kids.

> "A comprehensive analysis of hospital admissions and reported deaths across England suggests that COVID-19 carries a lower risk of dying or requiring intensive care among children and young people than was previously thought.
>
> Covid caused 25 deaths in that age group between March 2020 and February 2021, researchers reported in a series of preprints published on medRxiv. About half of those deaths were in individuals with an underlying disability with high health-care needs, such as tube feeding or assistance with breathing."

(A copy of the article in Nature.com titled "Deaths from COVID incredibly rare among children" is annexed as **Annexure A3** at **(Page** 37 **to _____).**

6. In an article in The Lancet titled "Children and young people remain at low risk of COVID-19 mortality", states that severe COVID-19 disease was rare in children.

> "In the USA, UK, Italy, Germany, Spain, France, and South Korea, deaths from COVID-19 in children remained rare up to February, 2021, at 0·17 per 100 000 population, comprising 0·48% of the estimated total mortality from all causes in a normal year (table, appendix p 2). Deaths from COVID-19 were

relatively more frequent in older children compared with younger age groups."

(A copy of the article in The Lancet, "Children and young people remain at low risk of COVID-19 mortality", is annexed as **Annexure A4 (Page** 38 **to** 39 **).**

7. A report in the BBC titled "COVID: Children's extremely low risk confirmed by study" states:

"The overall risk of children becoming severely ill or dying from Covid is extremely low, a new analysis of covid infection data confirms…those living with multiple chronic illnesses and neuro-disabilities were most at risk, though overall risk remained low."

(A copy of the article in the BBC titled "COVID: Children's extremely low risk confirmed by study" is annexed as **Annexure A5 (Page** 40 **to** 42 **).**

8. In an article published in Science Direct the authors compared children's mortality from COVID-19 with all-deaths and other relevant causes of death to provide parents, teachers, clinicians and policy makers with epidemiological information for decision making regarding children. The article states:

"The situation in each country was almost identical, and in accordance with early data from China i.e. COVID rarely kills children, even

compared with influenza, against which many children are already vaccinated. Our data show that for mortality COVID-19 is similar to flu, or less severe, in children whilst being the opposite in adults."

(A copy of the article, "Children's mortality from COVID-19 compared with all-deaths and other relevant cause of death: epidemiological information for decision-making by parents, teachers, clinicians and policymakers" is annexed as **Annexure A6 (Page 43 to 45).**

Serological Surveys indicate a large number of people including children already have antibodies to COVID-19

9. An Indian Express article dated 26th July 2021 titled "2 of 3 Indians have Covid-19 antibodies: ICMR serosurvey findings explained" reports that two-thirds of the general population above the age of 6 years had COVID-19 antibodies and that more than half of the children were sero-positive:

> "..Two-third of Indians above the age of 6 had SARS-CoV-2 antibodies, show findings of the fourth nationwide serological survey conducted by the Indian Council of Medical Research (ICMR) in June-July…
>
> ..The survey findings shows that more than half of the children (6 -17 years) were seropositive. It means they have been exposed to Covid-19 in the past months. The sero-prevalence

among children was 57.2 per cent in the age group 6-9 years and 61.6 per cent in the age group 10-17 years…"

(A copy of the Indian Express article dated 26th July 2021 and titled "2 of 3 Indians have Covid-19 antibodies: ICMR serosurvey findings explained" has been annexed as **Annexure A7 (Page 46 to 47)**

10. A news report titled "Delhi: 97% people have Covid -19 antibodies, shows sero survey" in the Indian Express Times reported that:

"Delhi has a seropositivity of 97 per cent for Covid-19 antibodies, the sixth serological survey conducted in the city has revealed, Delhi Health Minister Satyendar Jain said Thursday. Every district has a seropositivity of above 95 per cent, he said.

…

In children below the age of 18, the sero prevalence is 88 per cent, while it is 97 per cent to 98 per cent in adults."

(A copy of the Indian Express report dated 28th October 2021 titled "Delhi: 97% people have Covid -19 antibodies, shows sero survey", and available at https://indianexpress.com/article/cities/delhi/people-in-delhi-have-covid-19-antibodies-shows-sero-survey-7595390/is Annexed as **Annexure A8 (Page 48 to 49)**

Non disclosure of phase 3 trial results in adults and children for vaccines being administered in India

11. That Zydus Cadila vaccine has also received approval in August 2021 for emergency use to be administered in children and adults above 12 years. The phase 3 trial data for this vaccine is also not available in the public domain. The clinical trial process and data for both these vaccines, the COVAXIN vaccine being administered through the government immunization programme and the Zydus Cadila vaccine which has received emergency use approval in August 2021, are unknown and remain opaque to public scrutiny. This raises serious concerns regarding the suitability of these vaccines for use especially in children since phase 3 trial data of these vaccines in adults have not been published in peer reviewed scientific journals nor has the raw data related to these trials been put out for independent scientific scrutiny. Bharat Biotech reportedly submitted data from phase 2/3 trials for COVAXIN for those aged 15-18 years, conducted in India over a period of 3 months, to the Drug Controller General. This data has not been put out in the public domain or available for independent verification. Administering experimental vaccines to children which have not gone through complete phase 3 trials and for which safety and efficacy data from phase 3 trials in adults is not available raises serious ethical concerns and amounts to gross medical malpractice.

12. The current vaccination drive using Covaxin is based on limited understanding of short term risks from the vaccine since clinical trials have been truncated and the vaccine is being administered under emergency use to the population at large. As with many other vaccines

being administered under emergency authorization, risks of bias are high due to limited studies, all done by manufacturers. Trials to establish efficacy and safety of the Covid 19 vaccines are not conducted by independent research teams but by the pharmaceutical companies, who stand to gain financially from their products. Raw trial data for Covaxin is not yet accessible to be scrutinized by independent researchers. Lack of critical interpretation of side effects observed during trials, weak pharmacovigilance in most countries in the absence of control groups adds to the problem. Safety cannot be established if due scientific process is not adhered to. The clinical trial results for Covaxin phase 3 trials were due in 2023. Until we have the results of Phase 3 trials and unless we have sufficient long-term understanding, fully informed consent especially for administering these vaccines to children is medically, scientifically and ethically impossible.

COVID Vaccines do not prevent infection and transmission

13. For any vaccine to be recommended universally in public interest, the public health rationale underlying such a policy must be based essentially on efficacy and safety of vaccination and transmission of the disease. It has now been well established through peer reviewed scientific studies that vaccines do not prevent infection or transmission for Covid-19 and are not effective in preventing against infection from the new variants. The efficacy of vaccines in preventing infection or transmission has not been established. This is not being communicated

effectively to the public. Various studies have now been published that show that the vaccines do not prevent infection or transmission of the Covid 19 virus. There are many examples of outbreaks of the virus amongst fully vaccinated populations. Examples include Iceland and Israel where a high percentage of the population have been fully vaccinated, yet an increase of cases is being experienced. Therefore administering the vaccine through coercion or without informed consent to children cannot be a matter of public health since the vaccines are not an effective guarantee against infection and transmission.

14. On the 30th of December 2021, the ICMR Chief, Dr. Balram Bhargava stated in an interview that COVID vaccines do not prevent infection and are primarily disease modifying. Therefore there is no rationale for vaccinating a vulnerable group such as children with a vaccine that will not prevent them from getting the disease and transmitting it to others.

(The interview is available at https://timesofindia.indiatimes.com/videos/news/covid-vaccines-are-disease-modifying-dont-prevent-infection-icmr/videoshow/88597995.cms and a screen shot of the Times of India report on the same is annexed as **Annexure A9 (Page 50 to _____)**

Serious adverse events in children in the age group 15-18 who have been vaccinated in other countries

15. The potential benefit to an individual child of receiving a Covid-19 vaccine is statistically zero. Children play an insignificant role in transmission of Covid-19. There is therefore no demonstrable benefit to the wider society in vaccinating children. In a population cohort at minimal risk of severe disease such as young people and children, acquiring natural immunity will serve a better purpose, as it will be more comprehensive, longer lasting and cover broad range of virus variants. Serious adverse events and vaccine related deaths have been reported in the UK, the US and Europe especially in children who have been administered COVID vaccines. Adverse events recording systems show unprecedented levels of adverse events, including death, resulting from the administering of the Vaccines. There continue to be new side effects being reported and/or listed by regulatory bodies in various countries. These side effects are only the short-term side effects. These side effects include myocarditis, blood clots and facial nerve disorders, with new reports indicating a possible side effect related to a nerve/nervous system disease (Guillain-Barre syndrome). The long-term side effects are a completely unknown.

16. Changes to women's menstrual cycle have been reported in the UK. Blood clotting after the AstraZeneca (Covishield) vaccine is rare but can even cause death as has been reported. In Apr 2021, various European countries restricted the use of AstraZeneca (Covishield) to older

people. It is not recommended for the young, based on safety concerns.

(A copy of the article in The Guardian titled "Spain, Belgium and Italy restrict Astra Zeneca Covid vaccine to older people" dated 8th April 2021 is annexed as **Annexure A10 (Page 51 to 53).**

17. Associated with the mRNA vaccines is the risk of myocarditis (heart inflammation). Data from various countries such as the USA shows that the incidence of myocarditis increased after the receipt of the vaccine particularly after the second dose among young make recipients and Israel show that this risk for children is about 1 in 6000. Considering this, many European countries recently stopped the use of the Moderna vaccine for those under 30.

(A copy of the paper titled "Risk of Myocarditis from COVID 19 infection in people under age of 20: A population-Based Analysis" is annexed as **Annexure A11 (Page 54 to 60).**

18. A paper published in the New England Journal of medicine discusses the increased cases of myocarditis in young males after the second dose of the vaccine.

> "In most cases, symptoms of myocarditis developed within a few days after the second dose of vaccine. The incidence of myocarditis declined as the number of newly vaccinated persons decreased over time. This finding was suggestive of a possible causal relationship between two doses of the vaccine and the risk of myocarditis. Overall, we estimated that definite or probable cases of myocarditis occurred in the overall Israeli population at a rate of approximately 1 per 26,000 males and 1

> per 218,000 females after the second vaccine dose, with the highest risk again among young male recipients. This result may explain why a phase 3 trial of the vaccine, which included only 15,000 male and female recipients,[8] showed no cases of myocarditis. The mechanism of vaccine-induced myocarditis is not known but may be related to the active component of the vaccine, the mRNA sequence that codes for the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or to the immune response that follows vaccination."

(A copy of the paper in the New England Journal of Medicine titled "Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel" is annexed as **Annexure A12 (Page 61 to 70).**

19. As recently as last month, the NIH (USA) ordered a study on the Covid-19 vaccines impact menstrual cycle.

(A copy of an article in the New York Post titled "NIH orders $1.67M study on how COVID-19 vaccine impacts menstrual cycle" dated 7th September 2021 is annexed as **Annexure A13 (Page 71 to 73)**

20. It is important to note here that the above risks were not signaled in the initial vaccine trials: the trial size itself was too small to uncover rare risks (32,449for AstraZeneca/Covishield). That these risks have been found after mass vaccination is deeply concerning. The trial sizes for childrens vaccines in India are too small (525: Covaxin, 1000: ZyCov-D). Such low trial sizes cannot capture anything but the most obvious risks. Long term and more serious effects of these vaccines

would only be uncovered in larger numbers and when observed over a longer period of time.

21. The past history of emergency vaccines is very concerning. Swine flu vaccine, Pandemrix, was rolled out in response to the 2010 pandemic. It was later withdrawn when it was found that around one in every 55,000 jabs led to narcolepsy in children. Dengvaxia, a vaccine against Dengue, was withdrawn in 2017 after 19 children (1 in 44,000) died of possible Antibody-Dependent Enhancement (ADE).

(A copy of the British Medical Journal paper titled "Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis, dated 26th February 2013 is annexed as **Annexure A14 (Page 74 to 75).**

22. As of August 2021 in the USA, nearly 600,000 deaths have been officially attributed to COVID-19. Almost 5,000 deaths following inoculation have been reported to VAERS by late May 2021; specifically, "Over 285 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through May 24, 2021. During this time, VAERS received 4,863 reports of death (0.0017 %) among people who received a COVID-19 vaccine." (the Vaccine Adverse Events Reporting System (VAERS) is a passive surveillance system managed jointly by the CDC and FDA. Historically, VAERS has been shown to report about 1% of actual vaccine/inoculation adverse

events. By mid-June last year alone, deaths following COVID-19 inoculations had reached the ~6000 levels in the USA.

The data and scientific studies in countries where children have been given COVID Vaccines show that the vaccines have serious and significant adverse effects on them, which outweighs the adverse effects due to the COVID infection itself

23. In a paper published in Toxicology Reports titled "Why are we vaccinating children against COVID-19?" the authors undertake a detailed examination of the issues related to COVID-19 inoculations for children. They state that the bulk of the official COVID-19 attributed deaths per capita occur in the elderly with high comorbidities, and the COVID-19 attributed deaths per capita are negligible in children.

"The bulk of the normalised post inoculation deaths also occur in the elderly with high comorbidities, while the normalised post-inoculation deaths are smalls, but not negligible in children. Clinical trials for these inoculations were very short terms (a few months), had samples not representative of the total population, and for adolescents/children, had poor predictive power because of their small size…most importantly, the clinical trials did not address long-term effects that, if serious, would be borne by children/adolescents for potentially decades…the risk of death from COVID-19 decreases drastically as age decreases, and the longer term effects of the inoculations on lower age groups will increase their risk-benefit ratio, perhaps substantially."

The paper details the various short and long term adverse effects of the vaccination on children.

> "What are the potential mid- and long-term adverse health effects from the COVID-19 inoculation on children specifically, taking into account that they will be exposed not only to the spike protein component of the SARS-CoV-2 virus but also to the toxic LNP encapsulating-shell? This toxic combination will have bypassed many defensive safeguards (typically provided by the innate immune system) through direct injection [62]. As we have shown, the main reasons why we believe the spike protein could be harmful to children even though they don't seem to get sick from exposure to SARS-CoV-2 are 1) the bypassing of the innate immune system by inoculation, 2) the larger volume of spike protein that enters the bloodstream, and 3) the additional toxic effects of the encapsulating LNP layer."

(A copy of the paper "Why are we vaccinating children against COVID-19?" published in Toxicology Reports is annexed as **Annexure A15 (Page** 75 **to** 95 **).**

24. According to a paper published in the Lancet titled ***'COVID-19 herd immunity by immunisation: are children in the herd?'*** dated 19.04.2021, stated that using the same approach for delivering vaccines to adults and children will exacerbate hyperinflammatory conditions in children and ethically violates the risk-benefits principle:

> *"...Current vaccines that are authorised for emergency use, approved or in development, do not have a safety or*

immunogenicity profile in children. In the absence of a better understanding of the pathogenesis of this condition, ***using the same approach for delivering vaccines as in adults could exacerbate the incidence of this hyperinflammatory condition.***

Second, from a public health perspective, it will be necessary to immunise children if they are a major source of SARS-CoV-2 transmission and if the candidate vaccines block transmission. However, epidemiological reports up to now suggest that young children have a high likelihood of developing COVID-19 via household transmission, once a family member tests positive for COVID-19.1 There is little evidence of secondary infection from children to others in the transmission pathways of COVID-19. Although emerging data suggest that some candidate vaccines can block transmission, vaccinating children cannot be justified if it is to give direct protection despite minimal burden of disease or to help to block transmission if children do not constitute a substantial reservoir for transmission.

Third, from an ethical perspective, there is a balance between risk and benefit in offering a COVID-19 vaccine to children that will offer minimal or no direct benefit to the recipient, no benefit to the public, and as yet, unknown medium-term and long-term risks to the recipient…"

(A copy of the paper published in the Lancet titled 'COVID-19 herd immunity by immunisation: are children in the herd?' dated 19.04.2021 is annexed as **Annexure A16 (Page 96 to 97)**.

25. A paper published in the New England Journal of Medicine discusses the increased incidence of myocarditis in young male recipients after two dose of the vaccine and also concludes that the incidence of was higher than in the unvaccinated persons.

> "The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild…
>
> On the basis of data from an Israeli national database, the incidence of myocarditis after two doses of the BNT162b2 mRNA vaccine was low but higher than the incidence among unvaccinated persons and among historical controls. The risk of myocarditis was driven primarily by the increased incidence after the second dose of vaccine and in young male recipients."

(A copy of the paper in the New England Journal of Medicine titled "Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel" is annexed as **Annexure A17 (Page 98 to 107).**

26. A recent paper titled 'The Ethics of Drug Research in Children' by T.F. Ackerman suggests that clinical trials on children are justified only when the risk-benefit ratio is at least favourable:

> *"A second component of justice focuses on the fair distribution of the benefits of research participation. This feature is pertinent to the use of therapeutic research procedures. Involvement of children in these procedures is justified only when the risk-benefit ratio is at least as favorable as any alternative treatments available outside the research context."*

(A copy of the paper titled 'The Ethics of Drug Research in Children by T. F. Ackerman' (2001) available on doi:10.2165/00128072-200103010-00003' is annexed as **Annexure A18 (Page 108 to 120)**

Children are not capable of legal consent to the vaccines and the parents who give consent on their behalf are incapable of giving informed consent in the absence of studies and data about the benefits and adverse effects of the vaccines on children

27. There are deeply disturbing reports that government and health advisory groups are calling out in the media for the COVID-19 vaccine in children to enable schools reopening, contact sports or for admissions, etc. Any sort of such coercion of children or their parents to accept the COVID -19 vaccines that are still at research stage and about which no medium or long term side effects are known and against a disease which presents no material risk to children, is unethical and irresponsible. It violates the principles of medical freedom, informed consent and bodily autonomy which are to be preserved and protected, especially while dealing with vulnerable populations such as children.

28. Informed consent is the cornerstone of ethical medical practice. Introducing vaccinations especially for children in the absence of informed consent is unconstitutional and violates principle of informed self determination and bodily autonomy which flows from Article 21. Unless factually accurate information is made available, detailing risks as well as benefits, it is not possible for anyone, let alone children, to make a fully informed decision and give informed consent

29. Various disturbing news reports and orders have been issued which directly or indirectly have the effect of coercing children to get vaccinated. It appears to be a part of the public policy of the Union and State Governments to maximize the number of people receiving Covid 19 vaccines in as short a duration as is possible even without putting all 'information' in the public domain, enabling a citizen to make an 'informed' choice. This is unethical and has serious implication if this coercion is extending to vaccinating children.

30. In Master Hridaan Kumar Minor v. Union of India W.P.(C) 343/2019 & CM No. 1604/2019 & 1605/2019 (or "the Measles-Rubella case"), in order dated 15.01.2019, the Delhi High Court made it clear that parents must have information as to contra-indications before consent in any manner can be obtained:

> *"5. Before proceeding to examine whether consent in this manner can be obtained. It is clear that all parents must have full information as to (a) the particulars of the vaccine proposed to be administered; (b) contra indications and side effects of such a vaccine; (c) the date on which such vaccine would be administered to their wards/children; and (d) the personnel who would administer the same."*

(A copy of the order dated 15.01.2019 judgement in Master Hridaan Kumar Minor v. Union of India W.P.(C) 343/2019 & CM No. 1604/2019 & 1605/2019, is annexed as **Annexure A19 (Page** 121 **to** 128 **)**

31. In the Measles-Rubella case (Supra) the Hon'ble High Court of Delhi also made it mandatory to advertise the contra-indications of the Measles-Rubella vaccine:

> *"15. In view of the above, it is directed as under:*
> *(1) Directorate of Family Welfare shall issue quarter page advisements in various newspapers as indicated by the respondents, namely, The Hindustan Times, The Times of India, The Hindu, The Pioneer, The Indian Express, Delhi Tribune, Mail Today, The Asian Age, Navbharat Times, Dainik Jagran, Punjab Kesari, Hindustan, Amar Ujala, Navodaya Times, Hamara Samaj, Pratap, Daur-e-Jadeed, Jathedar, Jan Ekta. The advertisements shall also indicate that the vaccination shall be administered with Auto Disable Syringes to the eligible children by Auxiliary Nurse Midwifery.* ***The advertisement shall also clearly indicate the side effects and contraindications as may be finalised by the Department of Preventive Medicine, All India Institute of Medical Sciences.***
> *(2) The Head of Department of Preventive Medicine, All India Institute of Medical Sciences is directed to finalise the list of contraindications and risks associated with the vaccine being included in the aforesaid advertisements. Advertisements in two of the newspapers (one in English and the other in Hindi language) will also indicate the dates on which MR vaccine will be administered in respective schools. The website of DoE shall also clearly set out the above information…."*

32. Informed consent is necessary for medical procedures and bodily integrity is an integral part of the right to privacy flowing from Article 21 as has been settled in several judgments by the Hon'ble Supreme Court including Aarushi Dhasmana v. UOI & Ors (2013) 9 SCC 475, K. Puttaswamy v. UOI (2017) 10 SCC 1 and Common Cause v. UOI (2018) 5 SCC 1. Also, the Hon'ble Supreme Court in Kalpana Mehta & Ors. v. UOI & Ors. WP(C) No.558/2012 has framed questions on the

procedure by which a vaccine (HPV vaccine, in that case) was to be administered and thus recognized the factum that prior informed consent is a necessity for vaccination.

33. The draft "Charter of Patient's Rights" as issued by the Ministry of Health and Family Affairs, for public comments, which holds 'right to informed consent' as one of the patient's legal, fundamental rights states that:

> *"4. Every patient has a right that informed consent must be sought prior to any potentially hazardous test/treatment (e.g. invasive investigation / surgery / chemotherapy) which carries certain risks. It is the duty of the hospital management to ensure that all concerned doctors are properly instructed to seek informed consent, that an appropriate policy is adopted and that consent forms with protocol for seeking informed consent are provided for patients in an obligatory manner. It is the duty of the primary treating doctor administering the potentially hazardous test / treatment to explain to the patient and caregivers the main risks that are involved in the procedure, and after giving this information, the doctor may proceed only if consent has been given in writing by the patient / caregiver or in the manner explained under Drugs and Cosmetic Act Rules 2016 on informed consent.*
>
> > *a) Participation of patients in clinical trials must always be based on informed consent, given after provision of all relevant information. The patient must be given a copy of the signed informed consent form, which provides him / her with a record containing basic information about the trial and also becomes documentary evidence to prove their participation in the trial."*

(A copy of the Charter of Patient's Rights" as issued by the Ministry of Health and Family Affairs, is annexed as **Annexure A20 (Page** 129 **to** 155 **)**

COVID-19 Vaccine Mandates for Children

34. In an order no. DMC-SPO-2020/14198, Haryana State Disaster Management Authority, Government of Haryana notified that vaccinations of eligible persons (more than 15 years) is mandatory.

(A copy of the order no. DMC-SPO-2020/14198 dated 1st January 2022 by the Haryana State Disaster Management Authority, Government of Haryana is annexed as **Annexure A21 (Page** 156 **to** 158 **)**

35. In a letter dated 1st January 2022 by the District Educational Officer, YSR District, Kadapa, Andhra Pradesh, issued instructions to mandatorily vaccinate all children. The relevant parts of the same are reproduced below:

> *"In pursuance of the instructions issued by the Joint Collector (V, WS & D), YSR District in the reference cited, all the Deputy Educational Officers and Mandal Educational Officers in the district are requested to inform all the Headmasters of High Schools and Principals of Junior Colleges/AP Model Schools and Special Officers of KGBVS under their jurisdiction to complete vaccination (Covid-19) to all the students in the age group of 15-18 from 03.01.2022 to 10.01.2022 in their respective Sachivalams and see that all students are vaccinated."*

(A copy of the letter dated 1st January 2022 by the District Educational Officer, YSR District, Kadapa, Andhra Pradesh is annexed as **Annexure A22 (Page** 159 **to_____)**

36. A Deccan Herald article dated 4th January 2022 and titled 'Parents fume after some Karnataka schools make Covid-19 vaccinations mandatory', reported that schools in Karnataka were making vaccinations compulsory fueling fears that vaccinations may be compulsory to sit for board examinations despite government clarifications that COVID-19 vaccinations are voluntary:

> *"Such sentiments were also echoed by other parents that DH met after several schools made vaccination mandatory and sent out warning messages as the vaccination programme kicked off amid a Covid-19 surge. Parents revealed that some of the private unaided schools sent out messages on Sunday evening itself, mandating offline attendance for children on Monday following the vaccination session."*

(A copy of the Deccan Herald article dated 04.01.2022 and titled 'Parents fume after some Karnataka schools make Covid-19 vaccinations mandatory' has been annexed as **Annexure A23 (Page** 160 **to** 162**)**

37. A notice letter addressed to the 'The Principal Secretaries/Secretaries WCD/SJE (All States/UTs)' from the Ministry of Women and Child Development that vaccinations are compulsory for children:

> "F*urther, it is brought to the notice that in light of the compulsory vaccination of children against COVID-19 falling in the 15-18 age group, it is requested that all District Magistrates may be directed*

*to make appropriate arrangements on for vaccination of the Children living in CCIs as well, on pri*ority basis."

(A copy of the notice letter dated 4th January 2022 addressed to the 'The Principal Secretaries/Secretaries WCD/SJE (All States/UTs)' by the Director to the Government of India is annexed as **Annexure A24 (Page** 163 **to** 164 **)**.

38. In a letter dated 4th January 2022, the Council for the Indian School Certificate Examinations addressed to all heads of affiliated schools, the Chief Executive and Secretary made it mandatory for children to be vaccinated to sit in examinations. The relevant parts of the letter are reproduced below:

"*Considering the above, the CISCE would like to advise you to encourage all your parents and guardians to get their children in the age group of 15-18 years vaccinated at the earliest. Vaccination against the Covid-19 virus is the best protection which can be given to children at this stage. All candidates for the ICSE & ISC Year 2022 Examinations should be vaccinated before the start of the said examinations.*"

(A copy of the notice letter dated 4th January 2022 by the Council for the Indian School Certificate Examinations is annexed as **Annexure A25 (Page** 165 **to_____)**.

39. Another school, Lawrance Public Sr. Sec. School, Mohali, made it mandatory for students to be vaccinated and stated that unvaccinated children will not be allowed in offline classes.

(A copy of the notice letter dated 8th January 2022 by Lawrance Public Sr. Sec. School, Mohali is annexed as **Annexure A26 (Page** 166 **to____)**.

PRAYER

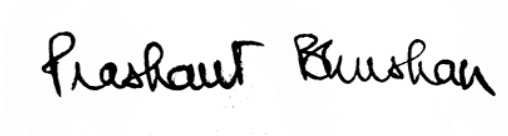
In view of the abovementioned facts and in the interest of public safety, it is respectfully submitted that this Hon'ble Court may be pleased to

a) Direct the respondents to release the entire segregated trial data for each of the phases of trials that have been undertaken with respect to the vaccines being administered in India for children along with the trial data for those vaccines in adults; and

b) Declare that vaccine mandates for children, in any manner whatsoever, even by way of making it a precondition for accessing educational institutions or sports facilities, is unconstitutional; and

c) Pass any other orders as this Hon'ble Court deems fit.

PETITIONER THROUGH:



(PRASHANT BHUSHAN)
COUNSEL FOR THE PETITIONER

DRAWN & FILED ON: 10th JANUARY 2022
PLACE: NEW DELHI

IN THE SUPREME COURT OF INDIA

(CIVIL ORIGINAL JURISDICTION)

I.A. NO. _____ OF 2021

IN

WRIT PETITION (CIVIL) NO. 607 OF 2022

IN THE MATTER OF:

Dr. JACOB PULIYEL ....PETITIONER

VERSUS

UNION OF INDIA & Ors ....RESPONDENTS

AFFIDAVIT

I, Dr. Jacob Puliyel, S/o Late Mr. P M Mammen, r/o 6A, 7 Raj Narayan Marg, Delhi – 110054, do hereby solemnly affirm and state on oath as under:

1. That I am the Petitioner in the aforementioned writ petition and being familiar with the facts and circumstances of the case, I am competent and authorized to swear this Affidavit.

2. That I have read and understood the contents of the application for directions **(Page** 1 **to** 26 **).** I state that the facts therein are true to the best of my knowledge, belief and nothing material has been concealed therefrom.

3. The annexures are true copies of their respective originals.

4. The source of the information is media reports, government orders and Supreme Court and High court judgments and other information which is available in the public domain.

5. That this petition is only motivated by public interest. I affirm that I have no personal interest in this matter.

NOTARY
Rajendra Kumar
Delhi
Regd. No. 5780
Date of Expiry
27th April-2023
GOVT. OF INDIA

6. That I have done whatsoever enquiry that was possible and I state that no relevant facts in my knowledge have been withheld.

DEPONENT

VERIFICATION:

I, the above named Deponent, do hereby verify that the contents of the above Affidavit are true and correct to my knowledge; that no part of it is false and that nothing material has been concealed therefrom.

Verified at New Delhi on 10th day of January 2022

NOTARY
Rajendra Kumar
Delhi
Regd. No. 5780
Date of Expiry
27th April-2023
GOVT. OF INDIA

DEPONENT

CERTIFIED THAT THE CONTENTS EXPLAINED TO THE DEPONENT EXECUTANT WHO IS SEEMED PERFECT TO UNDERSTAND & AFFIRMED DEPOSED BEFORE ME AT DELHI ON ..... INDENTIFIED BY
10 JAN 2022
IDENTITY THE EXECUTANT/DEPONENT WHO HAS SIGNED IN MY PRESENCE

IDENTITY THE EXECUTANT / DEPONENT WHO WAS SIGNED IN THE PRESENCE OF

ATTESTED
RAJENDRA KUMAR
NOTARY, DELHI-R-5780
GOVERNMENT OF INDIA
SUPREME COURT OF INDIA
COMPOUND, NEW DELHI
Register Pg./Sl. No..... 10 JAN 2022
Mobile No.: 9899446209

Guidelines for COVID-19 vaccination of children between 15-18 years and precaution dose to HCWs, FLWs & 60+ population with comorbidities

India's National COVID Vaccination Program is built on scientific and epidemiological evidence, WHO guidelines and global best practices. Anchored in systematic end-to-end planning, it is implemented through effective and efficient participation of States/UTs and the people at large.

Government of India's commitment to the vaccination program has been unwavering and proactive from the beginning, from strengthening Research and Development capacity, to encouraging and enabling manufacturing and vaccinating each and every adult Indian safely, as fast as possible.

As a consequence of reliance on scientific & epidemiological evidence and pro-active implementation, India's COVID-19 vaccination programme has achieved historical milestone of administering more than 141 crore doses so far. 90% of the adult population of the country has been covered with at least one dose and 62% of the adult population has been covered with both the doses.

For the COVID vaccination program, Government of India initiated early and proactive steps as far back as April 2020:

- "Task Force for Focused Research on Corona Vaccine" (constituted in April 2020), to encourage domestic R&D of Drugs, Diagnostics and Vaccines, headed by Principal Scientific Advisor to the Government of India.
- "National Expert Group on Vaccine Administration for COVID-19" (NEGVAC), (constituted in August 2020), to formulate a comprehensive action plan for vaccine administration, co-chaired by Member (Health) NITI Aayog and Union Health Secretary.
- "Empowered Group on Vaccine Administration for COVID-19" (constituted in January 2021), to facilitate optimal utilization of technology to make COVID vaccination all inclusive, transparent, simple and scalable, headed by CEO, National Health Authority.

India's COVID vaccination program incorporates recommendations of the foremost experts in the field of immunization, public health, disease control and information technology. Based on scientific and epidemiological evidence, the programme gives priority to strengthening the country's healthcare system by protecting the professionals, health and frontline workers, manning it, as well as protecting the most vulnerable population groups.

COVID vaccination in the country commenced with vaccination to all Health Care Workers. The program was expanded with time to include vaccination of Front Line Workers, citizens more than 60 years of age, citizens more than 45 years of age, and eventually citizens more than 18 years of age.

Under the National COVID Vaccination Program, from 16th January to 30th April 2021, 100% of vaccine doses were procured by Government of India and provided free of cost to State Governments. State Governments were in turn to administer vaccination free of cost to defined priority groups. To increase the pace of vaccination, participation of private hospitals was also enlisted where individuals could also choose to get vaccinated at a prescribed rate.

In response to the suggestions of many State Governments to be permitted the flexibility to procure vaccine directly and administer them as per their own prioritization based on local requirements, Government of India revised the Guidelines. Under the revised Guidelines effective from 1st May, 2021, Government of India was procuring 50% of the vaccine produced and was continuing to provide them to States free of cost for administering to priority groups. The State Government and private hospitals were also empowered to directly procure from the remaining 50% vaccine pool.

Many States subsequently communicated that they were facing difficulties in managing the funding, procurement and logistics of vaccines, impacting the pace of the National COVID Vaccination Program. It was also noted that smaller and remoter private hospitals also faced constraints.

Keeping in view the aforesaid aspects, the experiences gained from 1st May 2021 and the repeated requests received from States, the Guidelines for National COVID Vaccination Program were reviewed and revised. These Revised Guidelines became effective from 21st June 2021.

Under the Revised Guidelines, Government of India procured 75% of the vaccines being produced by the manufacturers in the country and provided it free of cost to States/UTs as has been the case from the commencement of the National Vaccination Programme. These doses were administered by the States/UTs free of cost to all citizens as per priority through Government Vaccination Centres.

Vaccine doses provided free of cost by Government of India have been allocated to States/UTs based on criteria such as population, disease burden and the progress of vaccination. Wastage of vaccine has affected the allocation negatively.

Government of India has also provided States/UTs advance information of vaccine doses to be supplied to them. States/UTs were expected similarly, to further allocate doses well in advance to districts and vaccination centers. They were also expected to put in the public domain the information about the above availability at district and vaccination center level, and widely disseminate it among the local population, maximizing the visibility and convenience of citizens.

In order to incentivize production by vaccine manufacturers and encourage new vaccines, domestic vaccine manufacturers were given the option to also provide vaccines directly to private hospitals. This was restricted to 25% of their monthly production. Later on, it emerged that the off take of private hospitals was much below the aforesaid 25%. Therefore, the Govt. of India procured more than 75% of vaccines being produced by the manufacturers in the country. These vaccines were provided free of cost to the States/UTs.

All citizens irrespective of their income status have all along been entitled to free vaccination. Those who have the ability to pay are encouraged to use private hospital's vaccination centres.

The CoWIN platform provides every citizen the facility of conveniently and safely pre-booking vaccination appointments. All government and private vaccination centers also provide onsite registration facility, available both for individuals as well as groups of individuals, for which detailed procedure have been finalized and published by States/UTs, in order to minimize any inconvenience to citizens.

Keeping in view the recent global surge of COVID-19 cases, detection of Omicron variant which has been categorized as a Variant of Concern (VOC), scientific evidence, global practices and the inputs/suggestions of 'COVID-19 Working Group of National Technical Advisory Group on Immunization (NTAGI)' as well as of 'Standing Technical Scientific Committee (STSC)' of NTAGI it has now been decided to further refine the scientific prioritization & coverage of COVID-19 vaccination as follows:

1. COVID-19 Vaccination of children in the age-group of 15-18 years to be started from 3rd January 2022. For such beneficiaries, vaccination option would be "Covaxin" only.
2. As a matter of abundant precaution, for those Health Care Workers (HCWs) & Front Line Workers (FLWs) who have received two doses, another dose of COVID-19 vaccine would be provided from 10th January 2022. The prioritization and sequencing of this precaution dose would be based on the completion of 9 months i.e. 39 weeks from the date of administration of 2nd dose.
3. All persons aged 60 years and above with comorbidities who have received two doses of COVID-19 vaccine, will on Doctor's advice be provided with a

precaution dose from 10th January 2022. The prioritization and sequencing of this precaution dose would be based on the completion of 9 months i.e. 39 weeks from the date of administration of second dose.

All citizens irrespective of their income status are entitled to free COVID-19 vaccination at Govt. Vaccination Centres. Those who have the ability to pay are encouraged to use Private Hospitals' Vaccination Centres.

Co-WIN features and provisions:

1. HCWs, FLWs and Citizens 60+ with co-morbidities:
   a. All HCWs, FLWs and citizens aged 60 years or above with comorbidities will be able to access the vaccination for precaution dose through their existing Co-WIN account.
   b. Eligibility of such beneficiaries for the precaution dose will be based on the date of administration of 2nd dose as recorded in the Co-WIN system.
   c. Co-WIN system will send SMS to such beneficiaries for availing the precaution dose when the dose becomes due.
   d. Registration and appointment services can be accessed through both, the online and the onsite modes.
   e. The details of administration of the precaution dose will be suitably reflected in the vaccination certificates.
2. New beneficiaries aged 15-18 years:
   a. All those aged 15 years or more will be able to register on Co-WIN. In other worlds, all those whose birth year is 2007 or before, shall be eligible.
   b. Beneficiaries can self-register, online through an existing account on Co-WIN or can also register by creating a new account through a unique mobile number, this facility is available for all eligible citizens presently.
   c. Such beneficiaries can also be registered onsite by the verifier/vaccinator in facilitated registration mode.
   d. Appointments can be booked online or onsite (walk-in).
   e. For such beneficiaries, option for vaccination would only be available for Covaxin as this is the only vaccine with EUL for the age-group 15-18.

These Guidelines will come into effect from 3rd January 2022 & will be reviewed from time to time.

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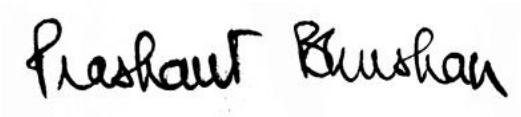

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ANNEXURE: A2

The Wire

10 Questions the Indian Govt Must Answer About Vaccines for Minors and Boosters

26/12/2021

Around 10 pm on December 25, 2021, Prime Minister Narendra Modi announced in a televised address that the Union health ministry would roll out COVID-19 vaccines for young adults aged 15-18 years as well as booster doses frontline and healthcare workers and the elderly (if they have a doctor's certificate).

Since the government didn't avail officials to elaborate on the decision at the late hour, here are 10 questions the Union health ministry and Prime Minister Modi should answer if the announcement is to make more sense.

1. On December 24, vaccination drive chief Vinod K. Paul, Indian Council of Medical Research chief Balram Bhargava and Union health secretary Rajesh Bhushan had said in a presser that their decisions are guided by science and that there isn't any scientific basis yet to necessitate paediatric vaccination. Are we to believe the science changed substantially between December 24 evening and December 25 night? If so, what exactly changed?

2. Which vaccines will frontline workers, healthcare workers and the elderly receive as booster doses? What will the rationale be for these decisions considering the Paul-Bhargava-Bhushan triumvirate admitted on December 24 that there haven't been studies thus far about Covaxin's

efficacy or its benefit as a booster dose – both against the omicron variant?

Addendum: Why has the emergency-approval for the Covavax vaccine, filed by Serum Institute, been delayed? Covovax was developed by Novavax and CEPI, and Novavax transferred the technology to Serum. This question arises because a) the WHO has already listed Covovax on its emergency-use vaccines roster, b) there has been a study from England saying the Covovax-equivalent there has been found to safely boost two doses of the AstraZeneca vaccine, and c) India is already exporting Covovax.

3. Did the Indian government wait to change its policy on vaccinating teenagers until the drug regulator had approved Covaxin for this age group? Because the government had approved Zydus Cadila's ZyCoV-D for teenagers in August and the evidence for the need to vaccinate children hasn't changed substantially since.

4. More worryingly, did the Indian government change its policy on vaccinating teenagers only because the drug regulator had approved Covaxin for this age group (considering the evidence at the moment on the need to vaccinate minors is iffy and debatable)? Put another way, if the regulator hadn't approved Covaxin – no matter how unlikely such rejection – would government officials have continued to say they're still unconvinced of the need to vaccinate children?

5. Covaxin maker Bharat Biotech has said it has formulated the vaccine such that the same dose works for those aged 15-18 years and for those older. How will this change the company's manufacturing and supply

calculi? Will existing stock start being diverted to vaccinate teenagers from January 3, 2022?

6. Bharat Biotech reportedly submitted data from phase 2/3 trials for Covaxin for those aged 15-18 years, conducted in India, to the Drug Controller General. Is this data in the public domain, for independent verification? Or must we wait until tens of thousands of teenagers have been vaccinated before we're offered a preprint paper?

Addendum: What about the deliberations of the National Technical Advisory Group on Immunisation, of the National Expert Group on Vaccine Administration for COVID-19 and of the Subject Expert Committee – all of which should have pointed the way for the drug regulator's decision?

7. The one other vaccine the drug regulator has approved for use among those aged 12-18 years is ZyCoV-D, made by Zydus Cadila. The phase 3 trial data for this product isn't available in the public domain either. Why?

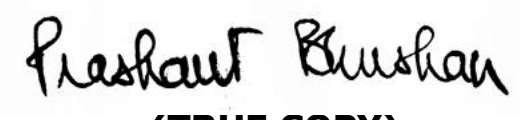
8. Why must elderly citizens get a doctor's certificate in order to receive booster doses while teenagers straightforwardly qualify for primary doses when the scientific evidence is ordered the other way: that SARS-CoV-2's effects become worse the older you are, especially if you're 60+, whereas the prevalence of disease, mild or severe, has been very low among minors? Remember that the vaccines' primary outcome is preventing severe disease, and transmission can be cut by better designing and enforcing COVID-appropriate behaviour.

9. How will informed consent work with people aged younger than 18 years? This isn't as simple as the buck stopping with their parents. For example, what happens when parents are opposed to a vaccine but their

child wants one, or vice versa? Or when one parent is in favour of vaccination but the other is against? The UK uses a test called the Gillick competence to arbitrate such cases. The test stipulates: "the parental right to determine whether or not their minor child below the age of sixteen will have medical treatment terminates if and when the child achieves sufficient understanding and intelligence to understand fully what is proposed."

10. Why is the prime minister making announcements about expanding the vaccination programme that are at odds with what representatives of the epidemiology and vaccination enterprises have been saying? And why is the prime minister making announcements related to healthcare at all instead of more informed officials who can answer questions from journalists and independent experts? (We may know the answer, but we must still ask.)

LINK: **https://science.thewire.in/health/10-questions-indian-govt-must-answer-covid-19-vaccines-teenagers-booster-doses/**



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News explainer

close-knit family structures in a country where adolescents tend to have frequent contact with their grandparents and often travel abroad for school.

Data show that children, and particularly adolescents, can play a significant part in coronavirus transmission, says Catherine Bennett, an epidemiologist at Deakin University in Melbourne, Australia. And concerns about transmission by children and adolescents are growing as new coronavirus variants emerge. It's possible that more-transmissible variants will develop a way to push through whatever it is in a young person's immune response that makes them more resistant to infection, says Bennett, making it all the more important that they are vaccinated.

Hopes of achieving herd immunity quickly through immunization have waned, so countries need to do the best that they can to keep transmission low, she adds: "You only need one poorly vaccinated population to generate global variants."

Is vaccinating children fair?

Chile, another country with a high COVID-19 vaccination rate, is also rolling out vaccines to those aged 12 and older.

But Miguel O'Ryan, a former member of two advisory committees to the government there who has pushed for aggressive vaccination campaigns, now finds himself wondering whether it's time to slow down. "Other countries, even our neighbours, are struggling very hard to get enough vaccines for their high-risk groups," says O'Ryan, who is a paediatric infectious-disease specialist at the University of Chile in Santiago.

In May, World Health Organization chief Tedros Adhanom Ghebreyesus said that wealthier countries that are vaccinating children are doing so at the expense of health-care workers and high-risk groups in other countries. But advocates for vaccinating children and young adults argue that it need not be a case of one or the other. Sam-Agudu points out that some wealthy countries bought more than enough doses to fully vaccinate their populations, and that sending vaccines abroad "should not preclude vaccinating children in higher-income countries".

By Heidi Ledford

DEATHS FROM COVID 'INCREDIBLY RARE' AMONG CHILDREN

Studies find that overall risk of death or severe disease from COVID-19 is very low in kids.

By Heidi Ledford

A comprehensive analysis of hospital admissions and reported deaths across England suggests that COVID-19 carries a lower risk of dying or requiring intensive care among children and young people than was previously thought.

COVID-19 caused 25 deaths in that age group between March 2020 and February 2021, researchers reported in a series of preprints published on medRxiv[1–3]. About half of those deaths were in individuals with an underlying disability with high health-care needs, such as tube feeding or assistance with breathing.

The studies did not evaluate rates of less severe illness or debilitating 'long COVID' symptoms that can linger months after the acute phase of the infection has past. "The low rate of severe acute disease is important news, but this does not have to mean that COVID does not matter to children," says paediatrician Danilo Buonsenso at the Gemelli University Hospital in Rome. "Please, let's keep attention – as much as is feasible – on immunization."

In one of the preprints, the researchers trawled for published accounts of COVID-19 among children and young people, and ultimately analysed data from 57 studies and 19 countries[3]. They then picked apart risk factors for severe disease and death from the data.

Study findings

Some conditions – including obesity and cardiac or neurological conditions – were associated with a higher risk of death or intensive-care treatment, the researchers found. But the absolute increase in risk was very small, study author Rachel Harwood, a paediatric surgical registrar at Alder Hey Children's Hospital in Liverpool, UK, said at a media briefing.

For the other two preprints, the researchers focused on England, where they found that of 6,338 hospital admissions for COVID-19, 259 children and young people required treatment in intensive-care units.

Black children were more likely than their white counterparts to require intensive care, both for COVID-19 and for paediatric multisystem inflammatory syndrome, a rare syndrome associated with coronavirus infection. But overall, the need for intensive care was "incredibly rare" among these patients, says study author Joseph Ward at the University College London Great Ormond Street Institute of Child Health.

DAN KITWOOD/GETTY

A child performs a lateral-flow COVID test.

Of 3,105 deaths from all causes among the 12 million or so people under 18 in England between March 2020 and February 2021, 25 were attributable to COVID-19 – a rate of about 2 for every million people in this age range. None had asthma or type-1 diabetes, the authors note, and about half had conditions that put them at a higher risk than healthy children of dying from any cause.

In some cases, efforts to shield children thought to be vulnerable to severe complications from COVID-19 might have "caused more stress and anxiety for families than benefit", says Elizabeth Whittaker, an infectious-disease specialist at Imperial College London.

The work does not tackle the spectre of long COVID, but other studies suggest that it does occur in children – including in those who had mild initial symptoms or were asymptomatic – but less frequently than in adults.

Buonsenso still hopes that schools will embrace measures such as masks and improved ventilation, and that parents will focus on immunization – for either their children, where possible, or themselves.

1. Ward, J. L. *et al*. Preprint at medRxiv https://doi.org/10.1101/2021.07.01.21259785 (2021).
2. Smith, C. *et al*. Preprint at medRxiv https://doi.org/10.1101/2021.07.07.21259779 (2021).
3. Harwood, R. *et al*. Preprint at medRxiv https://doi.org/10.1101/2021.06.30.21259763 (2021).

Children and young people remain at low risk of COVID-19 mortality

Since early reports from China stated that severe COVID-19 disease was rare in children,[1] we have analysed child COVID-19 mortality in seven countries. To put the deaths into a context that would help the understanding of parents, clinicians, and policy makers, we previously made comparisons of COVID-19 deaths with modelled mortality from all causes and other causes. Our first publication in April, 2020,[2] was followed by a trend analysis up to August, 2020.[3] We also update a data table online. Here, we update this analysis to February, 2021, in light of increases in adult mortality through the 2020–21 winter, and concerns about variant B.1.1.7, first identified in the UK in December, 2020 (probably circulating since September).[4]

In the USA, UK, Italy, Germany, Spain, France, and South Korea, deaths from COVID-19 in children remained rare up to February, 2021, at 0·17 per 100 000 population, comprising 0·48% of the estimated total mortality from all causes in a normal year (table, appendix p 2). Deaths from COVID-19 were relatively more frequent in older children compared with younger age groups. The differences between countries need careful interpretation because of small numbers, possible differences in case definition and death reporting mechanisms, and the related condition paediatric inflammatory multisystem syndrome temporally associated with COVID-19, which might not always be captured in these data. Overall, there was no clear evidence of a trend of increasing mortality throughout the period up to February, 2021, but additional deaths have clearly occurred in children and young people during periods of high community transmission (appendix p 3).

Although COVID-19 mortality data are contemporary and likely to accurately represent the reality in these countries, it is not possible to access such data for other causes of death. We therefore used estimates from the Global Burden of Disease 2017 database, which does not account for seasonality or changes in mortality patterns in this pandemic year. Nevertheless, the very low mortality we describe from COVID-19 compared with all-causes is likely to be of the correct magnitude. With the caveat that some children at high risk might be using extreme so-called shielding measures, children are overall not becoming seriously unwell with COVID-19,[5] and data from England show that children are also not requiring intensive care in large numbers.[6]

Some of the measures to counteract the devastating impact of the virus on adults are having unintended negative consequences for children.[7] The possible benefit to wider society of these measures should be constantly scrutinised to ensure proportionality in line with outcomes for all. Our evidence indicates that children continue to be mostly, but not completely, spared the worst outcome of the pandemic, particularly compared with older adults who have been much harder hit.[8] We continue to caution that the virus is likely to change over time, and that these conclusions should be kept under review.

We declare no competing interests.

*Sunil S Bhopal, Jayshree Bagaria, Bayanne Olabi, Raj Bhopal
sunil.bhopal@newcastle.ac.uk

	Population	All-cause deaths*		COVID-19 deaths†		COVID-19 deaths as percentage of all-cause deaths, %
		n	per 100 000	n	per 100 000	
USA						
0–4 years	19 810 275	23 844	120·36	67	0·34	0·28%
5–14 years	41 075 169	4990	12·15	67	0·16	1·34%
UK						
0–9 years	8 052 552	3793	47·10	7	0·09	0·19%
10–19 years	7 528 144	1109	14·73	22	0·29	1·98%
Italy						
0–9 years	5 090 482	1569	30·83	8	0·16	0·51%
10–19 years	5 768 874	772	13·38	10	0·17	1·30%
Germany						
0–9 years	7 588 635	2782	36·66	9	0·12	0·32%
10–19 years	7 705 657	1249	16·21	4	0·05	0·32%
Spain						
0–9 years	4 370 858	1369	31·31	8	0·18	0·58%
10–19 years	4 883 447	532	10·89	18	0·37	3·39%
France						
0–9 years	7 755 755	2916	37·60	7	0·09	0·24%
10–19 years	8 328 988	1068	12·82	4	0·05	0·38%
South Korea						
0–9 years	4 148 654	1519	36·61	0	0·00	0
10–19 years	4 940 455	814	16·48	0	0·00	0
Total	137 047 945	48 326	35·26	231	0·17	0·48%

The sources of these data are provided in the appendix (p 2). *Includes all deaths from approximately March 1, 2020, to Feb 1, 2021. †Includes all COVID-19 deaths reported from the start of the pandemic up to Feb 3, 2021 (USA), Jan 29, 2021 (UK), Jan 20, 2021 (Italy), Feb 9, 2021 (Germany), Feb 10, 2021 (Spain), Feb 11, 2021 (France), or Feb 3, 2021 (South Korea).

Table: **Age-specific data for seven countries showing estimated all-cause deaths compared with COVID-19 deaths**

Published **Online** March 10, 2021 https://doi.org/10.1016/S2352-4642(21)00066-3

This online publication has been corrected. The corrected version first appeared at thelancet.com/child-adolescent on March 24, 2021

For the **data table of COVID-19 deaths** see https://docs.google.com/document/d/e/2PACX-1vSty5XpnB4wbGYanBcuUu-AVk0OIHyhOGs0Eh1Ug23PwMFNjuIUPos47rTG_ql5gFfeLLsZk0nkC_UL/pub

See **Online** for appendix

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Prashant Bhushan

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ANNEXURE: A5

BBC

Covid: Children's extremely low risk confirmed by study

Published 9 July 2021

The overall risk of children becoming severely ill or dying from Covid is extremely low, a new analysis of Covid infection data confirms.

Data from the first 12 months of the pandemic in England shows 25 under-18s died from Covid.
Those living with multiple chronic illnesses and neuro-disabilities were most at risk, though the overall risk remained low.

The conclusions are being considered by the UK's vaccine advisory group.

Currently, under-18s are not routinely offered Covid vaccines, even if they have other underlying health conditions that put them at risk.
Covid in children graphic
Scientists from University College London, and the Universities of York, Bristol and Liverpool say their studies of children are the most comprehensive yet anywhere in the world.
They checked England's public health data and found most of the young people who had died of Covid-19 had underlying health conditions:

Around 15 had life-limiting or underlying conditions, including 13 living with complex neuro-disabilities
Six had no underlying conditions recorded in the last five years - though researchers caution some illnesses may have been missed

A further 36 children had a positive Covid test at the time of their death but died from other causes, the analysis suggests

Though the overall risks were still low, children and young people who died were more likely to be over the age of 10 and of Black and Asian ethnicity.

Researchers estimate that 25 deaths in a population of some 12 million children in England gives a broad, overall mortality rate of 2 per million children.

Current data shows some 128,301 people in the UK have died within 28 days of a positive coronavirus test since the pandemic started.

'Hospital stays rare'

Separately, scientists considered all children and young people in England who had an emergency hospital admission for Covid up to February 2021:

Some 5,800 children were admitted with the virus, compared to about 367,600 admitted for other emergencies (excluding injuries)

About 250 required intensive care

There were 690 children admitted for a rare inflammatory condition linked to Covid, called paediatric inflammatory multisystem syndrome (PIMS-TS)

Though the absolute risks were still small, children living with multiple conditions, those who were obese, and young people with heart and neurological illnesses were most at risk

Lead researcher Prof Russell Viner said complex decisions around vaccinating and shielding children required input from many sources - not their work alone.

But he said if there were adequate vaccines, their research suggested certain groups of children could benefit from receiving Covid jabs.

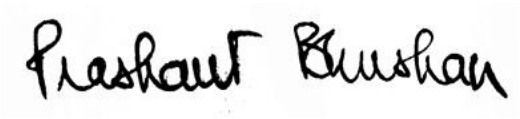
He added: "I think from our data, and in my entirely personal opinion, it would be very reasonable to vaccinate a number of groups we have studied, who don't have a particularly high risk of death, but we do know that their risk of having severe illness and coming to intensive care, while still low, is higher than the general population."

He said further vaccine data - expected imminently from other countries, including the US and Israel - should be taken into account when making the decision.

What is the risk of schools spreading coronavirus?
Will children get the coronavirus vaccine?
Dr Elizabeth Whittaker, from the Royal College of Paediatrics and Child Health and Imperial College London, said it was encouraging they were seeing very few seriously unwell children in hospital.

She added: "Although this data covers up to February 2021, this hasn't changed recently with the Delta variant. We hope this data will be reassuring for children and young people and their families."

Link: https://www.bbc.com/news/health-57766717#:~:text=The%20overall%20risk%20of%20children,under%2D18s%20died%20from%20Covid.



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ANNEXURE: A6

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Public Health 185 (2020) 19–20

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journal homepage: www.elsevier.com/locate/puhe

Letter to the Editor

Children's mortality from COVID-19 compared with all-deaths and other relevant causes of death: epidemiological information for decision-making by parents, teachers, clinicians and policymakers

Governments are grappling with the challenge of returning societies to quasi-normal following 'lockdowns' to control the coronavirus disease 2019 (COVID-19) pandemic. Policymakers, the public, and especially parents are understandably anxious about the implications of reopening nurseries and schools. In Europe, Norway, Denmark, France and Germany have already reopened schools. The UK government signalled its intention to do so from 1 June 2020 to vast unease and controversy amongst the public, not least from teachers' unions whose arguments against premature reopening have polarised opinion. Others have described 'collateral damage' to children through social distancing measures[1] and questioned compatibility with the UN convention on the rights of the child.

Although decisions about allowing children to exit their homes, and to restart schooling, are ultimately value judgements, we think that understanding current risks to children from COVID-19 can be aided through epidemiology and that this understanding should underpin decision-makers' and parents' views.[2] We accept that there is much to learn about this new disease, and that the virus is likely to change during the pandemic and add new complexities.

We synthesised information on COVID-19 in relation to other causes of death in line with a previous call for increased focus on age-specific mortality.[3] We examined mortality as an important outcome providing accurate data, while recognising that reports about a multisystem hyper-inflammatory state in children need investigation and may modify our conclusions in due course.[4] Fortunately, the number of hospitalisations and intensive care unit (ICU) admissions in children remains low.[5]

We examined age-specific data on COVID-19 deaths which had been collated from official government sources for seven countries up to 8–19 May 2020.[6] These countries were chosen due to data availability and high burden of adult COVID-19 death. The data were first extracted by S.B. and then cross-checked by S.B. and J.B. together to ensure accuracy. We obtained estimated numbers of deaths from other causes from Global Burden of Disease estimates[7] except for influenza for which we examined official government statistical websites and extracted age-specific death counts for up to the last five years (2015–2019). To help to compare like-with-like we adjusted mortality counts to reflect a three-month time period (Table 1).

For this time period, in these seven countries combined, 44 COVID-19 deaths were reported in 42,846 confirmed cases (this latter number is likely to be a massive underestimate; data were not available for France) in those aged 0–19 years (0–14 in USA). This compares with 13,200 estimated deaths from all-causes, including 1056 from unintentional injury, and 308 from lower respiratory tract infection (107 from influenza). The situation in each country was almost identical, and in accordance with early data from China[8] i.e. COVID rarely kills children, even compared with influenza, against which many children are already vaccinated. Our data show that for mortality COVID-19 is similar to flu, or less severe, in children whilst being the opposite in adults.

Our analysis should help parents, teachers and policymakers to make important decisions and possibly feel reassured about the direct impact of COVID-19 on children. Political leaders, communities, clinicians and parents should appreciate that the main reason we are keeping children at home and socially isolated is to protect adults. The ethics of this choice need to be publicly debated. Adults, especially those at increased risk, including those with comorbidities or the elderly, who are in close contact with children, need shielding. In children, at least in this wave of the pandemic and hopefully in the future, COVID-19 is a comparatively rare cause of death. We need to maintain close surveillance of COVID-19 in children in case this conclusion changes as the pandemic unfolds and the virus (SARS-CoV-2), evolves.

https://doi.org/10.1016/j.puhe.2020.05.047

Table 1
Age-specific data for seven countries showing population, estimated deaths from all and specific causes for three months, compared with COVID-19 cases and deaths from the beginning of the COVID-19 pandemic to 8–19 May 2020 (see note five for exact date for country, which varies by reporting method).

Country	Age	Population	All-cause deaths		Unintentional injury deaths		LRTI deaths		Influenza deaths	Confirmed COVID-19 cases	COVID-19 deaths		COVID-19 deaths as % of all deaths
			n	per 100,000	n	per 100,000	n	per 100,000	n	n	n	per 100,000	
USA	0-4 y	9,810,275	6503	32.83	522	2.63	159	0.80	46	4385	6	0.03	0.092%
	5-14 y	41,075,169	1361	3.31	194	0.47	35	0.09	43	17,523	7	0.02	0.514%
United	0-9 y	8,052,552	1034	12.84	34	0.42	34	0.42	4	972	2	0.02	0.193%
Kingdom	10-19 y	7,528,144	303	4.02	26	0.35	6	0.08	2	1245	9	0.12	2.975%
Italy	0-9 y	5,090,482	428	8.41	17	0.32	11	0.21	5	1774	4	0.08	0.935%
	10-19 y	5,768,874	211	3.65	20	0.34	3	0.05	3	3148	0	0.00	0.000%
Germany	0-9 y	7,588,635	759	10.00	36	0.47	14	0.18	1	3172	1	0.01	0.132%
	10-19 y	7,705,657	341	4.42	24	0.31	5	0.06	1	7350	2	0.03	0.587%
Spain	0-9 y	4,370,858	373	8.54	20	0.45	9	0.21	1	857	2	0.05	0.536%
	10-19 y	4,883,447	145	2.97	15	0.31	3	0.05	1	1591	5	0.10	3.448%
France	0-9 y	7,755,755	795	10.25	58	0.75	13	0.16	NA	NA	3	0.04	0.377%
	10-19 y	8,328,988	291	3.50	29	0.35	3	0.04	NA	NA	3	0.04	1.030%
Korea	0-9 y	4,148,654	414	9.99	39	0.93	10	0.24	NA	143	0	0.00	0.000%
	10-19 y	4,940,455	222	4.49	21	0.42	3	0.06	NA	614	0	0.00	0.000%
TOTAL		**137,326,595**	**13,200**	**9.62**	**1056**	**0.77**	**308**	**0.22**	**107**	**42,846**	**44**	**0.03**	**0.333%**

NA = not publicly available; coronavirus disease 2019 (COVID-19).
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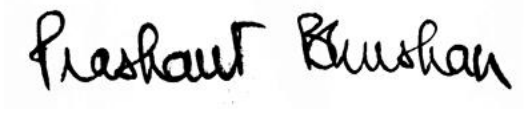
21 May 2020
Available online 30 May 2020



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ANNEXURE: A7

The Indian Express

2 of 3 Indians have Covid-19 antibodies: ICMR serosurvey findings explained

26th July, 2021

Two-third of Indians above the age of 6 had SARS-CoV-2 antibodies, show findings of the fourth nationwide serological survey conducted by the Indian Council of Medical Research (ICMR) in June-July. The survey results also suggest that about 40 crore people or one-third of the country's population is still vulnerable to the novel coronavirus.

The survey was conducted across the country in June and July. Its findings are significant because this is for the first time children aged 6-17 years were included in the national serosurvey. The results of the survey were released by DG, ICMR, Dr Balram Bhargava.

What is the ICMR serosurvey?

The ICMR has conducted the fourth round of national blood serum survey which tests for antibodies, known as a serosurvey, for Covid-19. The aim of the survey was to estimate the sero-prevalence of SARS-C0V-2 antibodies.

The survey was conducted in June and July, 2021 across 70 districts of 21 states. These are the same districts where three earlier rounds have been conducted during May-June (2020); August-September (2020); and December-January (2020-2021).

Who all did the survey cover?

The survey was conducted among 28,975 people. For the first time children aged 6-17 years were included in the survey. Besides, it included 7,252 healthcare workers.

What are the findings of the fourth round of national serosurvey?

The results of the IMCR's fourth round of national serosurvey shows that the overall sero-prevalence in the country was 67.6% in June and July, which is higher than the sero-prevalence rate recorded during the three earlier surveys – 0.7 percent during May-June (2020); 7.1 percent during August-September (2020); and 24.1 percent during December-January (2020-2021).

So, the latest findings of the survey suggest that two-third of the general population above 6 years have SARS-CoV-2 antibodies, which means that two-third of Indians have been exposed to novel coronavirus. It also shows that one-third of the population does not have antibodies, which suggests that about 40 crore people are still vulnerable to the novel coronavirus.

"In conclusion, two-thirds of the general population that is above the age of six years had SARS-CoV-2 infection. More importantly, a third of the population did not have any antibodies… 40 crore population of this country is still vulnerable," Bhargava said, addressing a press conference.

"States/districts/areas without antibodies run the risk of infection waves," Bhargava said.

The survey also shows that sero-prevalence was similar in rural and urban areas. It also suggests that 85 per cent healthcare workers had antibodies against SARS-CoV-2.

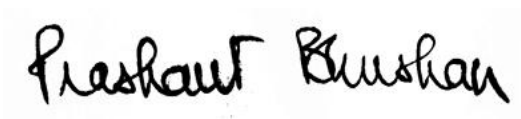
What does the survey say about children?

The survey findings shows that more than half of the children (6 -17 years) were seropositive. It means they have been exposed to Covid-19 in the past months. The sero-prevalence among children was 57.2 per cent in the age group 6-9 years and 61.6 per cent in the age group 10-17 years.

What are the implications of the latest findings of the serosurvey?

Bhargava says there is a "ray of hope" but there is "no room for complacency." He emphasised on the need of maintaining Covid-appropriate behaviour and curbs on community engagement. He said societal, public, religious and political congregations should be avoided.

LINK: https://indianexpress.com/article/explained/explained-icmr-covid-fourth-serosurvey-findings-7413949/



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ANNEXURE: A8

The Indian Express

97% people have Covid-19 antibodies, shows sero survey

Delhi: 97% people have Covid-19 antibodies, shows sero survey

Positivity in vaccinated people is 97-98%, while in non-vaccinated, it is 90%.

By: Express News Service | New Delhi |

Updated: October 28, 2021 4:21:26 pm

Health Minister Satyendar Jain said that a large part of Delhi's population has been affected by Covid-19 and the rest have been vaccinated. (Express photo by Praveen Khanna)

Delhi has a seropositivity of 97 per cent for Covid-19 antibodies, the sixth serological survey conducted in the city has revealed, Delhi Health Minister Satyendar Jain said Thursday. Every district has a seropositivity of above 95 per cent, he said.

Samples for the survey were collected in the last week of September. A total of 28,000 samples were collected — 100 each from 280 civic wards. This was the first such survey conducted after the deadly second wave hit the national capital in April and May.

A survey planned in April had to be abandoned midway because of the soaring case count.

"The seropositivity in women is slightly higher than that in men. In children below the age of 18, the sero prevalence is 88 per cent, while it is 97 per cent to 98 per

cent in adults. The survey included vaccinated and unvaccinated people. The unvaccinated have a prevalence of 90 per cent, and those who have been vaccinated is above 97 per cent," said Jain.

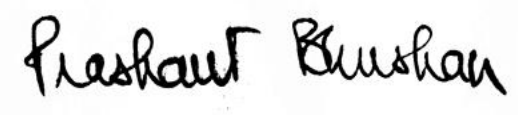
The minister said that a large part of Delhi's population has been affected by Covid-19 and the rest have been vaccinated. He, however, declined to comment on whether Delhi has now achieved herd immunity.

"The data shows clearly that sero positivity has increased slowly in Delhi. When the prevalence was 56 per cent, we thought it was a sign that a lot of people have got antibodies. Now it has increased to 97 per cent," he said.

Speaking about the status of vaccinated people, Jain said that sero prevalence was high in both vaccinated and unvaccinated people, but it was higher in those who have been vaccinated.

Sero surveys in other cities, conducted after the second wave and vaccination drives, also show high sero prevalence.

Link: https://indianexpress.com/article/cities/delhi/people-in-delhi-have-covid-19-antibodies-shows-sero-survey-7595390/



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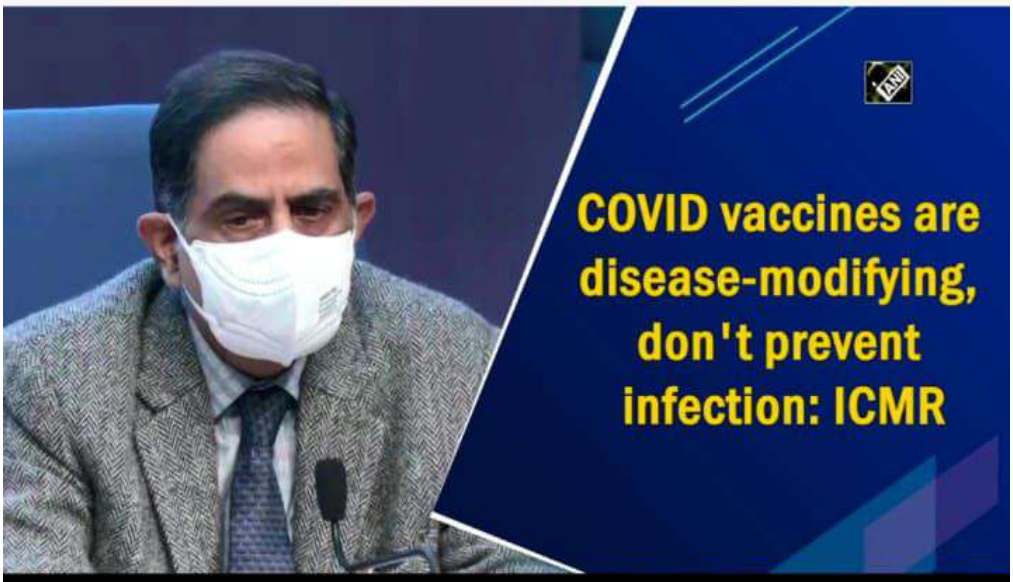

COVID vaccines are disease-modifying, don't prevent infection: ICMR

Dec 30, 2021, 09:49PM IST | Source: ANI |

518 Views

All COVID vaccines do not prevent infection and are primarily disease-modifying, said Dr Balram Bhargava, Director General, Indian Council of Me Research (ICMR) on December 30. He said, "All COVID vaccines, whether they are from India, Israel, US, Europe, UK or China, are primarily disease-modifying. They don't prevent infection. The precautionary dose is primarily to mitigate the severity of infection, hospitalisation, and death." He further added, "Use of masks before and after vaccination is a must and mass gatherings should be avoided... The treatment guidelines for the earlier and the currently circulating strains of coronavirus remain the same. Home isolation remains an important pillar."

Read less

Prashant Bhushan

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ANNEXURE: A10

The Guardian

Spain, Belgium and Italy restrict AstraZeneca Covid vaccine to older people

Thu 8 Apr 2021 11.22 BST

Italy, Spain and Belgium have joined other European countries in limiting the use of the Oxford/AstraZeneca vaccine to older age groups as the EU struggles to agree common guidelines to counter expected public hesitancy.

The European Medicines Agency (EMA) on Wednesday found a possible link between the vaccine and very rare cases of blood clots, although it said its benefits far outweighed the risks and did not announce any restrictions.

In Britain, the government's joint committee on vaccines and immunisation said healthy people aged 18 to 24 who were not at high risk of Covid should have the option of a different jab if one was available in their area.

Belgium's national and regional health ministers subsequently agreed to restrict the vaccine to the over-55s for a month, while Italy's health minister, Roberto Speranza, said late on Wednesday the shot should be offered only to those aged 60 and over.

Franco Locatelli, the head of the country's health council, said people who had already had the first dose of the AstraZeneca jab could proceed with the second, and officials stressed that while the shot was not recommended for under-60s, it was not prohibited.

After meeting regional health chiefs, Spain's health minister, Carolina Darias, also announced late on Wednesday that administration of the AstraZeneca vaccine would be temporarily suspended nationwide to people under the age of 60.

Spain's autonomous regions have given more than 2.1m first shots of the Anglo-Swedish shot under a patchwork of rules and at various paces. Authorities now have to decide whether to use a different vaccine for the second dose.

EU countries that have already imposed restrictions include Germany, which is limiting its use to under-60s and priority groups and has recommended that people under 60 who have had a first shot should receive a different second dose.

But countries are setting a range of age limits for the shot, with France restricting its use to people aged 55 and over, the Netherlands to those aged 60 and over, and Finland and Sweden to people aged 65 and over.

EU health ministers failed at an extraordinary meeting on Wednesday night to agree a coordinated approach despite a plea by Portugal, which holds the bloc's rotating presidency, to urgently seek common ground on the use of the vaccine.

"It is essential that we follow a coordinated European approach – an approach which does not confuse citizens, and that does not fuel vaccine hesitancy," the EU health commissioner, Stella Kyriakides, reportedly told ministers at the meeting.

The EMA said it received reports of 169 cases of the rare brain blood clot by early April, after 34m doses had been administered in the European Economic Area (EEA), adding that most occurred in women under 60 within two weeks of vaccination.

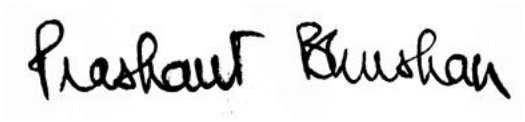
In Germany, Christian Bogdan, a member of the country's vaccine committee, said instances of the condition in women under 60 who had been given the AstraZeneca shot were 20 times higher than would normally be expected, representing what he called a "very clear risk signal".

Countries that have imposed age restrictions on the AstraZeneca vaccine now face the conundrum of what to do about younger people who have had a first dose. Some experts say different vaccines could work together to fight the virus because all target the same outer "spike" protein of the virus.

Germany has recommended that people under 60 who have had a first AstraZeneca shot should receive a different product for their second dose. Other countries are waiting for the results of a British trial launched in February to explore mixing doses of Pfizer and AstraZeneca vaccines.

France's top health advisory council is reportedly considering using mRNA vaccines such as those produced by Pfizer/BioNTech and Moderna as a second dose, but no formal decision has not been yet taken.

LINK : **https://www.theguardian.com/society/2021/apr/08/spain-belgium-and-italy-restrict-astrazeneca-covid-vaccine-to-older-people**



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ANNEXURE: A11

Risk of Myocarditis from COVID-19 Infection in People Under Age 20: A Population-Based Analysis

MedRxiv

ABSTRACT

Background There have been recent reports of myocarditis (including myocarditis, pericarditis or myopericarditis) as a side-effect of mRNA-based COVID-19 vaccines, particularly in young males. Less information is available regarding the risk of myocarditis from COVID-19 infection itself. Such data would be helpful in developing a complete risk-benefit analysis for this population.

Methods A de-identified, limited data set was created from the TriNetX Research Network, aggregating electronic health records from 48 mostly large U.S. Healthcare Organizations (HCOs). Inclusion criteria were a first COVID-19 diagnosis during the April 1, 2020 - March 31, 2021 time period, with an outpatient visit 1 month to 2 years before, and another 6 months to 2 years before that. Analysis was stratified by sex and age (12-17, 12-15, 16-19). Patients were excluded for any prior cardiovascular condition. Primary outcome was an encounter diagnosis of myocarditis within 90 days following the index date. Rates of COVID-19 cases and myocarditis not identified in the system were estimated and the results adjusted accordingly. Wilson score intervals were used for 95% confidence intervals due to the very low probability outcome.

Results For the 12-17-year-old male cohort, 6/6,846 (0.09%) patients developed myocarditis overall, with an adjusted rate per million of 876 cases (Wilson score interval 402 - 1,911). For the 12-15 and 16-19 male age groups, the adjusted rates per million were 601 (257 - 1,406) and 561 (240 - 1,313).

For 12-17-year-old females, there were 3 (0.04%) cases of myocarditis of 7,361 patients. The adjusted rate was 213 (73 - 627) per million cases. For the 12-15- and 16-19-year-old female cohorts the adjusted rates per million cases were

235 (64 - 857) and 708 (359 - 1,397). The outcomes occurred either within 5 days (40.0%) or from 19-82 days (60.0%).

Conclusions Myocarditis (or pericarditis or myopericarditis) from primary COVID19 infection occurred at a rate as high as 450 per million in young males. Young males infected with the virus are up 6 times more likely to develop myocarditis as those who have received the vaccine.

Background

Evidence has accumulated that myocarditis (used throughout, as in other studies, to include myocarditis, pericarditis or myopericarditis) is a rare side-effect of mRNA-based COVID-19 vaccines.[1-4] A recent update from the Advisory Committee on Immunization Practices (ACIP) included an analysis that weighed the benefits of COVID-19 vaccination through reduction in infections against the harm of the vaccine. The report used data from the Vaccine Adverse Events Reporting System (VAERS) and reported rates of myocarditis following mRNA vaccination. Risk for males under 30 was about 10 times that of males age 30 or over. The highest risk group was 12-17-year-old males after the 2nd dose, with an estimated 66.7 cases per million.[4] However, it is not known how this compares to the risk from the virus itself. Since relatively early in the pandemic, myocarditis has been recognized as a serious complication in hospitalized COVID-19 patients, including those with no prior history of cardiovascular disease, and there is histological evidence that inflammation and myocardial necrosis is present in the hearts of patients who succumbed to the disease.[5-7] However, myocarditis is not well studied in low risk COVID-19 patients. Several recently published papers have studied myocarditis in athletes, both college and professionals, but there is limited data on risk of myocarditis in other young people.[8-10] Although the ACIP report clearly demonstrated that the benefit of COVID-19 vaccination outweighs the risk in all age groups, a direct comparison of risk of myocarditis from disease vs. vaccination might allow for a more comprehensive risk-benefit assessment.

Methods

A de-identified, limited data set was extracted on June 24, 2021 from the TriNetX Research Network, a federated health research network that aggregates electronic health records from 53 mostly large U.S. Healthcare

Organizations (HCOs), including over 60 million people. For this study, the necessary data was available from 48 of the participating HCOs. The index date was the first COVID-19 encounter diagnosis or positive virus test, April 1, 2020 - March 31, 2021. We considered three age cohorts: 12-17 years old to match US myocarditis data following mRNA COVID-19 vaccination, and 12-15 and 16-19 years old to align with common age groupings for vaccination policy and an Israeli report of especially high risk in males age 16-19 following mRNA COVID-19 vaccination.[1,2,11] Given the demographics of earlier reports of mRNA vaccine-associated myocarditis, our report focuses on young males, but we include data for female cohorts for comparison purposes. To ensure a reasonable diagnosis history and relationship with the HCO, patients were required to have two unrelated outpatient visits: 1 month to 2 years before the index date, and another 6 months to 2 years before that. Patients were excluded for any prior cardiovascular condition, or if they received an mRNA vaccine prior to diagnosis of myocarditis. Anyone with a diagnosis of "other specified viral infection" was excluded if they lacked a positive COVID-19 virus or antibody test. Patients with a lone COVID-19 diagnosis and a proximal (±3 days) negative COVID test but no positive test within 14 days following COVID-19 diagnosis were also excluded. Only birth year was available. Birthday was assumed to have passed if the index date was on or after July 1. The primary outcome was diagnosis of myocarditis within 90 days. **Table 1** shows the ICD-10-CM diagnosis codes used. The probability of myocarditis was expected to be too low to rely on the Normal approximation to the Binomial distribution, so Wilson Score intervals were used in place of 95% confidence intervals based on the normal approximation.

Condition	ICD-10-CM Diagnosis Codes
COVID-19	B34.2, B97.29, J12.81, J12.82, U07.1, U07.2
Myocarditis (including pericarditis, myopericarditis)	B33.22, B33.23, I30.1, I40, I41, I51.4
Cardiovascular condition	B33.22, B33.23, I00-I99, R00, R01.1, R01.2, R03

While cases of myocarditis are expected to result in interaction with the health care system, there will be many missed COVID-19 cases that will not be detected in the HCO's electronic health records. We sought to estimate the proportion of missed COVID-19 cases. For each cohort, we queried the TriNetX Live Research Network to find people with matching demographics using similar engagement with the HCO: outpatient visit in the system in the two years ending March 31, 2021 (our study's ending date for index COVID-19 diagnosis

or positive virus test), as well as another outpatient visit six months to two years before that. Of these people, we queried to find out how many of them had a COVID-19 diagnosis or positive virus test in our study period, April 1, 2020 - March 31, 2021. This proportion was compared to the proportion of the population that had COVID-19 during that period. In the United States, there is no national data on infection rate by age. According to a systematic review and the working assumption of the Centers for Disease Control and Prevention, children may have infection rates similar to adults, with younger people having more mild or asymptomatic cases.[12,13] Accordingly, we used the estimated 9.2% population infection rate for April 2020 - March 2021.[14] The estimated proportion of COVID-19 cases for 12-17 year old males was 2.5%. We then multiplied the denominator of COVID-19 cases in our study by 3.7 (9.2 / 2.5) to arrive at an adjusted number of COVID-19 cases. Similar calculations were done for the other cohorts.

The missed COVID-19 cases can be broken down into three categories: not tested and no physician contact; tested outside the TriNetX system but no physician contact; and tested and received care outside the TriNetX system. We assumed this last group would have clinical courses similar to those followed up in the TriNetX database. All three groups of missed cases were expected to be substantial in size and in the absence of data to refine the estimate, we assumed all three groups would be of equal size. Based on these assumptions, we adjusted the number of myocarditis cases to reflect the missed cases arising from patients tested and followed up outside of TriNetX.

Results

For the 12-17-year-old male cohort, 6,846 patients met the study criteria (**Table 2**). There were 6 (0.09%) cases of myocarditis overall, corresponding to a rate of 1 case of myocarditis per 1,141 COVID-19 patients, or 876 cases per million patients (Wilson Score interval: 402 - 1,911). After adjusting for missed cases of COVID-19 and myocarditis, the adjusted cases per million was 450 (206 - 982).

	Males			Females		
	Age 12-17	Age 12-15	Age 16-19	Age 12-17	Age 12-15	Age 16-19
N (COVID-19 Patients)	6,846	4,114	5,097	7,361	4,280	6,687
Myocarditis, N(%)	6 (0.09%)	5 (0.12%)	5 (0.10%)	3 (0.04%)	2 (0.05%)	8 (0.12%)
Rate per Million (Wilson Score Interval)	876 (402 - 1,911)	1,215 (519 - 2,842)	981 (419 - 2,294)	408 (139 - 1,198)	467 (128 - 1,702)	1,196 (606 - 2,359)
Adjusted Rate per Million (Wilson Score Interval)	450 (206 - 982)	601 (257 - 1,406)	561 (240 - 1,313)	213 (73 - 627)	235 (64 - 857)	708 (359 - 1,397)

For the 12-15 and 16-19 male age groups, the number of myocarditis cases were 5 of 4,114 (0.12%) and 5 of 5,097 (0.10%), and the adjusted cases per million were 601 (257 - 1,406) and 561 (240 - 1,313).

For 12-17-year-old females the adjusted rate of myocarditis was 213 (73 - 627) per million cases. For the 12-15- and 16-19-year-old female cohorts the adjusted rates per million cases were 235 (64 - 857) and 708 (359 - 1,397).

When males and females were combined the adjusted rates per million cases for age 12-17, 12-15 and 16-19 were 328 (173 - 624), 416 (202 - 858) and 643 (376 - 1,100), respectively.

8/20 (40.0%) cases of myocarditis were diagnosed within 5 days of the index date, while the other 12/20 (60.0%) cases were diagnosed 19-82 days after the index date. Two patients were hospitalized, one and three days after the index date. There were no reported deaths.

Discussion

Based on existing reports, myocarditis after RNA COVID-19 vaccination occurs largely after the second dose. The highest risk subgroup is 12-17 year old males, with 66.7 cases per million second doses and 9.8 per million first doses for a combined total of 76.5 cases per million vaccine recipients.[1,2], Our results suggest that, even for this high-risk subgroup, the risk of myocarditis from COVID-19 infection is about 5.9 times as great, at a rate of 450 cases per million. Based on the background rate of myocarditis in this population, the expected rate in the absence of COVID-19 for 90 days would be less than 0.1.[15] For 12-17 year old females, myocarditis following mRNA COVID-19 vaccination was 1.1 and 9.1 per million following the first and second doses, for a total of 10.2 per million getting vaccinated.[4] Risk of myocarditis from COVID-19 infection was nearly 21 times that rate, with an adjusted rate of 213 cases per million. For both males and females, risk of myocarditis from COVID-19 infection was higher in the 16-19 year-old than the corresponding 12-17 cohort.

Time from COVID-19 diagnosis or positive virus test to myocarditis was split into two distinct groups: 8/20 (40.0%) within 5 days and the rest at 19-82 days following index COVID-19 diagnosis or positive virus test. This may represent a combination of acute COVID-19 myocarditis and post-COVID-19 myocarditis. However, some of the delayed diagnoses may represent patients hospitalized

outside the TriNetX system who later followed up with their primary care provider in the HCO. Two patients had no COVID-19 diagnosis, but diagnosis of myocarditis at 62 and 82 days after positive COVID-19 virus test. One had their first diagnosis of both COVID-19 and myocarditis 58 days after positive virus test. Three others had their first COVID-19 diagnosis in the system at 5, 13 and 32 days after positive virus test and myocarditis diagnosed at days 20, 63 and 40, respectively. It is likely that some of these 6 cases represent people who were hospitalized at a facility not in the TriNetX database, making the true hospitalization rate perhaps several times higher than the 2/20 (10.0%) in the database, though any hospitalizations are in the context of other COVID-19 symptoms and complications. Whatever the true hospitalization rate was, it was considerably lower than that reported in the VAERS, where more than three-fourths of reported cases of myocarditis were hospitalized.[16]. Cases have been described as generally mild.[2,17,18] Admission rates may settle at a much lower rate over time as the natural history becomes better understood.

Several studies have identified post-COVID19 myocarditis in collegiate and professional athletes at rates of 0.6 - 2.3%.[8-10] However, there are comprehensive testing protocols for high level collegiate and professional athletes that are not applicable to the general population, and these may over-estimate the rate of clinically significant disease. One study of college athletes at Big-Ten schools reported that if a published diagnostic strategy based on cardiac symptoms had been employed, just 0.31% would have been diagnosed.[9,19] In this study, rates were about 0.1% before downward adjustments for missed COVID-19 cases. This lower rate is likely due to some combination of missed cases for reasons explained above, and a somewhat younger population.

Reliance on diagnosis codes for myocarditis might underestimate or overestimate cases. More than 1 in 5 COVID-19 cases were based only on diagnosis codes. This may be due to presumed diagnosis based on a combination of symptoms and family exposure. It may also be due in part to testing that takes place outside the HCO and is not in the HCO's EHR, e.g. pharmacies, community testing sites, health departments. Myocarditis cases may also be missed due to insufficient follow-up for COVID-19 cases at the end of the study period.

Another limitation is the approach taken to account for missed cases of COVID-19. We assumed that infection rates are similar for 12-19-year-olds and the

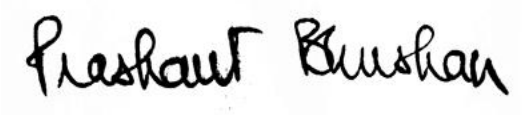
overall population, and that one-third of the extra COVID-19 cases not detected in the database were tested and seen by physicians with similar rates of myocarditis. There is no currently available data to support precise estimates. However, assuming no additional cases of myocarditis from any of the missed COVID-19 cases, rates of myocarditis in 12-17-year-old males would still be nearly three times as great from COVID-19 infection than from the vaccine.

With intense media and social media focus on COVID-19 vaccine side-effects, it is important to quantify and communicate to the public the risks of COVID-19 infection in young people. The ACIP report projected that mRNA vaccination in 12-17-year-old males would result in 215 fewer hospitalizations and 71 fewer intensive care unit stays. Benefits of the vaccine outweighed the risk of myocarditis from vaccination in all age groups, 12 years-old and up. Our results suggest that the risk of myocarditis from COVID-19 infection itself exceeds the known risk from vaccination by a considerable margin. In light of more infectious variants, the new school year nearing and many colleges now requiring COVID-19 vaccination (either for all students or just those living on campus), these results are especially timely. Whether considering all the risks and benefits of COVID-19 vaccination or just myocarditis, vaccination appears to be the safer choice for 12-19-year-old males and females.

Data Availability

The data set is licensed and is not publicly available.

LINK:
https://www.medrxiv.org/content/10.1101/2021.07.23.21260998v1.full-text



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ORIGINAL ARTICLE

Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

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ABSTRACT

BACKGROUND

Approximately 5.1 million Israelis had been fully immunized against coronavirus disease 2019 (Covid-19) after receiving two doses of the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) by May 31, 2021. After early reports of myocarditis during adverse events monitoring, the Israeli Ministry of Health initiated active surveillance.

METHODS

We retrospectively reviewed data obtained from December 20, 2020, to May 31, 2021, regarding all cases of myocarditis and categorized the information using the Brighton Collaboration definition. We analyzed the occurrence of myocarditis by computing the risk difference for the comparison of the incidence after the first and second vaccine doses (21 days apart); by calculating the standardized incidence ratio of the observed-to-expected incidence within 21 days after the first dose and 30 days after the second dose, independent of certainty of diagnosis; and by calculating the rate ratio 30 days after the second dose as compared with unvaccinated persons.

RESULTS

Among 304 persons with symptoms of myocarditis, 21 had received an alternative diagnosis. Of the remaining 283 cases, 142 occurred after receipt of the BNT162b2 vaccine; of these cases, 136 diagnoses were definitive or probable. The clinical presentation was judged to be mild in 129 recipients (95%); one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46). As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.

CONCLUSIONS

The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Mevorach can be contacted at mevorachd@gmail.com or at Hadassah Hebrew University Medical Center. Dr. Alroy-Preis can be contacted at sharon.alroy@moh.gov.il or at the Israeli Ministry of Health.

Drs. Mevorach and Anis, Ms. Cedar and Dr. Bromberg, and Drs. Keinan-Boker and Alroy-Preis contributed equally to this article.

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After the emergency use authorization of the BNT162b2 messenger RNA (mRNA) vaccine (Pfizer–BioNTech) against coronavirus disease 2019 (Covid-19) by the Food and Drug Administration,[1] authorization was also granted for use in Israel. On December 20, 2020, a national vaccination campaign was initiated that was based on a two-dose regimen spaced 21 days apart.[2] The campaign initially targeted health care workers and persons who were 60 years of age or older, and later the vaccine was offered to all persons who were at least 16 years of age. By May 31, 2021, approximately 5.12 million Israeli residents had received two vaccine doses.

At the beginning of the vaccination campaign, a program of passive surveillance was initiated for the monitoring of adverse events within 21 days after the first dose of vaccine and within 30 days after the second dose. Health care providers reported these data to the Ministry of Health, as required by Israeli law. After receipt of reports of myocarditis, the Ministry of Health subsequently initiated active surveillance beginning in February 2021 by requesting that all hospitals report cases of myocarditis, including cases that had been diagnosed since December 2020, with or without pericardial effusion and regardless of vaccination status. Since persons with suspected myocarditis are almost always hospitalized in Israel, such surveillance data should approximate all cases of myocarditis during the period of active surveillance.

The aims of the current study were to present the clinical and epidemiologic characteristics and follow-up findings of cases of myocarditis that were diagnosed in temporal proximity to vaccination and to examine a possible causal relationship between the vaccine and myocarditis.

Methods

Data Source and Case Definition

We retrospectively reviewed data regarding presumptive cases of myocarditis, including clinical and laboratory data and discharge summaries, from medical records obtained from the Ministry of Health database. The focus of the study was the 6 months from December 2020 through May 2021, which included periods of both active and passive surveillance. We used the codes for myocarditis (422.0-9x and 429.0x) of the *International Classification of Diseases, 9th Revision* (ICD-9), for screening. Records were reviewed by one of four board-certified cardiologists, with advice from a board-certified rheumatologist for verification of the diagnosis of myocarditis. All the reviewers were aware of the vaccination status of the patients.

The diagnostic criteria for myocarditis and degree of certainty of diagnosis were adapted from the case definition and classification of the Brighton Collaboration (Pandemic Emergency Response Process).[3] Cases were classified as definitive, probable, possible, having insufficient data, or having an alternative diagnosis. Cases of pericarditis with myocarditis were included among these cases, although pericarditis alone was not included in case counts. We also compared the classification according to the Brighton Collaboration with classifications of myocarditis issued by the Centers for Disease Control and Prevention (CDC) for adverse events after smallpox vaccination.[4-6] Additional details regarding the two classification systems are provided in the Methods section and Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Since the study was conducted as part of ongoing clinical surveillance for side effects related to the BNT162b2 vaccine as required by national guidelines, it received a waiver for review by an institutional review board. Pfizer–BioNTech had no role in the collection or analysis of the data or in the reporting of the data in this study.

Statistical Analysis

We used descriptive frequencies, percentages, means, and standard deviations to characterize cases of myocarditis according to age, sex, time elapsed since vaccination, length of hospital stay, and clinical outcome. Incidence curves were examined for the occurrence of new cases of myocarditis during the first 21 days after the first dose of vaccine and 30 days after the second dose, since passive surveillance had usually been terminated at that point. The data were analyzed separately for males and females and according to age group (16 to 19 years, 20 to 24 years, 25 to 29 years, 30 to 39 years, 40 to 49 years, and 50 years or older). To assess the incidence of myocarditis among vaccine recipients, we calculated risk differences, observed-to-expected ratios, and rate ratios between vaccinated and unvaccinated persons.

To calculate the risk difference, we determined the risk of myocarditis per 100,000 persons after

Table 1. Reported Myocarditis Cases, According to Timing of First or Second Vaccine Dose.*

Timing	First Vaccine Dose			Second Vaccine Dose			Both Doses
	No. of Vaccinations	Myocarditis Cases	Males/ Females	No. of Vaccinations	Myocarditis Cases	Males/ Females	Myocarditis Cases
Six-month study period	5,442,696	19	17/2	5,125,635	117	101/16	136
December 2020	987,013	0	0/0	0	0	0/0	0
January 2021	2,109,854	4	3/1	1,844,896	13	12/1	17
February 2021	1,613,909	6	5/1	1,546,184	47	41/6	53
March 2021	528,069	7	7/0	1,397,609	44	38/6	51
April 2021	152,765	1	1/0	253,701	13	10/3	14
May 2021	51,086	1	1/0	83,245	0	0	1

* Data are from medical records, including clinical and laboratory data and discharge summaries, from the Ministry of Health database from December 2020 through May 2021, according to the codes for myocarditis used in the *International Classification of Diseases, 9th Revision*. Cases of myocarditis were reported within 21 days after the first dose of vaccine and 30 days after the second dose. All cases were clinically reviewed, and only definite or probable cases are shown.

the first and second doses of vaccine according to age group and sex. This analysis included only the probable or definite myocarditis cases. In the calculation of the risk differences between the second and first doses, we used the cumulative incidence for a follow-up period of 21 days for both vaccine doses; we computed 95% confidence intervals for the risk difference using the Jeffreys–Perks method. The percentage of the myocarditis risk that could be attributed to the second dose was calculated by dividing the risk difference between the two vaccine doses by the risk after the second dose and expressing the quotient as a percentage.

We compared the observed incidence of myocarditis with the expected incidence using data obtained during the period from 2017 through 2019 in the pre–Covid-19 pandemic era by calculating standardized incidence ratios (after adjustment for age and sex) for all reported cases of myocarditis. We performed this analysis in all myocarditis cases that had occurred in temporal proximity to the vaccination without accounting for the adjudicated category of certainty, because historical cases of myocarditis had not been adjudicated by a team of clinical experts. We calculated approximate 95% confidence intervals for the true standardized incidence ratio by applying the Wilson and Hilferty approximation for chi-square percentiles.[7] In addition, to determine whether the standardized incidence ratios could have been overestimated owing to the overreporting of myocarditis cases because of a higher index of clinical suspicion during the surveillance period, we performed a sensitivity analysis in which we determined the minimal number of observed cases that would be needed to produce a significant difference in the standardized incidence ratios for male recipients after the second vaccine dose. This subgroup was chosen post hoc according to the apparent increase in risk observed in male teenagers and young adults.

We compared the incidence of myocarditis among recipients 30 days after the second vaccine dose with the incidence among unvaccinated persons starting on January 11, 2021 (when second vaccine doses were first administered in Israel) up to May 31, 2021, with data reported according to age group and sex. We computed the rate ratio between vaccinated and unvaccinated persons and 95% confidence intervals for each stratum and for the overall study population after adjustment

Table 2. Classification of Myocarditis Cases Reported to the Ministry of Health.*

Timing of Myocarditis Diagnosis	Brighton Collaboration Classification of Myocarditis					
	Level 1	Level 2	Level 3	Level 4	Level 5	All Levels
	number of cases					
All cases	118	153	3	9	21	304
Vaccinated persons						
≤21 days after first dose and 30 days after second dose	55	81	1	5	9	151
>21 days after first dose and 30 days after second dose	15	23	0	2	5	45
Unvaccinated persons	48	49	2	2	7	108

* In the Brighton Collaboration classification system for the diagnosis of myocarditis, level 1 indicates definite, level 2 probable, level 3 possible, level 4 insufficient data, and level 5 ruled out. Included are data for persons who had a delayed second dose of vaccine and who received a diagnosis of myocarditis 22 days or longer after the first dose and those in whom myocarditis developed more than 30 days after the second dose, so the diagnosis was not considered to have been made in temporal proximity to vaccination.

for age and sex using a negative binomial regression model. This analysis included only definite or probable myocarditis cases (Fig. S1).

Since we had no prespecified plan for adjustment of the width of confidence intervals for multiple comparisons in any of these approaches, no definite conclusions can be drawn from these data. We also assessed our findings according to the Bradford Hill causality criteria.

RESULTS

CASES OF MYOCARDITIS

Among 9,289,765 Israeli residents who were included during the surveillance period, 5,442,696 received a first vaccine dose and 5,125,635 received two doses (Table 1 and Fig. S2). A total of 304 cases of myocarditis (as defined by the ICD-9 codes for myocarditis) were reported to the Ministry of Health (Table 2). These cases were diagnosed in 196 persons who had received two doses of the vaccine: 151 persons within 21 days after the first dose and 30 days after the second dose and 45 persons in the period after 21 days and 30 days, respectively. (Persons in whom myocarditis developed 22 days or more after the first dose of vaccine or more than 30 days after the second dose were considered to have myocarditis that was not in temporal proximity to the vaccine.) After a detailed review of the case histories, we ruled out 21 cases because of reasonable alternative diagnoses. Thus, the diagnosis of myocarditis was affirmed for 283 cases. These cases included 142 among vaccinated persons within 21 days after the first dose and 30 days after the second dose, 40 among vaccinated persons not in proximity to vaccination, and 101 among unvaccinated persons. Among the unvaccinated persons, 29 cases of myocarditis were diagnosed in those with confirmed Covid-19 and 72 in those without a confirmed diagnosis.

Of the 142 persons in whom myocarditis developed within 21 days after the first dose of vaccine or within 30 days after the second dose, 136 received a diagnosis of definite or probable myocarditis, 1 received a diagnosis of possible myocarditis, and 5 had insufficient data. Classification of cases according to the definition of myocarditis used by the CDC[4-6] is provided in Table S1.

Endomyocardial biopsy samples that were obtained from 2 persons showed foci of endointerstitial edema and neutrophils, along with mononuclear-cell infiltrates (monocytes or macrophages and lymphocytes) with no giant cells. No other patients underwent endomyocardial biopsy. The clinical features of myocarditis after vaccination are provided in Table S3.

In the 136 cases of definite or probable myocarditis, the clinical presentation in 129 was generally mild, with resolution of myocarditis in most cases, as judged by clinical symptoms and inflammatory markers and troponin elevation, electrocardiographic and echocardiographic normalization, and a relatively short length of hospital stay. However, one person with fulminant

myocarditis died. The ejection fraction was normal or mildly reduced in most persons and severely reduced in 4 persons. Magnetic resonance imaging that was performed in 48 persons showed findings that were consistent with myocarditis on the basis of at least one positive T2-based sequence and one positive T1-based sequence (including T2-weighted images, T1 and T2 parametric mapping, and late gadolinium enhancement). Follow-up data regarding the status of cases after hospital discharge and consistent measures of cardiac function were not available.

The peak number of cases with proximity to vaccination occurred in February and March 2021; the associations with vaccination status, age, and sex are provided in Table 1 and Figure 1. Of 136 persons with definite or probable myocarditis, 19 presented after the first dose of vaccine and 117 after the second dose. In the 21 days after the first dose, 19 persons with myocarditis were hospitalized, and hospital admission dates were approximately equally distributed over time. A total of 95 of 117 persons (81%) who presented after the second dose were hospitalized within 7 days after vaccination. Among 95 persons for whom data regarding age and sex were available, 86 (91%) were male and 72 (76%) were under the age of 30 years.

Figure 1 (facing page). Timing and Distribution of Myocarditis after Receipt of the BNT162b2 Vaccine.

Shown is the timing of the diagnosis of myocarditis among recipients of the first dose of vaccine (Panel A) and the second dose (Panel B), according to sex, and the distribution of cases among recipients according to both age and sex after the first dose (Panel C) and after the second dose (Panel D). Cases of myocarditis were reported within 21 days after the first dose and within 30 days after the second dose.

COMPARISON OF RISKS ACCORDING TO FIRST OR SECOND DOSE

A comparison of risks over equal time periods of 21 days after the first and second doses according to age and sex is provided in Table 3. Cases were clustered during the first few days after the second dose of vaccine, according to visual inspection of the data (Fig. 1B and 1D). The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19); the overall risk difference was 3.19 (95% CI, 2.37 to 4.02) among male recipients and 0.39 (95% CI, 0.10 to 0.68) among female recipients. The highest difference was observed among male recipients between the ages of 16 and 19 years: 13.73 per 100,000 persons (95% CI, 8.11 to 19.46); in this age group, the percent attributable risk to the second dose was 91%. The difference in the risk among female recipients between the first and second doses in the same age group was 1.00 per 100,000 persons (95% CI, −0.63 to 2.72). Repeating these analyses with a shorter follow-up of 7 days owing to the presence of a cluster that was noted after the second vaccine dose disclosed similar differences in male recipients between the ages of 16 and 19 years (risk difference, 13.62 per 100,000 persons; 95% CI, 8.31 to 19.03). These findings pointed to the first week after the second vaccine dose as the main risk window.

OBSERVED VERSUS EXPECTED INCIDENCE

Table 4 shows the standardized incidence ratios for myocarditis according to vaccine dose, age group, and sex, as projected from the incidence during the prepandemic period from 2017 through 2019. Myocarditis after the second dose of vaccine had a standardized incidence ratio of 5.34 (95% CI, 4.48 to 6.40), which was driven mostly by the diagnosis of myocarditis in younger male recipients. Among boys and men, the standardized incidence ratio was 13.60 (95% CI, 9.30 to 19.20) for those 16 to 19 years of age, 8.53 (95% CI, 5.57 to 12.50) for those 20 to 24 years, 6.96 (95% CI, 4.25 to 10.75) for those 25 to 29 years, and 2.90 (95% CI, 1.98 to 4.09) for those 30 years of age or older. These substantially increased findings were not observed after the first dose. A sensitivity analysis showed that for male recipients between the ages of 16 and 24 years who had received a second vaccine dose, the observed standardized incidence ratios would have required overreporting of myocarditis by a factor of 4 to 5 on the assumption that the true incidence would not have differed from the expected incidence (Table S4).

RATE RATIO BETWEEN VACCINATED AND UNVACCINATED PERSONS

Within 30 days after receipt of the second vaccine dose in the general population, the rate ratio for the comparison of the incidence of myocarditis

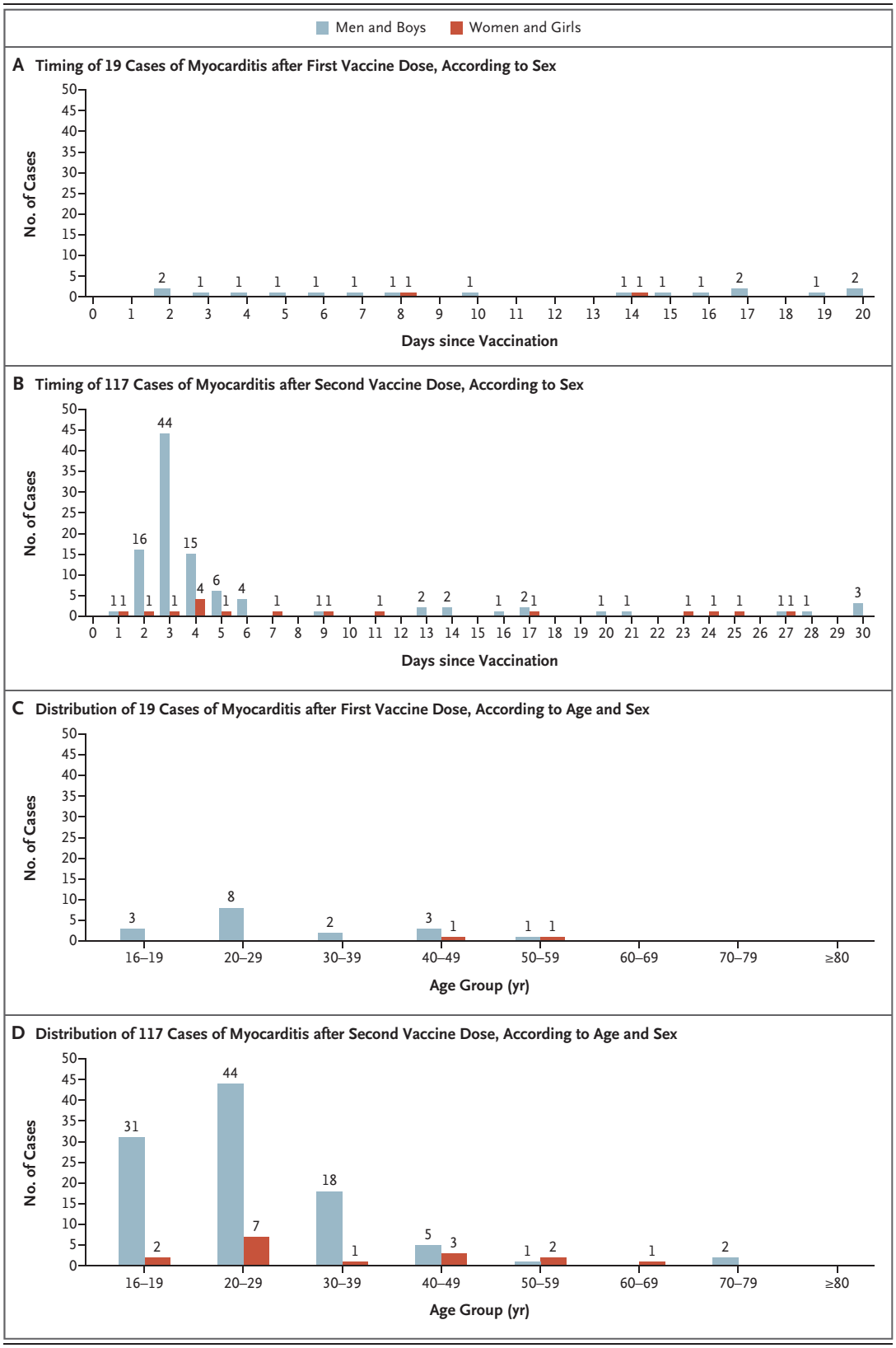

Table 3. Risk of Myocarditis within 21 Days after the First or Second Dose of Vaccine, According to Age and Sex.*

Age and Sex	First Dose			Second Dose			Risk Difference (95% CI)
	Recipients	Cases	Risk per 100,000 Persons	Recipients	Cases	Risk per 100,000 Persons	
	number			*number*			*no./100,000 persons*
Male recipients							
All ages	2,668,894	17	0.64	2,507,210	96	3.83	3.19 (2.37 to 4.02)
16–19 yr	224,518	3	1.34	199,115	30	15.07	13.73 (8.11 to 19.46)
20–24 yr	261,741	5	1.91	239,396	26	10.86	8.95 (4.42 to 13.55)
25–29 yr	246,638	3	1.22	228,988	16	6.99	5.77 (2.02 to 9.58)
30–39 yr	491,126	2	0.41	461,044	17	3.69	3.28 (1.41 to 5.18)
40–49 yr	458,268	3	0.65	433,069	5	1.15	0.50 (–0.82 to 1.84)
≥50 yr	986,603	1	0.10	945,598	2	0.21	0.11 (–0.29 to 0.52)
Female recipients							
All ages	2,773,802	2	0.07	2,618,425	12	0.46	0.39 (0.10 to 0.68)
16–19 yr	219,460	0	0	199,706	2	1.00	1.00 (–0.63 to 2.72)
20–24 yr	250,556	0	0	231,960	5	2.16	2.16 (0.13 to 4.24)
25–29 yr	235,575	0	0	219,113	0	0	0 (–0.83 to 0.89)
30–39 yr	481,045	0	0	451,791	1	0.22	0.22 (–0.37 to 0.84)
40–49 yr	472,083	1	0.21	444,916	2	0.45	0.24 (–0.61 to 1.11)
≥50 yr	1,115,083	1	0.09	1,070,939	2	0.19	0.10 (–0.26 to 0.46)

* Among vaccine recipients of all ages and both sexes, the overall difference in the incidence of myocarditis after the second dose as compared with the incidence after the first dose was 1.76 (95% confidence interval [CI], 1.33 to 2.19). The widths of the confidence intervals have not been adjusted for multiple testing.

Table 4. Standardized Incidence Ratios for 151 Cases of Myocarditis, According to Vaccine Dose, Age, and Sex.

Age and Sex	First Dose			Second Dose		
	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)
	number			*number*		
All recipients†	25	17.55	1.42 (0.92–2.10)	126	23.43	5.34 (4.48–6.40)
16–19 yr						
Male	3	1.86	1.62 (0.32–4.72)	32	2.35	13.60 (9.30–19.20)
Female	0	0.23	0	2	0.30	6.74 (0.76–24.35)
20–24 yr						
Male	5	2.33	2.14 (0.69–5.00)	26	3.05	8.53 (5.57–12.50)
Female	1	0.42	2.37 (0.03–13.20)	6	0.56	10.76 (3.93–23.43)
25–29 yr						
Male	3	2.17	1.39 (0.28–4.05)	20	2.87	6.96 (4.25–10.75)
Female	0	0.30	0	1	0.39	2.54 (0.03–14.14)
≥30 yr						
Male	10	8.13	1.23 (0.59–2.26)	32	11.04	2.90 (1.98–4.09)
Female	3	2.11	1.42 (0.29–4.15)	7	2.87	2.44 (0.98–4.09)

* Reference data regarding the background incidence of myocarditis were extracted from the Israel National Hospital Discharge Database for the years 2017 through 2019.

† Data are listed for the 151 vaccine recipients in whom myocarditis was diagnosed at any level of certainty within 21 days after the first dose and 30 days after the second dose; data for all vaccine recipients have been weighted according to age and sex.

between vaccinated and unvaccinated persons was 2.35 (95% CI, 1.10 to 5.02) according to the Brighton Collaboration classification of definite and probable cases and after adjustment for age and sex. This result was driven mainly by the findings for males in younger age groups, with a rate ratio of 8.96 (95% CI, 4.50 to 17.83) for those between the ages of 16 and 19 years, 6.13 (95% CI, 3.16 to 11.88) for those 20 to 24 years, and 3.58 (95% CI, 1.82 to 7.01) for those 25 to 29 years (Table 5). When follow-up was restricted to 7 days after the second vaccine dose, the analysis results for male recipients between the ages of 16 and 19 years were even stronger than the findings within 30 days (rate ratio, 31.90; 95% CI, 15.88 to 64.08). Concordance of our findings with the Bradford Hill causality criteria is shown in Table S5.

DISCUSSION

During a nationwide vaccination campaign conducted from December 2020 through May 2021 involving more than 5 million residents, the Israeli Ministry of Health recorded 136 cases of definite or probable myocarditis that had occurred in temporal proximity to the receipt of two doses of the BNT162b2 mRNA vaccine — a risk that was more than twice that among unvaccinated persons. This association was highest in young male recipients within the first week after the second dose. In our study, definite or probable cases of myocarditis among persons between the ages of 16 and 19 years within 21 days after the second vaccine dose occurred in approximately 1 of 6637 male recipients and in 1 of 99,853 female recipients.

In most cases, symptoms of myocarditis developed within a few days after the second dose of vaccine. The incidence of myocarditis declined as the number of newly vaccinated persons decreased over time. This finding was suggestive of a possible causal relationship between two doses of the vaccine and the risk of myocarditis. Overall, we estimated that definite or probable cases of myocarditis occurred in the overall Israeli population at a rate of approximately 1 per 26,000 males and 1 per 218,000 females after the sec-

Table 5. Rate Ratios for a Diagnosis of Myocarditis within 30 Days after the Second Dose of Vaccine, as Compared with Unvaccinated Persons (January 11 to May 31, 2021).

Age and Sex	Vaccinated Group		Unvaccinated Group		Rate Ratio (95% CI)
	Person-Days of Follow-up	Cases	Person-Days of Follow-up	Cases	
	number				
All recipients*	149,786,065	117	296,377,727	98	2.35 (1.10–5.02)
16–19 yr					
Male	6,018,541	31	19,135,706	11	8.96 (4.50–17.83)
Female	6,033,192	2	17,768,696	2	2.95 (0.42–20.91)
20–24 yr					
Male	7,088,335	27	20,926,320	13	6.13 (3.16–11.88)
Female	6,889,399	5	20,832,407	2	7.56 (1.47–38.96)
25–29 yr					
Male	6,590,263	18	20,944,595	16	3.58 (1.82–7.01)
Female	6,417,564	1	20,943,920	0	0
≥30 yr					
Male	53,577,403	26	82,419,957	40	1.00 (0.61–1.64)
Female	57,171,368	7	93,406,126	14	0.82 (0.33–2.02)

* Data for all vaccine recipients have been weighted according to age and sex.

ond vaccine dose, with the highest risk again among young male recipients. This result may explain why a phase 3 trial of the vaccine, which included only 15,000 male and female recipients,[8] showed no cases of myocarditis. The mechanism of vaccine-induced myocarditis is not known but may be related to the active component of the vaccine, the mRNA sequence that codes for the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or to the immune response that follows vaccination.

Although selection bias in this study is possible, we consider it unlikely, since we used data from the entire nation. A major limitation of the study is that the calculation of rate ratios was based on individual patient data in the vaccinated group as compared with aggregated data in the unvaccinated group. In addition, the diagnosis of myocarditis was not validated by myocardial biopsy, and acquisition bias could be present, because clinical assessors were aware of vaccination status. Misclassification may have taken place during surveillance, which could have resulted in the underdiagnosis of myocarditis among young patients with chest pain or discomfort who were not referred for evaluation for myocarditis because of a low level of suspicion, despite notifications by the Ministry of Health to health care providers. There was also a possibility of overdiagnosis of cases of myocarditis owing to increased public and medical awareness of this possible side effect of vaccination. However, our sensitivity analysis did not support the occurrence of overreporting as an explanation for our findings. Our calculations of risk difference and rate ratios were confined to cases that had met strict criteria for definite or probable myocarditis, which would tend to reduce ascertainment bias. Another limitation may be the use of the Israel National Hospital Discharge Database for the years 2017 through 2019 as a reference for the background incidence of myocarditis in the analyses of standardized incidence ratios. Those years were different from the period between 2020 and 2021 with respect to viral circulation — including influenza outbreaks in 2017, 2018, and 2019 but not in 2020 and 2021 and Covid-19 morbidity in 2020 and 2021 but not in 2017 through 2019 — and to the lack of systematic reporting of myocarditis during the earlier period. However, hospitalization rates for myocarditis during the period from 2017 through 2019 were similar to those in 2020,

and the databases used for these denominators are representative of the unvaccinated population. We were unable to adjust for potential confounders other than age and sex.

Finally, the rates of myocarditis in our study can be compared with those in the Clalit Health Services database in the study by Witberg et al.,[9] as now reported in the *Journal*. That study showed a somewhat lower incidence of myocarditis, possibly because of the different methods that were used. In our study, each vaccination date was recorded to ensure accurate follow-up of 21 days after the first dose and 30 days after the second dose, whereas Witberg et al. followed vaccinees for 42 days after the first dose. The study design may have led to an underestimation of myocarditis cases owing to a shorter follow-up for the second dose. In our study, the rate of myocarditis in the general unvaccinated population was 1 per 10,857 and can be compared with findings indicating that myocarditis was more common after SARS-CoV-2 infection than after vaccination, as reported previously by Barda et al.[10]

On the basis of data from an Israeli national database, the incidence of myocarditis after two doses of the BNT162b2 mRNA vaccine was low but higher than the incidence among unvaccinated persons and among historical controls. The risk of myocarditis was driven primarily by the increased incidence after the second dose of vaccine and in young male recipients.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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ANNEXURE: A13

New York post

NIH orders $1.67M study on how COVID-19 vaccine impacts menstrual cycle

4 January 2022

The National Institutes of Health has announced a $1.67 million study to investigate reports that suggest the COVID-19 vaccine may come with an unexpected impact on reproductive health.

It's been a little over six months since the three COVID-19 vaccines in the US — Pfizer, Moderna and Johnson & Johnson — became widely available to all adults. But even in the early days of vaccine rollout, some women were noticing irregular periods following their shots, as reported first by the Lily in April.

Shana Clauson, 45, spoke to the Washington Post's women's news site at the time, and again this week, about her experience after getting the jab — revealing that her period arrived earlier and heavier than what she considers normal. She was one of many who gathered on social media to share what they were seeing.

"Is this not being discussed, or is it even being looked at or researched because it's a 'woman's issue?' " Clauson speculated to the Lily last spring.

It would appear that the NIH heard Clauson and others' reports, as they announced on Aug. 30 that they intended to embark on just such research — aiming to incorporate up to half a million participants, including teens and transgender and nonbinary people.

Researchers at Boston University, Harvard Medical School, Johns Hopkins University, Michigan State University and Oregon Health and Science University

have been enlisted to embark on the study, commissioned by the NIH's National Institute of Child Health and Human Development (NICHD) and the Office of Research on Women's Health.

The approximately yearlong study will follow initially unvaccinated participants to observe changes that occur following each dose. More specifically, some groups will exclude participants on birth control or gender-affirming hormones, which may have their own impact on periods.

"Our goal is to provide menstruating people with information, mainly as to what to expect, because I think that was the biggest issue: Nobody expected it to affect the menstrual system, because the information wasn't being collected in the early vaccine studies," said NICHD director Diana Bianchi in a statement to the Lily — reportedly crediting their early coverage for helping to make the NIH aware.

The NIH suggests that changes to the menstrual cycle could arise out of several of life's circumstances during a pandemic — the stress of lifestyle changes or possibly contending with illness. Moreover, the immune and reproductive systems are intrinsically linked, and the notion that the immune-boosting vaccine may disrupt the typical menstrual cycle is plausible, as demonstrated by previous studies concerning vaccine uptake.

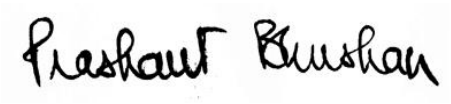
It's also worth noting the vaccine does not cause infertility and the Centers for Disease Control and Prevention recommends the shot even for pregnant women.

As changes to the menstrual cycle are "really not a life and death issue," explained Bianchi, the Food and Drug Administration — fast-tracking their work — prioritized only the most critical risks associated with the COVID-19 vaccine.

The NIH, too, pulled together the initiative at breakneck speed. Funding for such a study would typically take years to see approval.

"We were worried this was contributing to vaccine hesitancy in reproductive-age women," said Bianchi.

LINK: **https://nypost.com/2021/09/07/nih-to-study-how-covid-19-vaccine-impacts-menstrual-cycle/**



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Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis

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bmj.com

- Clinical review: Narcolepsy and excessive daytime sleepiness (*BMJ* 2004;329:724)
- Clinical review: Narcolepsy mistaken for epilepsy (*BMJ* 2001;322:216)

STUDY QUESTION

Is there an increased risk of narcolepsy in children and young people who received the AS03 adjuvanted A/H1N1 pandemic influenza vaccine in England?

SUMMARY ANSWER

After vaccination with AS03 adjuvanted pandemic A/H1N1 vaccine, children and young people have a significantly increased risk of developing narcolepsy.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Studies from Finland and Sweden have reported an increased risk of narcolepsy in children who received the AS03 adjuvanted pandemic vaccine. The current study found a similar risk in children in England, confirming that the association is not confined to Scandinavian populations.

Participants and setting

Children and young people with narcolepsy aged 4-18 with onset from January 2008 who received the diagnosis at sleep centres in England by July 2011.

Design

Retrospective analysis of records held by sleep centres in England complemented by review of cases reported by paediatric neurologists or identified in the national hospital episode statistics database. Vaccination histories were independently obtained from general practitioners. In each case, the population vaccine coverage was ascertained for children and young people in England of the same age at the time of onset of symptoms in the affected patient.

Primary outcome

The odds ratio for receipt of the AS03 adjuvanted pandemic vaccine before onset in patients with narcolepsy compared with the matched population after adjustment for the presence of high risk conditions that were an indication for vaccination.

Main results and the role of chance

Of the 23 centres in England contacted, 16 reported seeing cases in the relevant time period. A total of 245 possible cases were identified, of which 75 were retained for analysis, after we excluded patients with onset before January 2008 or an unconfirmed diagnosis. We found an increased odds ratio for receipt of the AS03 adjuvanted pandemic A/H1N1 vaccine before the onset of symptoms. The odds ratio for receipt of the AS03 adjuvanted pandemic A/H1N1 vaccine at any time before onset of narcolepsy in children and young people aged 4-18 in England was 14.4 (95% confidence interval 4.3 to 48.5). Alternative analyses with the date of first healthcare contact or date of diagnosis also gave significantly increased odds ratios. The attributable risk was estimated at between one per 57 500 to one per 52 000 doses.

Bias, confounding, and other reasons for caution

Despite attempts to minimise ascertainment bias by including only affected patients with a diagnosis before the public interest in the association, and by using two independent methods of case identification, there is potential for overestimation of risk because referral might be more rapid in vaccinated patients. Long term follow-up of the exposed cohorts is needed to properly evaluate the attributable risk.

Generalisability to other populations

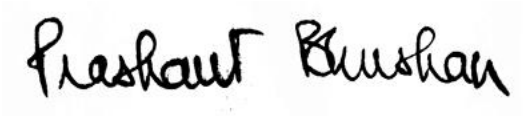
Failure to identify a signal in other European countries suggested that the risk reported from Finland and Sweden might be specific to those populations. Our study indicates that the risk is not restricted to Scandinavian populations. Further studies are needed to investigate whether there is a risk with other types of pandemic strain vaccine, with or without an adjuvant.

Study funding/potential competing interests

This study was funded by the Department of Health policy research programme (grant No 039/0031) and the Health Protection Agency.

Odds ratio (95% confidence intervals) for receipt of AS03 adjuvanted vaccine before onset of narcolepsy in children and young people aged 4-18 with diagnosis by July 2011

Interval before onset	No of patients vaccinated	Total No of patients eligible for vaccination in interval before onset	Expected proportion vaccinated after matching to risk group	OR (95% CI)
12 weeks	5	10	0.098	18.4 (3.7 to 91.6)
6 months	6	10	0.151	16.2 (3.1 to 84.5)
Any time	10	17	0.160	14.4 (4.3 to 48.5)



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Why are we vaccinating children against COVID-19?

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ABSTRACT

This article examines issues related to COVID-19 inoculations for children. The bulk of the official COVID-19-attributed deaths per capita occur in the elderly with high comorbidities, and the COVID-19 attributed deaths per capita are negligible in children. The bulk of the normalized post-inoculation deaths also occur in the elderly with high comorbidities, while the normalized post-inoculation deaths are small, but not negligible, in children. Clinical trials for these inoculations were very short-term (a few months), had samples not representative of the total population, and for adolescents/children, had poor predictive power because of their small size. Further, the clinical trials did not address changes in biomarkers that could serve as early warning indicators of elevated predisposition to serious diseases. Most importantly, the clinical trials did not address long-term effects that, if serious, would be borne by children/adolescents for potentially decades.

A novel *best-case scenario* cost-benefit analysis showed *very conservatively* that there are five times the number of deaths attributable to each inoculation vs those attributable to COVID-19 in the most vulnerable 65+ demographic. The risk of death from COVID-19 decreases drastically as age decreases, and the longer-term effects of the inoculations on lower age groups will increase their risk-benefit ratio, perhaps substantially.

1. Introduction

Currently, we are in the fifteenth month of the WHO-declared global COVID-19 pandemic. Restrictions of different severity are still in effect throughout the world [1]. The global COVID-19 mass inoculation is in its eighth month. As of this writing in mid-June 2021, over 800,000,000 people globally have received at least one dose of the inoculation and roughly half that number have been fully inoculated [2]. In the USA, about 170,000,000 people have received at least one dose and roughly 80 % of that number have been fully inoculated [2].

Also, in the USA, nearly 600,000 deaths have been officially attributed to COVID-19. Almost 5,000 deaths following inoculation have been reported to VAERS by late May 2021; specifically, "Over 285 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through May 24, 2021. During this time, VAERS received 4,863 reports of death (0.0017 %) among people who received a COVID-19 vaccine." [3] (the Vaccine Adverse Events Reporting System (VAERS) is a passive surveillance system managed jointly by the CDC and FDA [3]. Historically, VAERS has been shown to report about 1% of actual vaccine/inoculation adverse events [4]. See Appendix 1 for a first-principles confirmation of that result). By mid-June, deaths following COVID-19 inoculations had reached the ~6000 levels.

A vaccine is legally defined as any substance designed to be administered to a human being for the prevention of one or more diseases [5]. For example, a January 2000 patent application that defined vaccines as "compositions or mixtures that when introduced into the circulatory system of an animal will evoke a protective response to a pathogen." was rejected by the U.S. Patent Office because "The immune response produced by a vaccine must be more than merely some immune response but must be protective. As noted in the previous Office Action, the art recognizes the term "vaccine" to be a compound which prevents infection" [6]. In the remainder of this article, we use the term

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'inoculated' rather than vaccinated, because the injected material in the present COVID-19 inoculations prevents neither viral infection nor transmission. Since its main function in practice appears to be symptom suppression, it is operationally a "treatment".

In the USA, inoculations were administered on a priority basis. Initially, first responders and frontline health workers, as well as the frailest elderly, had the highest priority. Then the campaign became more inclusive of lower age groups. Currently, approval has been granted for inoculation administration to the 12–17 years demographic, and the target for this demographic is to achieve the largest number of inoculations possible by the start of school in the Fall. The schedule for inoculation administration to the 5–11 years demographic has been accelerated to start somewhere in the second half of 2021, and there is the possibility that infants as young as six months may begin to get inoculated before the end of 2021 [7].

The remainder of this article will focus on the USA situation, and address mainly the pros and cons of inoculating children under eighteen. The article is structured as follows:

Section 1 (the present section) introduces the problem.

Section 2 (Background):

1) provides the background for the declared COVID-19 "pandemic" that led to the present inoculations;
2) describes the clinical trials that provided the justification for obtaining Emergency Use Authorization (EUA) from the FDA to administer the inoculations to the larger population;
3) shows why the clinical trials did not predict either the seriousness of adverse events that have occurred so far (as reported in VAERS) or the potential extent of the underlying pre-symptomatic damage that has occurred as a result of the inoculations.

Section 3 (Mass Inoculation) summarizes the adverse events that have occurred already (through reporting in VAERS) from the mass inoculation and will present biological evidence to support the potential occurrence of many more adverse effects from these inoculations in the mid-and long-term.

Section 4 (Discussion) addresses these effects further

Section 5 (Summary and Conclusions) presents the conclusions of this study.

There are four appendices to this paper.

Appendix A provides some idea of the level of under-reporting of post-inoculation adverse events to VAERS and presents estimations of the actual number of post-inoculation deaths based on extrapolating the VAERS results to real-world experiences.

Appendix B provides a detailed analysis of the major clinical trials that were used to justify EUA for the inoculants presently being administered in the USA.

Appendix C summarizes potential adverse effects shown to have resulted from past vaccines, all of which could potentially occur as a result of the present inoculations.

Appendix D presents a novel *best-case scenario* cost-benefit analysis of the COVID-19 inoculations that have been administered in the USA.

2. Background

2.1. Pandemic history

In December 2019, a viral outbreak was reported in Wuhan, China, and the responsible coronavirus was termed Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [8,9]. The associated disease was called Coronavirus Disease 2019, or COVID-2019. The virus spread worldwide, and a global pandemic was declared by the WHO in March 2020 [10,11]. Restrictive measures of differing severity were implemented by countries globally, and included social distancing, quarantining, face masks, frequent hand sanitation, etc. [12,13]. In the USA, these measures were taken as well, differing from state-to-state [14]. At the same time, vaccine development was initiated to control COVID-19 [15]. In the USA, non-vaccine treatments were not encouraged at the Federal level, but different treatment regimens were pursued by some healthcare practitioners on an individual level [11,16,17].

By the end of May 2021, the official CDC death count attributed to COVID-19 was approaching 600,000, as stated previously. This number has been disputed for many reasons. First, before COVID-19 testing began, or in the absence of testing, after it was available, the diagnosis of COVID-19 (in the USA) could be made by the presumption of the healthcare practitioner that COVID-19 existed [4,18]. Second, after testing began, the main diagnostic used was the RT-PCR test. This test was done at very high amplification cycles, ranging up to 45 [19–21]. In this range, very high numbers of false positives are possible [22].

Third, most deaths attributed to COVID-19 were elderly with high comorbidities [1,22]. As we showed in a previous study [22], attribution of death to one of many possible comorbidities or especially toxic exposures in combinations [23] is highly arbitrary and can be viewed as a political decision more than a medical decision. For over 5 % of these deaths, COVID-19 was the only cause mentioned on the death certificate. For deaths with conditions or causes in addition to COVID-19, on average, there were 4.0 additional conditions or causes per death [24]. These deaths with comorbidities could equally have been ascribed to any of the comorbidities [22]. Thus, the actual number of COVID-19-based deaths in the USA may have been on the order of 35,000 or less, characteristic of a mild flu season.

Even the 35,000 deaths may be an overestimate. Comorbidities were based on the clinical definition of specific diseases, using threshold biomarker levels and relevant symptoms for the disease(s) of interest [25,26]. But many people have what are known as pre-clinical conditions. The biomarkers have not reached the threshold level for official disease diagnosis, but their abnormality reflects some degree of underlying dysfunction. The immune system response (including pre-clinical conditions) to the COVID-19 viral trigger should not be expected to be the same as the response of a healthy immune system [27]. If pre-clinical conditions had been taken into account and coupled with the false positives as well, the CDC estimate of 94 % misdiagnosis would be substantially higher.

2.2. Clinical trials

2.2.1. Clinical trials to gain FDA Emergency Use Authorization (EUA) approval

The unprecedented accelerated development of COVID-19 vaccines in the USA, dubbed Operation Warp Speed, resulted in a handful of substances available for clinical trials by mid-2020 [28]. These clinical trials were conducted to predict the safety and efficacy of the potential vaccines (which have turned out to be treatments/inoculations as stated previously), and thereby gain approval for inoculating the public at large [29]. An overview of the Pfizer clinical trials is presented in this section, and a more detailed description of the main clinical trials is shown in Appendix B.

Two types of inoculants have gained FDA EUA in the US: mRNA-based inoculants and viral vector-based inoculants, with the mRNA inoculants having the widest distribution so far. Comirnaty is the brand name of the mRNA-based inoculant developed by Pfizer/BioNTech, and Moderna COVID-19 Vaccine is the brand name of the mRNA-based inoculant developed by Moderna [30]. Both inoculants contain the genetic information needed for the production of the viral protein S (spike), which stimulates the development of a protective immune response against COVID-19 [31]. Janssen COVID-19 Vaccine is the brand name of the viral vector-based inoculant developed by Johnson and Johnson. Janssen COVID-19 vaccine uses an adenovirus to transport a gene from the coronavirus into human cells, which then produce the coronavirus spike protein. This spike protein primes the immune system to fight off potential coronavirus infection [32].

The results of these trials that allowed granting of EUA by the FDA

Table 1
Demographics (population for the primary efficacy endpoint). The number of participants who received vaccine and placebo, stratified by age.

AGE GROUP	Pfizer-BioNTech COVID-19 Vaccine (N = 18,242) n (%)	Placebo (N = 18,379) n (%)
≥12 through 15 years[b]	46 (0.3 %)	42 (0.2 %)
≥16 through 17 years	66 (0.4 %)	68 (0.4 %)
≥16 through 64 years	14,216 (77.9 %)	14,299 (77.8 %)
≥65 through 74 years	3176 (17.4 %)	3226 (17.6 %)
≥75 years	804 (4.4 %)	812 (4.4 %)

Symbols: b: "100 participants 12 through 15 years of age with limited follow-up in the randomized population received at least one dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the efficacy evaluation depending on the population analyzed. They contributed to exposure information but with no confirmed COVID-19 cases, and did not affect efficacy conclusions.", N: number of test subjects, n: number of controls.

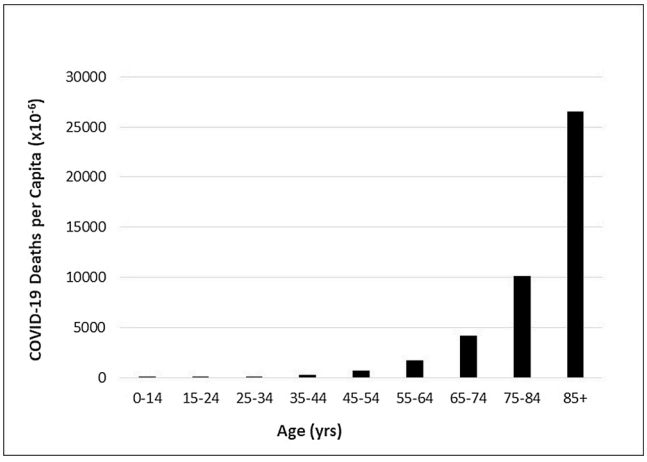

Fig. 1. COVID-19 Deaths per capita by age in the United States (as of Jun 5, 2021). Population-based on U.S. CDC WONDER Bridge-Race Population Estimate 2019. Data obtained from https://wonder.cdc.gov/bridged-race-v2019.html on 6/15/2021. Provisional COVID-19 deaths based on CDC data provided by the National Center for Health Statistics for the period 1/1/2020 – 6/5/2021. Data obtained from https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-by-Sex-and-Age/9bhg-hcku on 6/10/2021.

can be found in the inserts to the inoculation materials. For example, the Pfizer inoculation trial results are contained in the fact sheet for healthcare providers administering vaccine (vaccination providers) [33].

There were two clinical trials conducted to gain FDA EUA for Pfizer: a smaller Phase 1/2 study, and a larger Phase 1/2/3 study. The age demographics for the larger clinical study are as follows (from the Pfizer insert): "Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 (N = 20,033), 21.4 % (n = 4,294) were 65 years of age and older and 4.3 % (n = 860) were 75 years of age and older." Additionally: "In an analysis of Study 2, based on data up to the cutoff date of March 13, 2021, 2,260 adolescents (1,131 Pfizer-BioNTech COVID-19 Vaccine; 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) adolescents have been followed for at least 2 months after the second dose of Pfizer-BioNTech COVID-19 Vaccine. The safety evaluation in Study 2 is ongoing."

The relevant demographics are presented in Table 7 on p.31 of the Pfizer insert. The age component of those demographics is shown below in Table 1.

There are very minor differences between most of the data in the above table and the preceding narrative shown, and they are probably due to different time horizons. The major difference is the number of adolescents used and appears to result from a much later reporting time.

Fig. 1 uses the official large CDC numbers (coupled with USA census data estimates from CDC Wonder) to show the COVID-19 deaths per capita as a function of age, circa early June 2021. Unfortunately, the most critical range, 85+, has the least resolution. It is obvious that most of the deaths occurred in the 55 to 100+ range, and the remaining individuals in the other ranges (especially under 35) have negligible risk of dying from the disease.

The age distribution in Fig. 1 differs substantially from the age distribution in Table 1. Why is this important? When designing a trial for the efficacy and safety of a potential treatment, the focus should be on the target population who could benefit from that treatment. There is little rationale for including participants in a trial for whom the treatment would not be relevant or warranted.

For the COVID-19 Pfizer trials, based on the data from Fig. 1, the trial population should have been limited at most to the 45−100+ age segment, appropriately weighted toward the higher end where the deaths per capita are most frequent. That was almost the exact opposite of what was done in the Pfizer clinical trials. In Fig. 1, approximately 58 % of the deaths occurred in the age range 75+, whereas 4.4 % of the participants in the Pfizer clinical trial were 75 + . Thus, the age range most impacted by COVID-19 deaths was minimally represented in the Pfizer clinical trials, and the age range least impacted by COVID-19 deaths was maximally represented in the Pfizer clinical trials. This skewed sampling has major implications for predicting the expected numbers of deaths for the target population from the clinical trials.

Besides age, the other metric of importance in determining COVID-19 deaths is the presence of comorbidities. The more comorbidities, and the more severe the comorbidities, the greater the chances of death or severe adverse outcomes from COVID-19. It is not clear how well the number and severity of comorbidities in the clinical trial sample matched those reflected in Fig. 1, but the insert does mention the large number of conditions that excluded participation in the trials. In sum, the results from the clinical trials could not be expected to reflect the results that could occur (and have occurred) from mass inoculation of the public, given the unaffected nature of the bulk of the trial population from SARS-CoV-2 exposure.

The prior discussion on the clinical trials has focused on the efficacy and safety of the inoculants, and the relationship of the trial test population to the total target population. We have limited the focus so far to the safety and efficacy issues since these constituted the core of what was presented to the FDA for EUA approval. We have not focused on the trials from an early warning indicator perspective.

We will address summarily the science/early warning indicator issues associated with the Pfizer trials, and how the neglect of these issues has translated into disastrous consequences during the mass inoculation rollout. Standard practice for determining and understanding the impact of new technology (such as mRNA "vaccines") on a system involves measuring the state and flux variables of the system before the new technology intervention, measuring the state and flux variables of the system after the new technology intervention, and identifying the types and magnitudes of changes in the state and flux variables attributable to the intervention. This would be in addition to evaluating performance metrics before and after the intervention.

In Pfizer's proposed clinical trials for the mRNA "vaccine" (Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals - https://clinicaltrials.gov/ct2/show/NCT04368728), the focus was on determining 1) adverse events/symptoms, 2) SARS-CoV-2 serum neutralizing antibody levels, 3) SARS-CoV-2 anti-S1 binding antibody levels and anti-RBD binding antibody levels, and 4) effectiveness. These metrics are all related to safety at the symptom level and performance.

However, symptoms/diseases are typically end points of processes

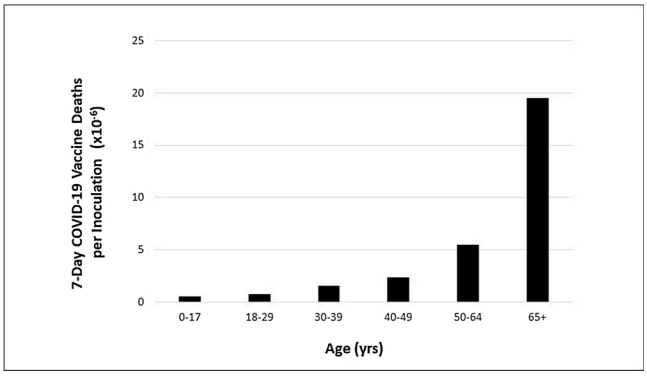

Fig. 2. Post-inoculation deaths per dose of inoculant. 7-day COVID-19 vaccine deaths per inoculation by age in the United States (as of 5/28/2021). Data shown includes the total number of all deaths up to 7 days after receiving the vaccine for both those administered 1 dose and the complete series of doses by age in the United States as of 5/28/2021 reported in VAERS (updated on 5/28/2021). COVID-19 Vaccinations (Inoculations) based on CDC data provided by ISSInfo up thru 5/28/2021. Data obtained from https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-Demographics-in-the-United-St/km4m-vcsb on 6/10/2021. COVID-19 Vaccinations Deaths based on CDC WONDER VAERS Database as of 5/28/2021, obtained from https://wonder.cdc.gov/controller/datarequest/D8;jsessionid=4B5522C8D1DA68F1A364646B0DA5 on 6/9/2021.

that can take months, years, or decades to surface. During that symptom/disease development period, many biomarker early warning indicators tend to exhibit increasing abnormalities that reflect an increasing predisposition to the eventual symptom/disease. Thus, serious symptoms/diseases that ordinarily take long periods to develop would be expected to be rare events if they occurred shortly following an inoculation. If the clinical trials that were performed by Pfizer and Moderna were designed to focus on efficacy and *only adverse effects at the symptom level of description* as an indicator of safety, the trial results would be limited to the identification of rare events, and the trial results would potentially under-estimate the actual pre-symptom level damage from the inoculations.

Credible safety science applied to this experiment would have required a much more expansive approach to determining effects on a wide variety of state and flux metrics that could serve as early warning indicators of potentially serious symptoms/disease, and might occur with much higher frequencies at this early stage than the rare serious symptoms. The only mention of these other metrics in the above proposal is in the Phase I trial description: "Percentage of Phase 1 participants with abnormal haematology and chemistry laboratory values", to be generated seven days after dose 1 and dose 2.

A paper published in NEJM in December 2020 [34] summarized the Phase 1 results. The focus was on local and systemic adverse events and efficacy metrics (antibody responses). The only metrics other than these reported were transiently decreased lymphocyte counts.

We view this level of reporting as poor safety science for the following reasons. Before the clinical trials had started, many published articles were reporting serious effects associated with the presence of the SARS-CoV-2 virus such as hyperinflammation, hypercoagulation, hypoxia, etc. SARS-CoV-2 includes the S1 Subunit (spike protein), and it was not known how much of the damage was associated with the spike protein component of SARS-CoV-2. A credible high-quality safety science experiment would have required state measurements of specific biomarkers associated with each of these abnormal general biomarkers before and after the inoculations, such as d-dimers for evidence of enhanced coagulation/clotting; CRP for evidence of enhanced inflammation; troponins for evidence of cardiac damage; occludin and claudin for evidence of enhanced barrier permeability; blood oxygen levels for evidence of enhanced hypoxia; amyloid-beta and phosphorylated tau for evidence of increased predisposition to Alzheimer's disease; Serum HMGB1, CXCL13, Dickkopf-1 for evidence of an increased disposition to autoimmune disease, etc. A credible high-quality safety science experiment would have required flux measurements of products resulting from the mRNA interactions, from the LNP shell interactions, from dormant viruses that might have been stimulated by the mRNA-generated spike protein, etc., emitted through the sweat glands, faeces, saliva, exhalation, etc.

Most importantly, these types of measurements would have shown changes in the host that did not reach the symptom level of expression but raised the general level of host abnormality that could predispose the host to a higher probability of serious symptoms and diseases at some point in the future. Instead, in the absence of high-quality safety science reflected in these experiments, all that could be determined were short-term adverse effects and deaths. This focus on symptoms masked the true costs of the mRNA intervention, which would probably include much larger numbers of people whose health could have been degraded by the intervention as evidenced by increased abnormal values of these biomarkers. For example, the trials and VAERS reported clots that resulted in serious symptoms and deaths but gave no indication of the enhanced predisposition to forming serious clots in the future with a higher base of micro-clots formed because of the mRNA intervention. The latter is particularly relevant to children, who have a long future that could be seriously affected by having an increased predisposition to multiple clot-based (and other) serious diseases resulting from these inoculations.

3. Mass inoculation

3.1. Adverse events reported for adults

This section describes the adverse effects that followed COVID-19 mass inoculation in the USA. The main source of adverse effects data used was VAERS. Because VAERS is used to estimate adverse event information by many other countries as well, a short overview of VAERS and its intrinsic problems is summarized in Appendix 1.

The period in the present study covered by the reported inoculations is mid-December 2020 to the end of May 2021. The population inoculated during this period is mainly adults. Child inoculations did not begin until mid-May. Because the different age groups were inoculated starting at different times based on priority, the elapsed times after inoculation will be different, and any adverse event comparisons across age groups will require some type of elapsed post-inoculation time normalization.

We examined VAERS-reported deaths by age group, normalized to:

1) the number of inoculations given
2) the period within seven days after inoculation.

This allows a credible comparison of very short-term adverse effects post-inoculation for all age groups. During this period, which is eight days post-inoculation (where day zero is the day of inoculation), sixty percent of all post-inoculation deaths are reported in VAERS.

Fig. 2 below shows the results circa late May 2021 [3]. The age band ranges are different from those in Fig. 1 because the CDC provides inoculation after-effect age bands differently from COVID-19 death age bands. In general, the inoculation deaths by age per inoculant roughly parallel the COVID-19 deaths by age per capita (the curve structures are very similar), with one exception: the 0–17 demographic. In the normalized COVID-19 death graph (Fig. 1), the deaths per capita in the 0–17 demographic are negligible, while in the normalized inoculant death graphs (Fig. 2) the normalized deaths are small, but not negligible. The members of the 65+ demographic, where the bulk of deaths are occurring in Figs. 1 and 2, have been receiving inoculations for five months, whereas the members of the youngest demographic have been receiving inoculations only for a few weeks. More time needs to pass

before more definitive conclusions can be drawn about the youngest demographic, and how its members are impacted adversely following the inoculations.

The high death rates from both COVID-19 and the inoculations in the 65+ demographic should not be surprising. In both cases, the immune system is challenged, and in both cases, a dysfunctional immune system characteristic of many elderly people with multiple comorbidities cannot respond adequately to the challenge.

3.1.1. Specific short-term adverse events reported in VAERS

The most comprehensive single evaluation of VAERS-reported adverse events (mainly for adult recipients of the COVID-19 "vaccines") we have seen is a non-peer-reviewed collection of possible side effects by Dr. Ray Sahelian [35]. We recommend reading this short data-rich summary of the broad types of events reported already, in the context that these events are very short-term. Dr. Sahelian identifies five mechanisms he believes are responsible for most of these events, with research potentially uncovering other mechanisms. These five mechanisms include:

1 "An overreacting inflammatory response is known as systemic inflammatory response syndrome (SIRS). This SIRS reaction, perhaps a cytokine storm, can range from very mild to very severe. It can begin the very first day of the shot or begin days or weeks later as a delayed reaction."
2 "Interaction of the spike proteins with ACE2 receptors on cell membranes. Such cells are found widely in the body including the skin, lungs, blood vessels, heart, mouth, gastrointestinal tract, kidneys, and brain."
3 "Interaction of spike proteins with platelets and/or endothelial cells that line the inside of blood vessels. This can lead to clotting or bleeding (low number of circulating platelets in the bloodstream). Some of the clots, even if tiny, cause certain neurological symptoms if the blood supply to nerves is compromised."
4 "Immediate or delayed release of histamine from mast cells and basophils (mast cell activation syndrome, MCAS)."
5 5. "Swelling of lymph nodes in various areas of the body could interfere with blood flow, put pressure on nerves causing pain, or compromise their proper function."

These reactions can be classified as Hyperinflammation, Hypercoagulation, Allergy, and Neurological, and can contribute to many symptoms and diseases, as VAERS is showing.

An excellent review of acute and potential long-term pathologies resulting from the COVID-19 inoculations [36] showed potential relationships to blood disorders, neurodegenerative diseases and autoimmune diseases. This review discussed the relevance of prion-protein-related amino acid sequences within the spike protein.

3.1.2. Potential mid- and long-term events and serious illnesses for adults and children from past vaccines

A detailed description of potential mid- and long-term events and serious illnesses for adults and children from past vaccines is presented in Appendix C. Most of these events and illnesses are not predictable, and most, if not all, would be possible for the COVID-19 inoculations in the mid- and long-term for adults and children.

3.1.3. Potential short-, mid-, and long-term risks of mass COVID-19 inoculation for children

3.1.3.1. Intrinsic inoculant toxicity. Children are unique relative to COVID-19. They have negligible risks of serious effects from the disease, as shown in Fig. 1. Given that the COVID-19 inoculants were only tested for a few months, and mid-or long-term adverse effects are unknown, any mid- or long-term adverse events that emerge could impact children adversely for decades.

We believe that mid-or long-term adverse effects are possible based on the recent emergence of evidence that would support the probability of mid-and long-term adverse effects from the COVID-19 inoculants, such as:

1) The spike protein itself can be a toxin/pathogenic protein:
2) S protein alone can damage vascular endothelial cells (ECs) by downregulating ACE2 and consequently inhibiting mitochondrial function [37].
3) it is concluded that ACE2 and endothelial damage is a central part of SARS-CoV2 pathology and may be induced by the spike protein alone [38].
4) the spike protein of SARS-CoV-1 (without the rest of the virus) reduces ACE2 expression, increases angiotensin II levels, exacerbates lung injury, and triggers cell signaling events that may promote pulmonary vascular remodeling and Pulmonary Arterial Hypertension (PAH) as well as possibly other cardiovascular complications [39].
5) the recombinant S protein alone elicits functional alterations in cardiac vascular pericytes (PCs) [40]. This was documented as:
6) increased migration
7) reduced ability to support EC network formation on Matrigel
8) secretion of pro-inflammatory molecules typically involved in the cytokine storm
9) production of pro-apoptotic factors responsible for EC death. Furthermore, the S protein stimulates the phosphorylation/activation of the extracellular signal-regulated kinase 1/2 (ERK1/2) through the CD147 receptor, but not ACE2, in cardiac PCs, the S protein may elicit vascular cell dysfunction, potentially amplifying, or perpetuating, the damage caused by the whole coronavirus [40].
10) "even in the absence of the angiotensin-converting enzyme 2 receptors, the S1 subunit from SARS-CoV-2 spike protein binding to neutral phospholipid membranes leads to their mechanical destabilization and permeabilization. A similar cytotoxic effect of the protein was seen in human lung epithelial cells." [125].
11) The LNP layer encapsulating the mRNA of the inoculant is highly inflammatory in both intradermal and intranasal inoculation [41] and "Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine" [42]. "Humans are likely developing PEG antibodies because of exposure to everyday products containing PEG. Therefore, some of the immediate allergic responses observed with the first shot of mRNA-LNP vaccines might be related to pre-existing PEG antibodies. Since these vaccines often require a booster shot, anti-PEG antibody formation is expected after the first shot. Thus, the allergic events are likely to increase upon re-vaccination" [43].

    There is also the possibility that the components of the LNP shell could induce the ASIA Syndrome (autoimmune/inflammatory syndrome induced by adjuvants), as shown by studies on post-inoculation thyroid hyperactivity [44] and post-inoculation subacute thyroiditis [45].
12 The spike protein has been found in the plasma of post-inoculation individuals, implying that it could circulate to, and impact adversely, any part of the body [46].
13 The spike protein of SARS-CoV-2 crosses the blood-brain barrier in mice [47], and "the SARS-CoV-2 spike proteins trigger a pro-inflammatory response on brain endothelial cells that may contribute to an altered state of BBB function" [48].
14 The spike proteins manufactured in vivo by the present COVID-19 inoculations could potentially "precipitate the onset of autoimmunity in susceptible subgroups, and potentially exacerbate autoimmunity in subjects that have pre-existing autoimmune diseases", based on the finding that anti-SARS-CoV-2 protein

antibodies cross-reacted with 28 of 55 diverse human tissue antigens [49].

15 "The biodistribution of ChaAdOx1 [Astra Zeneca's recombinant adenovirus vaccine candidate against SARS-CoV-2] in mice confirmed the delivery of vaccine into the brain tissues [50]. The vaccine may therefore spur the brain cells to produce CoViD spike proteins that may lead to an immune response against brain cells, or it may spark a spike protein-induced thrombosis. This may explain the peculiar incidences of the fatal cerebral venous sinus thrombosis (CVST) observed with viral vector-based CoViD-19 vaccines" [51,52].

A complementary perspective to explain adenovirus-based vaccine-induced thrombocytopenia is that "transcription of wildtype and codon-optimized Spike open reading frames enables alternative splice events that lead to C-terminal truncated, soluble Spike protein variants. These soluble Spike variants may initiate severe side effects when binding to ACE2-expressing endothelial cells in blood vessels." [100].

16 A Pfizer Confidential study performed in Japan showed that "modRNA encoding luciferase formulated in LNP comparable to BNT162b2″ injected intramuscularly concentrated in many organs/tissues in addition to the injection site [53]. The main organs/sites identified were adrenal glands, liver, spleen, bone marrow, and ovaries. While damage to any of these organs/sites could be serious (if real for humans), adverse effects on the ovaries could be potentially catastrophic for women of childbearing or pre-childbearing age.

The main objective of credible biodistribution studies (of inoculants for eventual human use) is to identify the spatio-temporal distribution of the actual inoculant in humans; i.e., how much of the final desired product (in this case, expressed protein antigen/spike protein) is produced in different human tissues and organs as a function of time. That's not what was reported in the Pfizer Confidential study.

Rats were used for the in vivo studies; the relationship of their biodistribution to that of humans is unclear. They were injected in different locations (hindpaw/intramuscular); the relationship to human injections in the deltoid muscle is unclear. They were injected with "modRNA encoding luciferase formulated in LNP comparable to BNT162b2″; it is unclear why they weren't injected with BNT162b2, it is unclear why spike protein expression wasn't evaluated rather than LNP concentration, and it is unclear how well the biodistribution from the actual inoculant used in the experiments compares to the biodistribution from BNT162b2.

They were injected once per rat. Given that a second injection would not be in the same exact location as the first, and that the circulatory system might have changed due to clotting effects from the first injection and other potential vascular complications, it is unclear how the biodistribution change with the second injection would compare with the first. If a booster injection is given to counter variants, it is unclear how its biodistribution would be altered as a consequence of the preceding two injections.

Clotting will occur with the highest probability where the blood flow is reduced (and more time is available for LNP-endothelial cell interaction). It is unclear whether the clotting process would show *positive feedback* behaviour where the initial inoculation constricts the flow in low-velocity regions even further by enhanced clotting, and subsequent inoculations further amplify this reduced flow-enhanced clotting cycle.

The rats were injected under pristine conditions; how that compares with humans, who have been, are being, and will continue to be exposed to multiple toxic substances in combination, is open to question. We know these combinations can act synergistically to adversely impact myriad organs and tissues throughout the body [23]. We don't know how these toxic exposures in humans affect the permeability of the blood/tissue barriers, and especially the ability of the injected material to diffuse into the bloodstream (and also the ability of the manufactured spike proteins to diffuse from the bloodstream into the surrounding tissue).

Higher-level primates should have been used for these short-term experiments, to obtain a more realistic picture of the biodistribution of inoculant in human organs and tissues. In other words, these laboratory experiments may be just the tip of the iceberg of estimating the amount of inoculant that concentrates in critical organs and tissues of human beings.

The many studies referenced above indicate collectively that the mRNA-based COVID-19 inoculations (the most prolific inoculations used in the USA for COVID-19 so far) consist of (at least) two major toxins: the instructions for the spike protein (mRNA) and the mRNA-encapsulating synthetic fat LNP. The vaccine is injected into the deltoid muscle, at which time it contributes to inflammation at the injection site due in part to the LNP and potentially to anaphylaxis from the LNP PEG-2000 component. Some of the injected material stays at the injection site, where it combines with cells through endocytosis to express spike protein on the cell surface, stimulating the adaptive immune system to eventually produce antibodies to the spike protein [54].

The remainder of the injected material enters the lymphatic system and the bloodstream, and is distributed to tissues and organs throughout the body: e.g., "Drugs administered by the intramuscular (IM) route are deposited into vascular muscle tissue, which allows for rapid absorption into the circulation" [55]. The basis of this process is that the bulky muscles have good vascularity, and therefore the injected drug quickly reaches the systemic circulation and thereafter into the specific region of action, bypassing the first-pass metabolism [56]. The widespread distribution is greatly enhanced by the LNP PEG-2000 coating as follows: building from the success of PEGylating proteins to improve systemic circulation time and decrease immunogenicity [57]. PEG coatings on nanoparticles shield the surface from aggregation, opsonization, and phagocytosis, prolonging systemic circulation time. [57]. PEG coatings on nanoparticles have also been utilized for overcoming various biological barriers to efficient drug and gene delivery associated with other modes of administration. [57]

In the bloodstream, one possible outcome is that the LNPs coalesce with the endothelial cells on the inner lining of the blood vessels and transfer the mRNA to the cells through endocytosis. The endothelial cells would then express the spike protein on their surface. Platelets flowing by the spike protein express ACE2 receptors on their surface; therefore, one possible outcome would be activation of the platelets by the spike protein and initiation of clotting. Another possible outcome would be the modified endothelial cells being recognized by innate immune system cells as foreign. These immune killer cells would then destroy parts of the endothelium and weaken the blood-organ barriers. The LNPs would inflame the endothelium as well, both increasing barrier permeability and increasing the blood vessel diameter. This weakening of the blood-organ barriers would be superimposed on any inflammation due to the myriad toxic contributing factors operable [4]. The newly-formed cells with spike proteins would penetrate the blood-organ barriers and bind to tissue with expressed ACE2 receptors. Any LNPs that did not coalesce with the endothelial cells, but remained intact, could also pass through the permeable blood-organ barrier, and coalesce directly with the organ cells. This could lead to an attack by innate immune system cells, and be a precursor to autoimmunity [4].

In the preceding discussion of the Pfizer biodistribution studies, the issue of multiple inoculations on changes in biodistribution was raised. Similarly, the alteration of effects as described above by multiple inoculations must be considered. Each inoculation will have positive aspects and negative aspects. The positive aspects are the formation of antibodies in the muscle cells and lymphatic system. The negative aspects include, but are not limited to, the potential clotting effects and permeability increases for that fraction of the inoculant that enters the bloodstream. The first inoculant dose can be viewed as priming the immune system. The immune response will be relatively modest. The second inoculant dose can be expected to elicit a more vigorous immune

Table A1
Expected deaths from non-COVID-19 causes for inoculees (Thousands).

Potential covid deaths/# non-covid expected	Mean time location/five months									
	0	%REP	1/3	%REP	1/2	%REP	2/3	%REP	1	%REP
0	723	0.5	482	0.74	362	0.98	242	1.47	4.77	75
.5	1085	0.33	723	0.5	543	0.66	363	0.98	7.14	50
1	1446	0.25	964	0.37	724	0.49	484	0.74	9.51	37

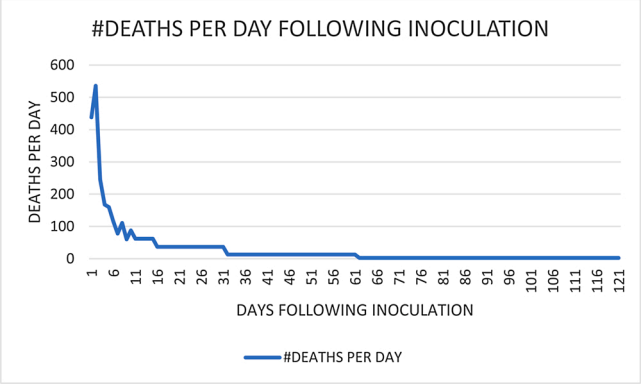

Fig. A1. Figure A1-1 is a plot of number of deaths from COVID-19 inoculation (reported to VAERS and obtained from the CDC search engine CDC Wonder) as a function of days from inoculation (zero reflects day of inoculation). If there were no effect from the inoculation, as claimed by the CDC and other official government agencies, the curve would be essentially a straight horizontal line, reflecting normal expected deaths in a non-COVID-19 year. The curve is stepped past the tenth day because the data after that point is provided in bands by CDC Wonder. The knee of the curve, which will denote the beginning of the transition of 1) deaths **from** inoculation to 2) deaths **expected**, appears somewhere in the range between day ten and day thirty.

Table A2
Actual COVID-19 inoculation-based deaths.

Actual COVID-19 inoculation-based deaths from vaers reporting				
	Separate Groups		Overlapping Groups	
Expected Deaths Reported	37	20	37	20
Range Of Days Inoculation Deaths	0–30	0–30	0–30	0–30
Total Reported Deaths Over Range	2901	2901	2901	2901
Total Expected Deaths Over Range	1147	620	1147	620
Inoculation-Based Deaths Reported	1754	2281	2901	2901
Expected Deaths Reported/Total Expected	.0077	.0041	.0077	.0041
Total Actual Inoculation-Based Deaths Using Expected Ratio (Above)	227792	556341	376753	707561

Table A3
Possible COVID-19 inoculation-based deaths.

Possible COVID-19 inoculation-based deaths from vaers reporting				
	Separate Groups		Overlapping Groups	
Expected Deaths Reported	10	15	10	15
Range Of Days Inoculation Deaths	0–30	0–30	0–30	0–30
Total Reported Deaths Over Range	2901	2901	2901	2901
Total Expected Deaths Over Range	310	465	310	465
Inoculation-Based Deaths Reported	2591	2436	2901	2901
Expected Deaths Reported/Total Expected	.0021	.0031	.0021	.0031
Total Actual Inoculation-Based Deaths Using Expected Ratio (Above)	1233810	785806	1381429	935806

response. This will enhance the desired antibody production in the muscle cells and lymphatic system, but may also enhance the immune response to both the blood vessel-lining endothelial cells displaying the spike protein and the platelets, causing more severe damage. If a booster (s) inoculation is also required, this may further enhance both the positive and negative immune responses resulting from the second inoculation. While the positive effects are reversible (antibody levels decrease with time), adverse effects may be cumulative and irreversible, and therefore injury and death rates may increase with every additional inoculation [58].

These effects can occur throughout the body in the short term, as we are seeing with the VAERS results. They can occur in the mid- and long-term as well, due to the time required for destructive processes to have full effect and the administration of further inoculations. For example, micro-clots resulting from the inoculation that were insufficient to cause observable symptoms could in effect raise the baseline for thrombotic disease [92]. Lifestyle activities that contribute to enhanced blood clotting would have less distance to travel to produce observable symptoms, and thus the serious effects of clotting would have been accelerated [59,60]. As an example: the risk of venous thrombosis is approximately 2- to 4-fold increased after air travel [61]. How much this rate would increase after the inoculations, where microthrombi have formed in some recipients, is unknown. These potential baseline-raising effects could impact the interpretation of the VAERS results, as we show at the end of Appendix 1.

3.1.3.2. Adverse inoculant effects on children. What are the potential mid- and long-term adverse health effects from the COVID-19 inoculation on children specifically, taking into account that they will be exposed not only to the spike protein component of the SARS-CoV-2 virus but also to the toxic LNP encapsulating-shell? This toxic combination will have bypassed many defensive safeguards (typically provided by the innate immune system) through direct injection [62]. As we have shown, the main reasons why we believe the spike protein could be harmful to children even though they don't seem to get sick from exposure to SARS-CoV-2 are 1) the bypassing of the innate immune system by inoculation, 2) the larger volume of spike protein that enters the bloodstream, and 3) the additional toxic effects of the encapsulating LNP layer.

3.1.3.2.1. Potential mid-term adverse health effects. Examination of the myriad post-COVID-19 inoculation symptoms/biomarker changes for the 0–17 age demographic reported to VAERS circa mid-June 2021 provides some indication of very early damage [84]. Main region-s/systems affected adversely (VAERS symptoms/biomarkers shown in parentheses) include:

- Cardiovascular (blood creatine phosphokinase increased, cardiac imaging procedure abnormal, echocardiogram abnormal, electrocardiogram abnormal, heart rate increased, myocarditis, palpitations, pericarditis, tachycardia, troponin I increased, troponin increased, fibrin D-Dimer increased, platelet count decreased, blood pressure increased, bradycardia, brain natriuretic peptide increased, ejection fraction decreased, migraine)
- Gastrointestinal (abdominal pain, diarrhoea, vomiting, alanine aminotransferase increased, aspartate aminotransferase increased.)
- Neural (gait disturbance, mobility decreased, muscle spasms, muscle twitching, seizure, tremor, Bell's Palsy, dyskinesia)

- Immune (C-Reactive Protein increased, red blood cell sedimentation rate increased, white blood cell counts increased, inflammation, anaphylactic reaction, pruritis, rash, lymphadenopathy)
- Endocrine (heavy menstrual bleeding, menstrual disorder)

In addition, there were large numbers of different vision and breathing problems reported.

All the major systems of the body are impacted, and many of the major organs as well. Given the lag times in entering data into VAERS and the fact that inoculations of children started fairly recently, we would expect the emphasis to be immediate symptomatic and biomarker reactions. More time is required for organ and system damage to develop and emerge. Cardiovascular problems dominate, as our model for spike protein/LNP circulation and damage predicts, and it is unknown how reversible such problems are. Many of the VAERS symptoms listed above were also found in COVID-19 adult patients [64].

Consider the example of Multisystem Inflammatory Syndrome in Children (MIS-C). It has emerged in VAERS with modest frequency so far, and it also occurred about a month after COVID-19 infection [65]. In both cases, the presence of the spike protein was a common feature. Many of its characteristic symptoms are those listed above from VAERS. MIS-C has similarities with known disease entities like Kawasaki Disease (KD), toxic shock syndrome (TSS) and macrophage activation syndrome (MAS)/secondary hemophagocytic lymphohistiocytosis (HLH) [66]. One presentation of MIS-C is in adolescents with a high disease burden as evidenced by more organ systems involved, almost universally including cardiac and gastrointestinal systems, and with a higher incidence of shock, lymphopenia, and elevated cardiac biomarkers indicating myocarditis [67]. Since the first reports of children developing MIS-C, it was evident that others presented with some of the classic symptoms of the well-recognized childhood illness KD [68]. Further, despite KD being ordinarily incredibly rare in adults, patients with MIS-A have also been reported with KD-like features. [68] Thus, an examination of the adverse effects from COVID-19 as evidenced through these diseases might shed some light on what can be expected further down the line from the inoculations.

The following section addresses Kawasaki disease (KD) and Multisystem Inflammatory Syndrome in Children (MIS-C) [65].

KD is an acute vasculitis and inflammation that predominantly affects the coronary arteries and can cause coronary artery aneurysms. Other KD manifestations include systemic inflammation of arteries, organs, and tissues, with consequent hepatitis and abdominal pain; lung interstitial pneumonitis, aseptic meningitis due to brain membrane inflammations; myocarditis, pericarditis, and valvulitis; urinary tract pyuria, pancreatitis; and lymph-node enlargement [69]. In general, although almost all children fully recover, some of them later develop coronary artery dilation or aneurysm [70]. Etiologically and pathologically, numerous studies indicate that KD is triggered by an abnormal autoimmune response caused by an infection [71]. The infection hypothesis is supported by epidemiology data showing that an infectious disease is involved at least as a starting point. Previously proposed infectious agents include Herpesviridae, retroviruses, Parvovirus B19, bocavirus, and bacterial infections such as staphylococci, streptococci, Bartonella, and Yersinia infections [72].

SARS-CoV-2 adds to these infectious agents by eliciting autoantibodies likely via molecular mimicry and cross-reactivity with autoantigens [72,73].

Then, the formation of antigen–antibody immune complexes can lead to KD symptoms via activation of the receptors of mast cells, neutrophils, and macrophages with consequent release of pro-inflammatory cytokines and increase of blood vessel permeability; activation of the complement system, stimulation of neutrophils and macrophages to secrete proteases and more proinflammatory cytokines [74], thus merging into the “cytokine storm” that characterizes MIS-C [75]. Indeed, features of KD are raised levels of Interleukin (IL)-6, IL-8, IL-15, and IL-17, with the cytokine level predicting coronary aneurysm formation in KD patients [76,77]

3.1.3.2.2. Potential long-term adverse health effects. In the long-term, SARS-CoV-2-induced KD vasculitis can lead to severe pathologies. Vasculitis has a predilection for coronary arteries with a high complication rate across the lifespan for those with medium to large coronary artery aneurysms [78]. The cytokine-induced inflammation produces endothelial dysfunction and damage to the vascular wall, leading to aneurysmal dilatation. Successively, vascular remodeling can also occur, but this does not imply resolution of the disease or reduction of risk for future complications. A rigorous follow-up to detect progressive stenosis, thrombosis and luminal occlusion that may lead to myocardial ischemia and infarction becomes mandatory [78]. Of equal importance, among other long-term outcomes, children with KD may have increased risks not only for ischemic heart disease, but also for autoimmune disorders, cancer as well as an increased all-cause mortality [71].

Additional questions regarding mass inoculation of children and adolescents include:

a) Do children, being asymptomatic carriers of SARS-CoV-2, transmit the virus?
b) Do recently vaccinated people, infected with SARS-CoV-2, transmit the virus?

There is evidence of children transmitting SARS-CoV-2 in community settings, but the existing literature is heterogeneous with regards to the relative rate at which they do so compared to adults [79].

Studies from South Korea and Thailand found a very limited number of secondary cases [80,81]. On the contrary, a large contact tracing study from India concluded that the highest probability of transmission was between case-contact pairs of similar age and that this pattern of enhanced transmission risk was highest among children 0–4 years of age as well as adults 65 years of age and older [80]

With regard to the second question, it was shown that household members of healthcare workers inoculated with a single dose of either Pfizer or Astra Zeneca COVID-19 inoculant were at significantly reduced risk of PCR-confirmed SARS-CoV-2 infection but at non-statistically significant reduced risk of hospitalization, compared to household members of uninoculated healthcare workers, fourteen days after inoculation [82]. This finding again underlines the association of severe disease to the characteristics of the infected person and not directly to the transmission, implying that the elderly should be inoculated and not the children.

3.2. Novel best-case scenario cost-benefit analysis of COVID-19 inoculations for most vulnerable

Traditional cost-benefit analyses are typically financial tools used to estimate the potential value of a proposed project. They involve generating cost streams over time, benefit streams over time, and then comparing the net present value of these two streams (including risk) to see whether the risk-adjusted discounted benefits outweigh the risk-adjusted discounted costs. Appendix D presents a detailed non-traditional *best-case scenario* pseudo-cost-benefit analysis of inoculating people in the 65+ demographic in the USA. In this incarnation of a cost-benefit analysis, the costs are the number of deaths resulting from the inoculations, and the benefits are the lives saved by the inoculations. The time range used was from December 2019 to end-of-May 2021. No discounting was done; an inoculation-based death occurring immediately post-inoculation was given the same importance/weighting as an inoculation-based death months after inoculation.

Why was this non-traditional approach selected for a cost-benefit analysis? In a traditional non-financial cost-benefit analysis relative to inoculations, the adverse events prevented by the inoculations would be compared with the adverse events resulting from the inoculations. Presently, in the USA, definitions, test criteria, and reporting incentives

for COVID-19 and its inoculants have shifted over time, and we believe a standard approach could not be performed credibly. Appendix Da presents some of the problems with the COVID-19 diagnostic criteria on which the above statements are based.

In contrast to the pandemic buildup phase, where many who died *with* COVID-19 were assumed to have died *from* COVID-19 by the medical community and the CDC, the post-inoculation deaths reported in VAERS are assumed by the CDC to be mostly from causes other than the inoculations. We wanted to use a modified cost-benefit analysis that would have less dependence on arbitrary criteria and subjective judgments.

The approach selected can be viewed as a *best-case scenario* pseudo-cost-benefit analysis. We assume the inoculations prevent ***all*** the deaths ***truly*** attributable to COVID-19 (these are the total deaths attributed to COVID-19 officially minus 1) the number of false positives resulting from the PCR tests run at very high amplification cycles and 2) the number of deaths that could have been attributed to one of the many comorbidities that were typical of those who succumbed, as shown in our results section) over the period December 2019 to end-of-May 2021, and relate that number to the deaths ***truly*** attributable to the inoculation (from January 2021 to end-of-May 2021) based on our computations in the results section. The results show ***conservatively*** that there are five times the number of deaths ***truly*** attributable to each inoculation vs those ***truly*** attributable to COVID-19 in the 65+ demographic. As age decreases, and the risk for COVID-19 decreases, the cost-benefit increases. Thus, if the best-case scenario looks ***poor*** for benefits from the inoculations, any realistic scenario will look ***very poor***. For children the chances of death from COVID-19 are negligible, but the chances of serious damage over their lifetime from the toxic inoculations are not negligible.

4. Discussion

Two issues arise from these results.

First, where is the data justifying inoculation for children, much less most people under forty? It's not found on Fig. 1, where the most vulnerable are almost exclusively the elderly with many comorbidities [83]. Yet, in the USA, Pfizer has been approved to inoculate children 12–17, and the goal is to accomplish this by the start of the school year in the Fall. As stated previously, there are plans to inoculate children as young as six months starting before the end of 2021.

What is the rush for a group at essentially zero risks? Given that the inoculations were tested only for a few months, only very short-term adverse effects could be obtained. It is questionable how well even these short-term effects obtained from the clinical trials reflect the short-term effects from the initial mass inoculation results reported in VAERS. Figs. 1 and 2 reflect only these very short-term results. A number of researchers have suggested the possibility of severe longer-term autoimmune, Antibody-Dependent Enhancement, neurological, and other potentially serious effects, with lag periods ranging from months to years. If such effects do turn out to be real, the children are the ones who will have to bear the brunt of the suffering. There appear to be no benefits for the children and young adults from the inoculations and only Costs!

The second issue is why the deaths shown on Fig. 2 were not predicted by the clinical trials. We examined the Pfizer trial results (based on a few months of testing) and did not see how (potentially) hundreds of thousands of deaths could have been predicted from the trials' mortality results. Why this gap?

As we showed in the clinical trials section, 17.4 % of the Pfizer sample members were over 65, and 4.4 % were over 75. When the later phases of the trials started in late July 2020, the managers knew the COVID-19 age demographics affected from the July 2020 analog of Fig. 1. Rather than sampling from the age region most affected, they sampled mainly from the age region least affected! And even in the very limited sampling from the oldest groups, it is unclear whether they selected from those with the most serious comorbidities. Our impression is that the sickest were excluded from the trials, but were first in line for the inoculants.

It is becoming clear that the central ingredient of the injection, the recipe for the spike protein, will produce a product that can have three effects. Two of the three occur with the production of antibodies to the spike protein. These antibodies could allegedly offer protection against the virus (although with all the "breakthrough" cases reported, that is questionable), or could suppress serious symptoms to some extent. They could also cross-react with human tissue antigen, leading to potential autoimmune effects. The third occurs when the injected material enters the bloodstream and circulates widely, which is enabled by the highly vascular injection site and the use of the PEG-2000 coating.

This allows spike protein to be manufactured/expressed in endothelial cells at any location in the body, both activating platelets to cause clotting and causing vascular damage. It is difficult to believe this effect is unknown to the manufacturer, and in any case, has been demonstrated in myriad locations in the body using VAERS data. There appears to be modest benefit from the inoculations to the elderly population most at risk, no benefit to the younger population not at risk, and much potential for harm from the inoculations to both populations. It is unclear why this mass inoculation for all groups is being done, being allowed, and being promoted.

5. Overall conclusions

The people with myriad comorbidities in the age range where most deaths with COVID-19 occurred were in very poor health. Their deaths did not seem to increase all-cause mortality as shown in several studies. If they hadn't died with COVID-19, they probably would have died from the flu or many of the other comorbidities they had. We can't say for sure that many/most died from COVID-19 because of: 1) how the PCR tests were manipulated to give copious false positives and 2) how deaths were arbitrarily attributed to COVID-19 in the presence of myriad comorbidities.

The graphs presented in this paper indicate that the frail injection recipients receive minimal benefit from the inoculation. Their basic problem is a dysfunctional immune system, resulting in part or in whole from a lifetime of toxic exposures and toxic behaviors. They are susceptible to either the wild virus triggering the dysfunctional immune system into over-reacting or under-reacting, leading to poor outcomes or the injection doing the same.

This can be illustrated by the following analogy. A person stands in a bare metal enclosure. What happens when the person lights a match and drops it on the floor depends on what is on the floor. If the floor remains bare metal, the match burns for a few seconds until extinguished. If there is a sheet of paper on the floor under the match, the match and the paper will burn for a short time until both are extinguished. If, however, the floor is covered with ammonium nitrate and similar combustible/explosive materials, a major explosion will result! For COVID-19, the wild virus is the match. The combustible materials are the toxic exposures and toxic behaviors. If there are no biomarker 'footprints' from toxic exposures and toxic behaviors, nothing happens. If there are significant biomarker 'footprints' from toxic exposures and toxic behaviors, bad outcomes result.

Adequate safety testing of the COVID-19 inoculations would have provided a distribution of the outcomes to be expected from 'lighting the match'. Since adequate testing was not performed, we have no idea how many combustible materials are on the floor, and what the expected outcomes will be from 'lighting the match'.

The injection goes two steps further than the wild virus because 1) it contains the instructions for making the spike protein, which several experiments are showing can cause vascular and other forms of damage, and 2) it bypasses many front-line defenses of the innate immune system to enter the bloodstream directly in part. Unlike the virus example, the injection ensures there will always be some combustible materials on the

floor, even if there are no other toxic exposures or behaviors. In other words, the spike protein and the surrounding LNP are toxins with the potential to cause myriad short-, mid-, and long-term adverse health effects even in the absence of other contributing factors! Where and when these effects occur will depend on the biodistribution of the injected material. Pfizer's own biodistribution studies have shown the injected material can be found in myriad critical organs throughout the body, leading to the possibility of multi-organ failure. And these studies were from a single injection. Multiple injections and booster shots may have cumulative effects on organ distributions of inoculant!

The COVID-19 reported deaths are people who died **with** COVID-19, not necessarily **from** COVID-19. Likewise, the VAERS deaths are people who have died **following** inoculation, not necessarily **from** inoculation.

As stated before, CDC showed that 94 % of the reported deaths had multiple comorbidities, thereby reducing the CDC's numbers attributed strictly to COVID-19 to about 35,000 for all age groups. Given the number of high false positives from the high amplification cycle PCR tests, and the willingness of healthcare professionals to attribute death to COVID-19 in the absence of tests or sometimes even with negative PCR tests, this 35,000 number is probably highly inflated as well.

On the latter issue, both Virginia Stoner [85] and Jessica Rose [86] have shown independently that the deaths **following** inoculation are not coincidental and are **strongly related to** inoculation through strong clustering around the time of injection. Our independent analyses of the VAERS database reported in Appendix 1 confirmed these clustering findings.

Additionally, VAERS historically has under-reported adverse events by about two orders-of-magnitude, so COVID-19 inoculation deaths ***in the short-term*** could be in the hundreds of thousands for the USA for the period mid-December 2020 to the end of May 2021, potentially swamping the *real* COVID-19 deaths. Finally, the VAERS deaths reported so far are for the very short term. We have no idea what the death numbers will be in the intermediate and long-term; the clinical trials did not test for those.

The clinical trials used a non-representative younger and healthier sample to get EUA for the injection. Following EUA, the mass inoculations were administered to the very sick (and first responders) initially, and many died quite rapidly. However, because the elderly who died following COVID-19 inoculation were very frail with multiple comorbidities, their deaths could easily be attributed to causes other than the injection (as should have been the case for COVID-19 deaths as well).

Now the objective is the inoculation of the total USA population. Since many of these potential serious adverse effects have built-in lag times of at least six months or more, we won't know what they are until most of the population has been inoculated, and corrective action may be too late.

All the authors contributed equally and approved the final version of the manuscript.

Author's contribution

Kostoff RN contributed to this paper with conception, data analysis, and writing the manuscript; Calina D contributed to data analysis, writing the manuscript, and editing; Kanduc D participated in data analysis and writing the manuscript; Briggs MB participated in data analysis, results validation, and graphics development; Vlachoyiannopoulos P participated in writing the manuscript; Svistunov AA participated in editing and reviewing the manuscript; Tsatsakis A participated in editing and reviewing the manuscript; all the authors contributed equally and approved the final version of the manuscript.

Ethical approval

Not applicable.

Declaration of Competing Interest

The authors declare that they have no competing interests. Aristides Tsatsakis is the Editor-in-Chief for the journal but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article.

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Not applicable.

Appendix A

EXPECTED DEATHS IN 65+ DEMOGRAPHIC VS COVID-19 INOCULATION DEATHS

The goal of this appendix is to estimate the number of actual deaths from the COVID-19 inoculation based on the number of deaths following inoculation reported in VAERS [93,94,101]. The approach used will:

1) identify the number of deaths following COVID-19 inoculation that would have been **expected** without COVID-19 inoculation (i.e., pre-COVID-19 death statistics);
2) relate the VAERS **expected** death data to the actual number of deaths **expected** based on historical death statistics; and
3) apply this ratio to scale-up the deaths attributed to COVID-19 inoculation reported in VAERS to arrive at actual deaths attributable to COVID-19 inoculation.

For example, if ten deaths could be shown in VAERS to reflect expected pre-COVID-19 deaths, and the actual number of expected pre-COVID-19 deaths from historical data was 100, the scaling factor of deaths would be ten to translate VAERS-reported deaths to actual deaths. Then, the deaths reported in VAERS that can be attributed to the COVID-19 inoculation will be multiplied by the expected deaths scaling factor, ten, to arrive at the actual number of deaths resulting from the COVID-19 inoculation. Thus, if VAERS shows fifty deaths that can be attributed to the COVID-19 inoculation, then the actual number of deaths attributed to COVID-19 will be 500 with these assumptions [3].

The basis for our approach is the following statement from the USA Federal government: "Healthcare providers are required to report to VAERS the following adverse events after COVID-19 vaccination [33] and other adverse events if later revised by FDA" [96,102,103]. "Serious AEs regardless of causality.", including death [3,95].

If there had been full compliance with this requirement in VAERS, then the VAERS-reported deaths would have equaled the sum of

1) actual expected deaths (based on past statistics)

2) actual deaths over and above expected deaths that could be attributed to the COVID-19 inoculations.

Based on this requirement, we will generate a rough estimate (in the simplest form possible) of the number of deaths that would have occurred in the 65+ demographic if there had been no COVID-19 "pandemic". Then, we will relate this number to the number of deaths reported to VAERS following COVID-19 inoculations in the 65+demographic. This would provide a "floor" for estimating the fraction of actual deaths reported to VAERS. This will be followed by parameterizing potential deaths attributable to the COVID-19 inoculations and displaying the effects on ratio of reported deaths to actual deaths. We will perform a global analysis and a local analysis, to see whether major or minor differences occur. The local analysis (Section A1-a2) may be somewhat easier to comprehend than the global analysis, but both come to similar conclusions.

A1-a Deaths Following COVID-19 Inoculations Reported to VAERS Compared to Expected Deaths

A1-a . Problems with VAERS

Before we discuss numbers of adverse events reported by VAERS, we need to identify potential shortcomings of, and problems with, VAERS, so these numbers of adverse events can be understood in their proper context. As stated previously, VAERS is a passive surveillance system managed jointly by the CDC and FDA, and historically has been shown to report about 1% of actual vaccine/inoculation adverse events (confirmed by the first principles analysis that follows in this appendix). There is no evidence that even the 1% reported have been selected randomly.

Some of this gross underreporting of adverse events reflects a major conflict-of-interest of CDC with respect to VAERS. CDC provides funding for administration of many vaccines, including the COVID-19 inoculations. Prior to COVID-19, the CDC provided about five billion dollars annually to the Vaccines for Children Program alone [102].

For COVID-19, the CDC has received many billions of dollars in supplemental funding for myriad activities, including vaccine distribution. It is difficult to separate out the CDC funding available for vaccine distribution from other CDC COVID-19 related activities, but one budget item (of many) should illustrate the magnitude of the effort: "Coronavirus Response and Relief Supplemental Appropriations Act, 2021 (P.L. 116–260): P.L. 116–260 provided $8.75 billion to CDC to plan, prepare for, promote, distribute, administer, monitor, and track coronavirus vaccines to ensure broad-based distribution, access, and vaccine coverage." [3]. Low reporting rates of actual adverse events in VAERS should not be surprising, since the same organization that receives multi-billions of dollars in funding annually for promoting and administering vaccines also has responsibility for monitoring the safety of these products (whose liability has been waived).

In addition, the 1% reporting rates came from a thirty-day tracking study [22], and therefore are strictly applicable to *very near-term* adverse events. For mid-term and especially long-term events, the reporting rates would be much lower, since the links between inoculation and adverse events would be less obvious. That doesn't mean these non-very-short-term adverse events don't exist; it just means they haven't been tracked. Absence of evidence is not evidence of absence. Thus, the VAERS numbers should be viewed as a very low "floor' of the numbers and types of adverse events from COVID-19 inoculations that exist in the real-world.

A1-a2 Global analysis

We used 2019 death statistics from CDC to start the analysis. According to search results from CDC Wonder [104] obtained 11 June 2021, there were 2,117,332 deaths from all causes for people aged 65+ in the United States in 2019. Assuming uniformity throughout the year, there would have been~882,000 deaths occurring the first five months of the year, and that number will be used as the expected deaths for the first five months of 2021. From the same source, the population estimate is~54,000,000 for the 65+ age range. From CDC COVID-19 data tracker, the number of people 65+ vaccinated with at least one dose is~44,000,000 [24]

For those who were inoculated somewhere in the time frame 1 January 2021 to 31 May 2021, the number who would have been expected to die in the period from inoculation to 31 May will be a function of the duration of this period. For example, if all 44,000,000 people had been fully inoculated on 1 January 2021, then the number expected to die post-inoculation from non-COVID-19 inoculation causes would be simply (44,000,000/54,000,000) x 882,000, or~723,000 deaths. Conversely, if all 44,000,000 people had been fully inoculated on 31 May 2021, then the number expected to die post-inoculation from non-COVID-19 inoculation causes would be extremely small [24].

For an accurate estimation of the number expected to die post-inoculation from non-COVID-19 causes, one would need to integrate the time between inoculation and 31 May over the inoculation temporal distribution function. For present purposes, we will do a very rough approximation by modeling the inoculation distribution function as a delta function occurring at a mean temporal location. In other words, we compress all inoculations an individual receives into one, identify the mean temporal location from the actual inoculation distribution function, and compute the expected deaths based on the distance from 31 May to the temporal mean point.

From a graph of inoculation trends in the CDC data tracker [101] the distribution appears to be non-symmetrical pyramidal, rising to a peak in mid-April. This is slightly over the 2/3 point in the five-month range of interest. We will approximate the mean time point as 2/3 of the distance.

Table A1 displays the mean time normalized to the five-month study window vs potential deaths from COVID-19 inoculation (not expected from prior census data) normalized to the deaths expected from prior census data. Each cell represents the percent of deaths reported in VAERS following inoculation relative to total deaths (number of deaths expected from prior census data plus number of deaths following COVID-19 inoculation not contained in the expected death group). The model on which the table is based is as follows: there are two classes of deaths for the period following COVID-19 inoculation. One is the deaths expected from prior census data, and the other is deaths attributable mainly to COVID-19 inoculation. There would be potentially substantial overlap between the two in this age group (and perhaps other age groups as well). We assume that we can tag those individuals who would be expected to die based on prior census data. The remaining deaths attributable to COVID-19 inoculation not contained within the tagged group are classified as potential COVID deaths in Table A1.

Consider the cell (2/3,0). The mean time is about mid-April 2021 and the only deaths occurring are those expected (some may have died because of the inoculation, but they were sufficiently ill that they would have died during that period without the inoculation). There were 723,000 expected deaths and~3560 reported, yielding a ratio of deaths reported in VAERS to actual deaths of ½%.

Consider the cell (1/2,1). The mean time would have been about mid-March 2021 and the inoculation distribution would have resembled an isosceles triangle. The total deaths occurring are those expected and an equal number whose deaths were attributed to COVID-19 inoculation but did not overlap with those in the tagged expected group (there still could have been some/many in the latter group that may have died because of the

inoculation, but they were sufficiently ill that they would have died during that period without the inoculation). There were 724,000 total deaths that occurred during that period and ~3560 reported, yielding a ratio of deaths reported in VAERS to actual deaths of ½%. [3]

So, according to Table A1, focusing on the parameter most closely reflecting the actual inoculation distribution (2/3), the reporting percentages of actual to total are about 1%. This mirrors the Harvard Pilgrim study results (referenced in our vaccine safety study) which were obtained through an entirely different empirical approach [4]. At least for deaths reporting, there appears to be an approximately two order of magnitude difference between actual and reported deaths in VAERS.

Table A1 used two parameters to examine a broad spectrum of possible results, the mean time and the number of deaths solely attributable to COVID-19 inoculation. The mean time parameter was fairly well known and constrained in interpretation, because it was based on an empirical inoculation distribution function. The number of deaths solely attributable to COVID-19 inoculation is completely unknown.

As will be shown in the next section, the numbers of deaths reported in VAERS are strongly related to the inoculation date by clustering, but those who died might also have been those who would have died anyway because they were expected to die. There were probably some of each in that group reported. But we have no idea of the total number whose death could be directly attributed to COVID-19 inoculation and who were not in the group expected to die. For all we know, there could have been ten million people in that group, and only an extremely small fraction of that total group was reported in VAERS.

Suppose, for example, that the actual number of deaths reported in VAERS came from two groups: 90 % were from the inoculation-attributable death group and 10 % were from the expected death group. Assume there is no overlap between the two groups. In that case, what VAERS shows is not that 1% of actual expected deaths were reported, but rather that 1/10 of one percent of the expected deaths were reported. If that metric is used as the standard to scale up to total deaths, then the number in the actual inoculation-attributable death group is not 100 times the VAERS reported deaths, but rather 1000 times the VAERS-reported deaths! The point is we can't "reverse-engineer" the reported VAERS death numbers to get the actual inoculation-attributable deaths because it depends on the unknown contribution of each of the two groups (expected deaths and inoculation-attributable deaths) to the VAERS reported deaths, and we can't separate those out.

All this analysis shows is that, at best, only about 1% of the number expected to die was reported, and because the number reported in VAERS included deaths from both groups, the fraction from each actual group of deaths could not be determined. Realistically, we may have to wait until mid-2022, when the 2021 total deaths for each age group are finalized, to ascertain whether we can see increases in all-cause mortality that could have come from the inoculation-attributable deaths.

A1-a3 Local Analysis

Another way of estimating VAERS reporting efficiency is to perform a local analysis, focused on clustering about date of COVID-19 inoculation. For the 65+demographic, the post-inoculation deaths cluster near the vaccination date, providing evidence of a ***strong link to the inoculation***.

Following the approach in the first section of this appendix, we calculate the deaths expected in any ten-day period based on 2019 pre-COVID-19 death statistics. For the inoculated group, the number of deaths expected for any ten-day period are (2,117, 332 deaths/per year) x (44,000,000/54,000,000 fraction of population in age range inoculated) x (10/365 fraction of year), or ~47,270 deaths.

BEST-CASE SCENARIO

Consider the ten days following inoculation (including day of inoculation). Approximately 2,000 deaths were reported in VAERS. Assume hypothetically that all these deaths were in the expected category; this can be viewed as a *best-case scenario*. In this *best-case scenario*, where the concentration of deaths is the highest and is normalized to the expected number of non-COVID-19 inoculation deaths (excluding deaths due solely to COVID-19 inoculation), 2,000/47,270 % of actual deaths (inoculation-related or not), or 4.23%, are reported in VAERS. Thus, at best, VAERS is underreporting by a factor of ~20.

Suppose in that ten-day interval there had been 10,000 deaths that could be directly attributed to COVID-19 inoculation in addition to the expected deaths. This would have given a ratio of 2,000/57,270 actual total deaths, or 3.5 % reported in VAERS. This latter approach requires less assumptions than the former approach, but still yields results of only a few percent actual deaths reported in VAERS.

The Harvard Pilgrim electronic tracking study of post-vaccination events reported to VAERS performed in 2010 [4] showed a 1 % reporting rate for a thirty-day period. In the present case, ~2900 post-inoculation deaths were reported to VAERS within thirty days of inoculation, or ~82 % of total deaths for the 65+demographic. Substituting thirty days for ten in the above computation yields 141,810 expected non-COVID-19 post-inoculation deaths for the thirty-day period, or 2% that are reported in VAERS. The Harvard study used an electronic system that automatically tracked every event that occurred, no matter how small. Because of the effort (time and cost) required to submit event reports to VAERS, we suspect that only the more serious events, such as death, would be reported, and even in this case, the numbers reported are miniscule.

We also did an analysis for sixty days post-inoculation. In the present case, ~3300 post-inoculation deaths were reported to VAERS within sixty days of inoculation, or ~93 % of total deaths for the 65+demographic. Substituting sixty days for ten in the above computation yields 283620 expected non-COVID-19 post-inoculation deaths for the thirty-day period, or 1.2 % that are reported in VAERS. Remember, this normalization is based only on expected deaths. If 100,000 deaths attributable mainly to the COVID-19 inoculation beyond those that overlapped with the expected group occurred during this period, then the denominator would have to be increased by 100,000, yielding a VAERS reporting rate of 0.86 %.

Thus, both the global and local analyses, and the Harvard Pilgrim empirical analysis, are converging on the same two orders-of-magnitude difference between the actual number of deaths that occurred in the USA and those reported in VAERS. Depending on how many people have really died as a result of the COVID-19 inoculation, this reporting rate could well be a fraction of a percent!

A1-a3a Local Clustering Analysis

We end this appendix with one more example from the local analysis. Some background perspective is required. In the buildup to the pandemic (putting aside the issue of high false positives from PCR tests run at high numbers of amplification cycles), almost anyone who died **with** COVID-19 was assumed to have died **from** COVID-19, irrespective of the number of potentially lethal comorbidities they had. The CDC admitted later that about

94 % of the deaths attributed to COVID-19 would ordinarily have been attributed to one of the comorbidities.

For this example, we adopt a similar philosophy for the COVID-19 inoculations. People in the 65+ demographic who have died following inoculation are divided into two groups: those who died **from** the inoculation and those who died as **expected** based on pre-COVID-19 death data. The two groups range from being entirely separate to completely overlapping. We will examine two cases: entirely separate and completely overlapping.

How are the members of each group determined? The death **from** inoculation group consists of those whose deaths cluster significantly around the date of inoculation. The deaths expected group are the number who would have died in the absence of COVID-19. We allow for overlap, where each person who died can be double-valued (a member of both groups), but not double-counted.

To obtain a relatively precise estimate of expected deaths, we would want to select a region of time where the distribution function has substantially leveled off. From Fig. A1, the thirty-sixty-day range appears reasonable. However, there is a time issue here. Given the lag time in data reported by VAERS, most of the data in this range will probably have come from inoculations in January and February, and early-mid March, approximately 35 percent of the total inoculations. Therefore, we could multiply the thirty-sixty-day average number of deaths by ~3 to obtain ~40 expected deaths per day. An even simpler way to estimate the expected deaths reported in VAERS is to use the 15−30-day average shown, which will represent most of the range. This value is ~37, which is close to the ~40 obtained with the above approximation. This analysis should be re-run in three-four months, when more of the long-range data has been filled in.

Table A2 shows the results of our analysis. As stated previously, two separate cases were analyzed: completely separate groups and completely overlapping groups. Two values of daily expected deaths were used: the 37 as described above, and 20 to account for potentially lower expected death reporting when the VAERS data has filled in more completely.

Thus, based on the deaths reported in VAERS following COVID-19 inoculation, and assuming the inoculation-related deaths are reported in the same ratio as expected deaths, the actual number of deaths strongly related to the COVID-19 inoculation should be scaled up by factors of 100−200. For the broadest definition of VAERS coverage provided by CDC Wonder, which includes the USA and all territories, protectorates, and possessions, the total deaths following COVID-19 were ~5200 in early June 2021. Using our scaling factors, this translates into somewhere between one-half million and one-million deaths, and this has not taken into account the lag times associated with entering data into VAERS. Compared with the ~28,000 deaths the CDC stated were due to COVID-19 and not associated morbidities for the 65+ age range, the ***inoculation-based deaths are an order-of-magnitude greater than the COVID-19 deaths!*** It should be remembered these are only the **very-short-term inoculation-based deaths**, and could increase dramatically if mid- and long-term adverse effects come to fruition.

We end this appendix with an even more unsettling possibility. The main assumption upon which the results in Table A2 were based is that the post-inoculation temporal distribution function shown in Fig. A1 could be divided into two regions. The strongly varying region originating from the inoculation date reflected deaths from the inoculation, and the essentially flat region that followed reflected expected deaths (that flat region also started at the inoculation date, and formed the base on which the highly varying region is positioned). This model excludes the possibility that deaths from the inoculation extend well beyond the limits of the highly varying region.

We know in general this is not true. There can be lag effects such as ADE in the Fall viral season, and longer-term effects such as autoimmune diseases. We postulate that there are other effects from the inoculation that could result in the same flat death profile as that for expected deaths.

Consider the following. Some of the damage we have seen following the inoculations in VAERS includes coagulation/clotting effects and neurological effects of all types [63]. If these effects are not lethal initially, they raise the level of dysfunction. Thus, platelet aggregation has increased to a new base level, and micro-clots have raised the probability of serious clots forming from other lifestyle factors [105]. Death of specific neurons can increase the risk of Alzheimer's disease or Parkinson's disease, and can accelerate the onset of these and many other diseases. Thus, the adverse impacts of the COVID-19 inoculations could be viewed as raising the level of expected deaths in the future. Any deaths of this nature reported in VAERS would need to be viewed as inoculation-driven, and the expected deaths used in the computations would be reduced accordingly.

Consider Table A3 below. The "expected deaths reported" have been reduced below their counterparts in Table A2 to illustrate parametrically how the total inoculation-based deaths would change from VAERS reporting if this baseline effect is operable. While Table A2 used values of 37 and 20 for expected deaths, Table A3 uses values of 10 and 15.

Thus, if the baseline of the host for coagulation/clotting, inflammation, hypoxia, neurodegeneration, etc., has been raised by the inoculations, translating into an increase in expected deaths and accelerated deaths, then it is entirely plausible that the VAERS death numbers reflect over a million deaths from COVID-19 inoculations so far. These are very short-term-effects only, and time will tell whether the large potential waves of ADE-driven deaths and autoimmune-driven deaths come to pass.

Appendix B

DETAILED ANALYSIS OF MAJOR COVID-19 INOCULANT CLINICAL TRIALS

A2-a Clinical Trials in the Mainly Adult Population

Definitions. *Efficacy* is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances – comparing a vaccinated group with a placebo group [106].

Effectiveness refers to how well a vaccine performs in the real world [107]

Relative Risk (RR) is computed by dividing the percentage of patients that contracted disease in the vaccine arm by the percentage of patients that contracted disease in the placebo arm.

Relative Risk Reduction (RRR) is computed by subtracting the RR from 1.

Absolute Risk Reduction (ARR) is computed by subtracting the percentage that contracted disease in the vaccine arm from the percentage that contracted disease in the placebo arm.

Absolute Risk = probability = incidence.

Cumulative Incidence represents the number of new cases in a period of time / population at risk.

Incidence Density is the number of new cases of a given disease during a given period in specified population; also, the rate at which new events occur in a defined population.

Immunogenicity is the ability of a molecule or substance to provoke an immune response or the strength or magnitude of an immune response. It can be a positive (wanted) or negative (unwanted) effect, depending on the context.

Immune Response is an integrated systemic response to an antigen (Ag), especially one mediated by lymphocytes and involving recognition of Ags by specific antibodies (Abs) or previously sensitized lymphocytes [108]

Safety data for Pfizer and Moderna trials:

There were two major COVID-19 inoculant clinical trials: Pfizer/BioNTech and Moderna.

The Pfizer clinical trials were titled officially "a phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of sars-cov-2 rna vaccine candidates against covid-19 in healthy individuals" [98]. The "Actual Study Start Date" was 29 April 2020, the "Estimated Primary Completion Date" was 2 November 2020, and the "Estimated Study Completion Date" is 2 May 2023. Thus, the mass inoculation rollout so far has been conducted in parallel with the Pfizer Phase III Clinical Trial. For all practical purposes, the mass global inoculation of the Pfizer inoculant recipients can be considered Phase III 2.0 of the Clinical Trials! The inclusion criteria for the official Phase III Clinical Trials incorporated (as stated in the title and in the protocol document) healthy individuals, while the criteria for mass inoculation went well beyond healthy individuals. In essence, we have an official Phase III Clinical Trial with ~43,000+ healthy individuals, and an unofficial Phase III Clinical Trial with billions of individuals covering a wide spectrum of health levels [98].

The Pfizer Phase III trials were initiated July 2020, the efficacy data were submitted to the FDA for EUA approval in November 2020, and FDA approval was granted in December 2020. Six deaths occurred in the Pfizer trial, two in the inoculated group and four in the placebo group (which received saline) [33]. The two inoculated, both over the age of 55, died of cardiovascular causes. One died three days after inoculation and the other died 62 days after inoculation [109]. These two deaths were comparable (in frequency and cause) to placebo group deaths and perhaps more importantly, similar to the general population at that age. In the case of Moderna, there were 13 deaths, six in the inoculated group, seven in the placebo group (normal saline placebo, a mixture of sodium chloride in water 0.90 % w/v) at 21–57 days after the inoculation ([103]b).

In a report by the Norwegian National Medicines Association, published on 15 January 2021, there were 23 elderly people (all over the age of 75 and frail) in nursing homes, who died at various intervals from the time of inoculation with mRNA inoculant The report then suggested that, following the assessment, 13 of the 23 deaths would have been a direct result of the side effects of inoculation. It is possible that the other 10 deaths were post-inoculation, but not directly related to side effects, so not necessarily related to the inoculant itself [109].

It is no surprise that frail elderly people can be fatally destabilized by adverse reactions associated with post-inoculation inflammation, which in a young adult would have been considered minor. It is also no surprise that frail elderly people with comorbidities can be fatally destabilized from COVID-19 infection, which in a young adult or child would have been considered minor. A frail elderly person can be fatally destabilized by a simple coughing fit! This does not mean that these deaths are not events that need to be taken very seriously; on the contrary, if confirmed, they should guide inoculation policies in this category of patients from now on. Specifically, each case should be carefully assessed and an inoculation decision made based on the risk-benefit ratio [110].

In light of these data, the question may arise as to why there were no inoculant-attributed deaths in clinical testing of inoculants. The answer is that neither Pfizer nor Moderna included frail patients and included only a small number of very elderly patients - those over 75 accounted for 4.4 % of the total tested for Pfizer and 4.1 % for Moderna. While they could not in fact determine a causal relationship between inoculation and death, they also could not rule out that the inoculations had accelerated the deterioration of the condition of those patients [33].

Effectiveness data

As defined previously, the effectiveness of a vaccine lies in its ability to prevent a particular disease. If designed, tested, and administered correctly, authorized vaccines are effective in preventing disease and protecting the population. Like medicines, vaccines are not 100 % effective in all vaccinated people. Their effectiveness in a person depends on several factors. These include: age; other possible diseases or conditions; time elapsed since vaccination; previous contact with the disease.

To be declared safe and effective, a vaccine against COVID-19 infection must pass a series of tests and must meet regulatory standards, like any other vaccine or drug approved on the pharmaceutical market [111].

Regarding Pfizer and Moderna trials:

The first important note is that maximum efficiency does not come immediately, because the immune response needs time.

In the case of Pfizer, the chance of developing COVID-19 becoming virtually the same between the inoculated and placebo groups increases up to 12 days after the first inoculation, then gradually decreases for those inoculated. The inoculum efficiency between the first and second doses is 52 % [106], but it is unclear what long-term protection a single dose provides. After the second dose, the effectiveness rises to 91 % and only beyond 7 days after the second dose is 95 % reached. However, the ARR for the latter case is only 0.7 % [112]. In other words, within 12 days after the first dose we can get COVID-19 as if we had not been inoculated. Another important aspect is that we still do not know if the Pfizer inoculant prevents severe cases. Seven days after the second dose, there were four severe cases of COVID-19, one in the inoculated group and three in the placebo group, which is far too low for us to make a statistical assessment. There are as yet no data on the inoculant's ability to prevent community transmission. Realistically, the effectiveness of the inoculant in preventing asymptomatic cases has not been tested.

For Moderna, the effectiveness is only 50 % in the first 14 days after the first dose and reaches a maximum of 92.1 % on the edge of the second dose (ARR of 1.1 %, which is 28 days, not 21 as in the case of Pfizer) [46]. Moderna also did not test the long-term efficacy of a single dose. Then, 14 days after the second dose, the effectiveness rises to 94.1 %, with the amendment being an average. Thus, in people over 65 it was 86.4 %, compared to 95.6 % in the 18–65 age range ([103]). It is a minor difference from Pfizer, which declares equal efficiency in all age groups. An important observation is the statement by Moderna that their inoculant prevents severe cases, but only more than 14 days after both doses [126]. All 30 severe cases were in the placebo group, suggesting 100 % efficacy. After a single dose, there were two severe cases among those inoculated and four in the placebo group [33]. Last, but not least, unlike Pfizer, Moderna tested the presence of asymptomatic infection by RT-PCR before the second dose: there were 39 asymptomatic cases in the placebo group and 15 in the inoculated group. It is difficult to draw definitive conclusions due to the small number of cases. These data suggest that the inoculant reduces, but does not prevent, asymptomatic transmission [126].

A2-b Ongoing Clinical Trials in the Pediatric Population

In a recent Phase III study performed in the pediatric population, Comirnaty (Pfizer) was tested on a group of 2,260 children, aged 12–15, years who had no previous clinical signs of SARS-CoV-2 infection. They were divided into two groups, one placebo (978 children) and the other with Comirnaty (1005 children). In the Comirnaty group, of the 1005 children in whom the serum was administered, none developed COVID-19 disease,

compared with the placebo group in which 16 children in 978 had clinical signs of the disease. The Pfizer study showed that the children's immune response was comparable to the immune response in the 16–25 age group (measured by the level of antibodies against SARS-CoV-2). It could be concluded that in this study, Comirnaty was 100 % effective in preventing SARS-CoV-2 infection, although the actual rate could be between 75 % and 100 %. [63]. The results will be evaluated by the FDA and EMA.

The predictive value (for mass inoculation results) of the Comirnaty trial for the children aged 12–15 years is questionable. There were 1005 children who were inoculated with Comirnaty. Using the rule of three in statistics, where to obtain a predictive result of 1/x with high confidence (e.g., 1 in a thousand), 3x participants are required for the test sample. For the Comirnaty test sample of 1005, an adverse event of about 1/340 could be detected with high confidence.

What does this mean in the real world? In the USA, there are approximately 4,000,000 children in each age year for adolescents. Thus, there are 16,000,000 children in the 12–15 age band. A serious adverse event, including death, that occurred at a 1/800 rate would not be detectable with high confidence in a sample of 1005 people. Thus, the results of the trials for 1005 children would allow for 20,000 children to suffer a non-trial-detected serious adverse event, including death, when extrapolated to potential inoculation of all children in the 12–15 age group! Given that the risk of contracting COVID-19 with serious outcomes is negligible in this population, ***proceeding with mass inoculation of children 12–15 years old based on the trials that were conducted cannot be justified on any cost-benefit ratio findings***.

Also, the evaluation of efficacy in children aged 6 months to 11 years has recently begun and continues [24]. Pfizer began enrolling children under 12 to evaluate the COVID-19 mRNA inoculant. Also, Comirnaty will be evaluated in a new clinical trial for children aged 6 months to 11 years. In the first phase, the study will enroll 144 people and will identify the required dose for 3 age groups (6 months - 2 years, 2–5 years and 5–11 years). After a 6-month follow-up period, the parents/guardians of children in the placebo group will have the option of allowing their children to receive the inoculation. The results are expected in the second half of 2021.

Moderna also began a study to evaluate the mRNA inoculation in children aged 6 months to 12 years. Both companies have already started testing vaccines in 14-year-olds. In the US, children make up 23 % of the population [113].

Data on the risks and benefits of possible inoculation in children and adolescents are currently insufficient and no recommendation can be made. Specifically, mass child inoculations cannot be recommended until the benefits and minimal projected risks have been demonstrated in a sufficiently large trial to provide confidence that mass inoculation will have an acceptable level of adverse effects relative to the demonstrated benefits. On the other hand, children often experience COVID-19 asymptomatically, and the SARS-CoV-2 infection progresses harmlessly. Currently, in the context of limited inoculation capacities, there is no indication of urgent inoculation of children. In the context of declining incidences of SARS-CoV-2 infections and demonstrated low serious adverse effects from COVID-19 infections for children and adolescents, the issue of inoculating children and adolescents is no longer paramount. Authorized forums must calculate what prevails for children and adolescents: the benefits or risks.

A2-c Clinical Trial Issues for Other Categories

Although people with severe comorbidities such as obesity or oncological conditions were not initially included in the clinical trials that led to obtaining EUA, they were included in subsequent studies, some even ongoing. In their case, it seems that the efficacy was lower compared to the results obtained initially with healthy adults.

The interim analysis of data from a prospective observational study indicates the need to prioritize cancer patients for timely (respectively 21-day) booster administration in the case of administration against COVID-19 with Comirnaty. According to the study, the effectiveness of a single dose of Comirnaty among cancer patients is low, but the immunogenicity of patients with solid cancers increased at 2 weeks after receiving the second dose of inoculant 21 days after the first dose. Because the study was conducted in the UK, participants inoculated before December 29, 2020 received two doses of Comirnaty 21 days apart, and those who started the regimen after this date were scheduled to receive a second dose of Comirnaty 12 weeks apart. first administration. Thus, the study continues to collect data from participants receiving Comirnaty 12 weeks after the first dose.

Approximately 21 days after a single dose of Comirnaty, the proportion of study participants who tested positive for anti-S IgG antibodies was [114]:

94 % among healthy participants;

38 % among patients with solid cancers;

18 % among patients with hematological cancers.

Among participants who received the 21-day booster and for whom biological samples were available two weeks after the second dose, the following proportions of confirmation as seropositive for anti-S IgG antibodies were reported [114].

100 % of healthy participants, compared to 86 % of the same group of participants who did not receive the second dose;

95 % of patients with solid cancers, compared with 30 % of the same group of participants who did not receive the second dose;

60 % of patients with hematological cancers, compared with 11 % of the same group of participants who did not receive the second dose.

Two other studies suggest low immunogenicity in the context of Comirnaty administration in patients with hematological cancers. In one study, patients with chronic lymphocytic leukemia (CLL) had significantly reduced immune response rates to COVID-19 inoculation compared to healthy participants of the same age. Considerable variations in post-administration immune response have been reported among patients with CLL depending on their stage of treatment

The effectiveness of Comirnaty administration was also evaluated in elderly patients with multiple myeloma [115]. 21 days after administration of the first dose of Comirnaty inoculation (before receiving the second dose), 20.5 % of patients with multiple myeloma compared to 32.5 % of control participants had neutralizing antibodies against SARS-CoV-2. One possible explanation could be that the therapy negatively affects the production of antibodies. However, the administration of the second dose is important for the development of the immune response in these patients [115].

Preliminary data from the v-safe surveillance system, the v-safe pregnancy registry and the Vaccine Adverse Event Reporting System (VAERS) do not indicate obvious safety signals regarding pregnancy or the associated neonatal implications with mRNA injections against COVID-19 *in the third trimester of pregnancy* [3]. The study included 35,691 pregnant women [116]. Compared to non-pregnant women, pregnant women reported more frequent pain at the injection site as an adverse event associated with mRNA COVID-19 vaccination, and headache, myalgia, chills, and fever were reported less frequently. In the context where initial clinical trials of messenger RNA-based inoculants have not evaluated the efficacy and safety of innovative technology among pregnant women, these preliminary data *from the third trimester only* help to inform both pregnant women and health professionals in making the inoculation decision. However, continuous monitoring through large-scale longitudinal studies remains necessary to investigate the effects associated with maternal anti-COVID-19 inoculation on mothers, pregnancies, the neonatal period and childhood.

On the other hand, the inoculation landscape has become even more complex due to new circulating viral variants. Authorities recommend genomic surveillance and adaptation in order to be effective against new variants (different from the initial strain that was detected at the end of 2019). The efficacy data of Comirnaty against circulating viral variants are highlighted in a very recent study in Israel which showed that the protection offered by the Pfizer inoculant against variant B.1.351 (first identified in South Africa) is lower [112].

The results have not yet been submitted to the expertise of specialists. The study compared nearly 400 adults who were diagnosed with COVID-19 at least 14 days after receiving one or two doses of the inoculant to the same number of uninoculated people. It was found that B.1.351 represents approximately 1 % of the COVID-19 cases studied. But among patients who received two doses of inoculant, the prevalence rate of the variant was eight times higher than in those not inoculated - 5.4 % compared to 0.7 %. This suggests that Comirnaty is less effective against variant B.1.351, compared to the original variant and variant B.1.1.7. The limitation of the study comes from the small number of adult people studied, but it is an alarm signal for a closer study of these cases. In addition, it seems that at present, the prevalence of this variant is low. On the other hand, in early April, Pfizer announced that according to the results of the Phase III study in the adult population, Comirnaty also demonstrated 100 % efficacy in the prevention of Covid-19 disease caused by SARS-CoV-2 variant B.1.351 (9 cases of Covid-19 were recorded, all in the placebo group, and after sequencing it was found that 6 had been determined by B.1.351) [117].

Appendix C

MID- AND LONG-TERM ADVERSE EFFECTS FROM PRIOR VACCINES

A 2020 study emphasizing mid- and long-term adverse effects from prior vaccines [4] identified the following sixteen mid- and longer-term potential issues concerning vaccines. These include:

3.1. Antibody-Dependent Enhancement (where enhanced virus entry and replication in a number of cell types is enabled by antibodies);

-1a. *Intrinsic Antibody-Dependent Enhancement* (where non-neutralizing antibodies raised by natural infection with one virus may enhance infection with a different virus);

-1b. *Immune Enhancement* (enhancement of secondary infections via immune interactions);

-1c. *Cross-Reactivity* (an antibody raised against one specific antigen has a competing high affinity toward a different antigen.);

-1d. *Cross-Infection Enhancement* (infection enhancement of one virus by antibodies from another virus);

3. 2. Vaccine-Associated Virus Interference (where vaccinated individuals may be at increased risk for other respiratory viruses because they do not receive the non-specific immunity associated with natural infection);

3. *Vaccine-Associated Imprinting Reduction* (where vaccinations could also reduce the benefits of 'imprinting', a protection conferred upon children who experienced infection at an early age)

4. *Non-Specific Vaccine Effects on Immune System* (where previous infections can alter an individual's susceptibility to unrelated diseases);

5. *Impact of Infection Route on Immune System* (where immune protection can be influenced by the route of exposure/delivery);

6. *Impact of Combinations of Toxic Stimuli* (where people are exposed over their lifetime to myriad toxic stimuli that may impact the influence of any vaccine);

7. *Antigenic Distance Hypothesis* (negative interference from prior season's influenza vaccine (v1) on the current season's vaccine (v2) protection may occur when the antigenic distance is small between v1 and v2 ($v1 \approx v2$) but large between v1 and the current epidemic (e) strain ($v1 \neq e$).);

8. *Bystander Activation* (activation of T cells specific for an antigen X during an immune response against antigen Y);

9. *Gut Microbiota* (Impact of gut microbial composition on vaccine response);

10. *Homologous Challenge Infection Enhancement* (the strain of challenge virus used in the testing assay is very closely related to the seed virus strain used to produce the vaccine that a subject received);

11. *Immune Evasion* (evasion of host response to viral infection);

12. *Immune Interference* (interference from circulating antibody to the vaccine virus);

-12a. *Original Antigenic Sin* (propensity of the body's immune system to preferentially utilize immunological memory based on a previous infection when a second slightly different version of that foreign entity (e.g. a virus or bacterium) is encountered.);

13. *Prior Influenza Infection/Vaccination* (effects of prior influenza infection/vaccination on severity of future disease symptoms);

14. *Timing between Viral Exposures* (elapsed time between viral exposures);

15. *Vaccine-Associated Enhanced Respiratory Disease* (where vaccination enhances respiratory disease); and

16. *Chronic Immune Activation* (continuous innate immune responses).

Most of these events are not predictable, and most, if not all, would be possible for the COVID-19 inoculant in the mid- and long-term for adults and children.

3.3. Mid- and Long-Term Serious Illnesses for Adults and Children from Past Vaccines

As stated in the aforementioned 2020 study on vaccine safety: "The biomedical literature is very sparse with studies on long-term vaccine effects, especially long-term adverse effects. Large numbers of people and long periods of time are required to identify such adverse events, and draw statistically-valid connections between vaccinations and disease. These efforts would be very resource-intensive, and there appears to be little motivation among the vaccine producers and regulators to make these resources available for such studies. Thus, the following examples reflect the extremely small tip of an extremely large iceberg of long-term adverse vaccine effects." [4]

"The two main categories of diseases reported in the biomedical literature triggered by past vaccinations are "Autoimmune (e.g., Systemic Lupus Erythematosus, Psoriasis, Arthritis, Multiple Sclerosis, Hepatitis, Uveitis, Pseudolymphoma, Guillain-Barre Syndrome, Thrombocytopenic Purpura, etc.) and Neurological (e.g., Central Demyelinating Diseases, Developmental Disability, Febrile seizures, Narcolepsy, Encephalomyelitis, Autonomic Dysfunction, etc.). Others include Diabetes, Gastrointestinal, Joint-related, Necrobiotic Granuloma, Neutropenia, Pulmonary Fibrosis, etc."

"Vaccinations may also contribute to the mosaic of autoimmunity [118]. Infrequently reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barre syndrome, and vasculitis".

"Studies have demonstrated a latency period of years between HiB vaccination and diabetes mellitus, and between HBV vaccination and demyelinating events [118] latency periods can range from days to years for postinfection and postvaccination autoimmunity".

"Most of the extra cases of IDDM appeared in statistically significant clusters that occurred in periods starting approximately 38 months after

immunization and lasting approximately 6–8 months. Immunization with pediatric vaccines increased the risk of insulin diabetes in NOD mice. Exposure to HiB immunization is associated with an increased risk of IDDM." [4]

Thus, even the sparse past vaccine studies that went beyond the short-term showed latency effects of serious diseases occurring ***three years or more*** post-vaccination.

Appendix D

COST-BENEFIT ANALYSIS OF COVID-19 INOCULATIONS

This appendix presents a non-traditional *best-case scenario* pseudo-cost-benefit analysis of the COVID-19 inoculations for the 65+ demographic in the USA. In this incarnation of a cost-benefit analysis, the costs are the number of deaths resulting from the inoculations, and the benefits are the lives saved by the inoculations. The time range used was from December 2019 to end-of-May 2021.

It is assumed, in this best-case scenario, that all the deaths truly attributable to COVID-19 only could have been eliminated by the inoculations given (about half the USA population has been inoculated at this time) [88,119]. It can be conceptualized as the vaccines having been available in Summer 2019, and subsequent administration having eliminated all the deaths experienced that were truly attributable to COVID-19. If the cost-benefit ratio is ***poor*** for this *best-case scenario*, it will be ***very poor*** for any real-world scenario [120].

We will use Figs. 1 and 2 as starting points to conduct a cost-benefit analysis of COVID-19 inoculations for the most vulnerable demographic, those 65 + . We start with the official government numbers for COVID-19 and post-inoculation deaths, and modify them to arrive at actual deaths resulting from COVID-19 and the inoculations. We compare the two numbers (appropriately normalized) to ascertain costs vs benefits .

As Fig. 1 shows, there are three age bands that comprise the 65+ demographic. We weight the COVID-19 deaths per capita in each band by the band's population, and divide the sum of these three products by the total 65+ population to arrive at an average COVID-19 deaths per capita of 0.0087 for the total 65+ demographic.

Fig. 2 contains two normalizations. First, the deaths were normalized by total inoculations given, not by people inoculated or people who had completed the full series of inoculations. We will retain the normalization by total inoculations given, since it will provide the ***most conservative results*** (largest denominator) for estimation purposes. Second, the deaths were normalized/restricted to those occurring within seven days post-inoculation. This normalization was done to compare across age bands, where the inoculations started at very different points in time. For the present cost-benefit purpose, where we are concentrating on the 65+ band, we remove this latter normalization, and include all post-inoculation deaths. Removing this normalization increases deaths per inoculation by about 40 % to a value of 0.000032, and offers a more credible comparison to the numbers from Fig. 1.

Thus, based on the CDC's official numbers, there are an average COVID-19 deaths per capita of 0.0087 and an average deaths per inoculation of 0.000032 for the 65+ demographic. The chances of a person 65+ dying from an inoculation relative to their chances of dying from COVID-19 are approximately 0.0037, or about 1/270, based on these official CDC figures.

However, as we have shown previously, three corrections to these numbers are required to convert them to real-world effects. First, as the Harvard Pilgrim study has shown and as our results in Appendix 1 confirm, VAERS is underreporting actual deaths by about two orders of magnitude. Applying this correction alone to the above 1/270 ratio changes the risk benefit to about 1/3., Second, as the CDC has stated, approximately 94 % of the COVID-19 deaths could have been attributed to any of the comorbidities these patients had, and only 6% of the deaths could actually be attributed to COVID-19. As we pointed out, if pre-clinical comorbidities had been included, this number of 6% would probably be decreased further. For ***conservative*** purposes, we will remain with the 6%. Applying this correction to the 1/3 risk-benefit ratio changes it to 5/1! Third, as a comprehensive survey of false positives from RT-PCR tests concluded: "evidence from external quality assessments and real-world data indicate enough a high enough false positive rate to make positive results highly unreliable over a broad range of scenarios" [127]. Because of the myriad RT-PCR tests performed in the USA to screen for/diagnose COVID-19 using different values for Ct and different procedures, a specific number for false positives cannot be obtained at this point in time. Again, these false positives would reduce the 6% number, perhaps substantially. And again, for ***conservative*** purposes, we will remain with the 6% number.

Thus, our ***extremely conservative*** estimate for risk-benefit ratio is about 5/1. In plain English, people in the 65+ demographic are five times as likely to die from the inoculation as from COVID-19 under the most favorable assumptions! This demographic is the most vulnerable to adverse effects from COVID-19. As the age demographics go below about 35 years old, the chances of death from COVID-19 become very small, and when they go below 18, become negligible.

It should be remembered that the deaths from the inoculations shown in VAERS are short-term only (six months for those inoculated initially), and for children, extremely short-term (one month) [3]. Intermediate and long-term deaths remain to be identified, and are possible from ADE, auto-immune effects, further clotting and vascular diseases, etc., that take time to develop. Thus, the long-term cost-benefit ratio under the *best-case scenario* could well be on the order of 10/1, 20/1, or more for all the demographics, increasing with decreasing age, and an order-of-magnitude higher under real-world scenarios! In summary, the value of these COVID-19 inoculations is not obvious from a cost-benefit perspective for the most vulnerable age demographic, and is not obvious from any perspective for the least vulnerable age demographic.

Appendix Da

PROBLEMS WITH TEST CRITERIA FOR DETERMINING COVID-19

Consider the criteria for determining whether an RT-PCR test result is positive for SARS-CoV-2. The CDC instruction (until 1 May 2021) specifies running the RT-PCR tests for 45 amplification cycles. Then, to interpret the data: when all controls exhibit the expected performance, a specimen is considered positive for SARS-CoV-2 if all SARS-CoV-2 marker (N1, N2) cycle threshold growth curves cross the threshold line within 40.00 cycles (< 40.00 Ct). The RNase P may or may not be positive as described above, but the SARS-CoV-2 result is still valid ([103]a).

Many false positives are possible in the upper part of this cycle threshold range, especially in areas of low prevalence. In particular, virus culture has been found to be unfeasible in cases with a Ct value exceeding 33. A prospective cohort study involving the first 100 COVID-19 patients in Singapore also showed that attempts to culture the virus failed in all PCR-positive samples with a Ct value >30" [121]. During mass testing in Germany, it was found "that more than half of individuals with positive PCR test results are unlikely to have been infectious" [122]. Another study

found that tests with low specificity (deriving from use of many cycles) cannot provide strong evidence for the presence of an infection [123]. A systematic review of PCR testing concluded "Complete live viruses are necessary for transmission, not the fragments identified by PCR. Prospective routine testing of reference and culture specimens and their relationship to symptoms, signs and patient co-factors should be used to define the reliability of PCR for assessing infectious potential. Those with high cycle threshold are unlikely to have infectious potential." [89].

As skeptics have argued, in the buildup of the pandemic, the rapid increase in numbers of COVID-19 cases was due in part to the high values of cycle threshold used in the tests. Unfortunately, the true numbers of false positives will probably be unobtainable if an audit were performed, since these values are not reported with the test results: all currently-available nucleic acid tests for SARS-CoV-2 are FDA-authorized as qualitative tests, and Ct values from qualitative tests should never be used to direct or inform patient management decisions. Therefore, it is not good for laboratories to include Ct values on patient reports [124].

After mass inoculations started, a large number of "breakthrough" cases emerged, and a total of 10,262 SARS-CoV-2 vaccine breakthrough infections had been reported from 46 U.S. states and territories as of April 30, 2021 [18]; the number of reported COVID-19 vaccine breakthrough cases is likely a substantial undercount of all SARS-CoV-2 infections among fully vaccinated persons. The national surveillance system relies on passive and voluntary reporting, and data might not be complete or representative. Many persons with vaccine breakthrough infections, especially those who are asymptomatic or who experience mild illness, might not seek testing [18].

This negative outcome of increased "breakthrough" cases motivated the CDC to change a number of reporting and test procedures and issue new regulations for identifying and investigating hospitalized or fatal vaccine breakthrough cases starting 1 May 2021, stating: "For cases with a known RT-PCR cycle threshold (Ct) value, submit only specimens with Ct value $\leq$28 to CDC for sequencing. (Sequencing is not feasible with higher Ct values.)". Thus, the Ct values for sequencing were lowered from the high false positive range allowed during the pandemic buildup to a limit that would eliminate many of these false positives in the 'breakthrough case' identification phase [101].

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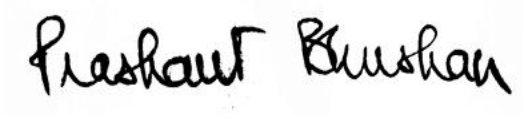

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COVID-19 herd immunity by immunisation: are children in the herd?

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The scourge of COVID-19 has been global, but the most affected subgroups in the population have largely been older people and individuals with comorbid conditions that predispose them to increasingly severe disease and poor outcomes. Overall, the disease burden in children has been reasonably mild, even in those with comorbidities, such as oncological conditions. Protection from severe disease in children might be related to a lower expression of host factors required for viral replication, and to differences in the magnitude and timing of innate or adaptive immune responses. Data for recorded COVID-19 cases show that only 7% of children younger than 18 years with severe disease required intensive care, whereas 53% of adults who had severe disease required intensive care.[1–3] Multisystem inflammatory syndrome in children, arguably the most dreaded presentation, typically presents between 3 and 6 weeks after SARS-CoV-2 exposure.[4] Most patients at presentation have a negative nasopharyngeal RT-PCR but are positive for serology. This temporal association and low PCR positivity rate suggest a postinfectious mechanism rather than acute viral infection. Children of African or Hispanic race or ethnicity are more frequently affected, whereas children of Asian or White race or ethnicity appear to be less often affected,[5,6] and genetic susceptibility might account for this over-representation. The reasonably low incidence of COVID-19 in the general population of children, the unusual manifestation with multisystem inflammatory syndrome in older children and adolescents, and the absence of epidemiological data that incriminates children in the transmission of SARS-CoV-2, pose important immunological, ethical, and economic conundrums that require careful examination before the deployment of any COVID-19 vaccine in children.

The following clinical observations are relevant for formulating COVID-19 vaccines for deployment in children.

First, from an immunological perspective, the milder spectrum of disease in children might correlate with SARS-CoV-2 antigen processing and immunopathogenesis in children. Few immunological studies in children with multisystem inflammatory syndrome report abnormal immunophenotypes of plasmablasts,[7,8] elevated SARS-CoV-2 IgG, and proinflammatory cytokines.[8] Current vaccines that are authorised for emergency use, approved or in development, do not have a safety or immunogenicity profile in children. In the absence of a better understanding of the pathogenesis of this condition, using the same approach for delivering vaccines as in adults could exacerbate the incidence of this hyperinflammatory condition.

Second, from a public health perspective, it will be necessary to immunise children if they are a major source of SARS-CoV-2 transmission and if the candidate vaccines block transmission. However, epidemiological reports up to now suggest that young children have a high likelihood of developing COVID-19 via household transmission, once a family member tests positive for COVID-19.[1] There is little evidence of secondary infection from children to others in the transmission pathways of COVID-19. Although emerging data suggest that some candidate vaccines can block transmission, vaccinating children cannot be justified if it is to give direct protection despite minimal burden of disease or to help to block transmission if children do not constitute a substantial reservoir for transmission. For other infections that can be prevented by vaccine, such as invasive pneumococcal disease, immunisation of children not only prevented infections in children, but also conferred indirect benefit by decreasing disease in older people, because of its effect on carriage reduction and blockage of transmission.[9] For COVID-19, the reverse might be the case, with adults having to be vaccinated to confer protection on young children.

Third, from an ethical perspective, there is a balance between risk and benefit in offering a COVID-19 vaccine to children that will offer minimal or no direct benefit to the recipient, no benefit to the public, and as yet, unknown medium-term and long-term risks to the recipient. Other important considerations include the economic and practical considerations in deploying a new vaccine into the routine childhood immunisation programmes. Without additional data and public enlightenment on the benefits of immunising young

children, this deployment could further threaten childhood immunisation coverage that is already precariously low in several settings.

Finally, because individuals are not equally susceptible and contagious, our current target to vaccinate 65–70% of the population to archive herd immunity might be an overestimate.[10] If young children are excluded, there will be more vaccines available for the more epidemiologically susceptible subgroups. Initiating efficacy trials in youths aged 12–18 years is a welcome development, but a new strategy might ultimately be required for immunising younger children, should this become necessary.

I declare no competing interests.

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Vaccine development lessons between HIV and COVID-19

The SARS-CoV-2 pandemic has many parallels to the early days of the HIV epidemic. Both began with efforts to identify the causative pathogen, followed by rapid development of diagnostics, animal models, therapeutics, and preventive vaccines. After targeting of the gp120 and gp160 HIV envelope proteins proved ineffective, development of candidate vaccines to prevent HIV expanded to encompass DNA and viral vector vaccines, with the intent of inducing both humoral and cellular immunity. In recent years, mRNA has been harnessed as a newer platform for the development of candidate HIV vaccines.[1] Advancing the evidence from HIV vaccines, research supporting vaccines against other pathogens has also influenced SARS-CoV-2 vaccine design, including structure-based design of stabilised epitope-scaffold proteins for respiratory syncytial virus,[2] DNA vaccines for MERS-CoV,[3] and ongoing global molecular surveillance for the design of influenza vaccines.[4] Collectively, the knowledge gained through these preclinical, manufacturing, and clinical development experiences has allowed for a rapid pivot to apply these approaches to SARS-CoV-2 vaccine research. The success of several large efficacy trials of HIV candidate vaccines has been used to advance SARS-CoV-2 vaccine research and development via existing public–private partnerships and networks such as the HIV Vaccine Trials Network and their established connections with local investigators and community advocates.

The most noteworthy difference between responses to SARS-CoV-2 and HIV is the time to authorisation and rollout of effective preventive vaccines. Emergency use authorisation of initial vaccines against COVID-19 was granted by the US Food and Drug Administration and European Medicines Agency less than 1 year after initial publication of the genetic sequence of SARS-CoV-2. By stark contrast, after more than 30 years of research, only six efficacy trials of candidate HIV vaccines have been completed,[5] of which only one showed partial efficacy in preventing acquisition of new HIV-1 infection (risk lowered by 31%).[6] Much of this discrepancy is due to inherent biological differences between HIV and coronaviruses, such as HIV's substantially higher mutation rate due to reverse transcription and evasion of immune responses after HIV integration into the host genome. Nonetheless, there is much that can be learned

Prashant Bhushan
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ORIGINAL ARTICLE

Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel

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ABSTRACT

BACKGROUND

Approximately 5.1 million Israelis had been fully immunized against coronavirus disease 2019 (Covid-19) after receiving two doses of the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) by May 31, 2021. After early reports of myocarditis during adverse events monitoring, the Israeli Ministry of Health initiated active surveillance.

METHODS

We retrospectively reviewed data obtained from December 20, 2020, to May 31, 2021, regarding all cases of myocarditis and categorized the information using the Brighton Collaboration definition. We analyzed the occurrence of myocarditis by computing the risk difference for the comparison of the incidence after the first and second vaccine doses (21 days apart); by calculating the standardized incidence ratio of the observed-to-expected incidence within 21 days after the first dose and 30 days after the second dose, independent of certainty of diagnosis; and by calculating the rate ratio 30 days after the second dose as compared with unvaccinated persons.

RESULTS

Among 304 persons with symptoms of myocarditis, 21 had received an alternative diagnosis. Of the remaining 283 cases, 142 occurred after receipt of the BNT162b2 vaccine; of these cases, 136 diagnoses were definitive or probable. The clinical presentation was judged to be mild in 129 recipients (95%); one fulminant case was fatal. The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95% CI, 8.11 to 19.46). As compared with the expected incidence based on historical data, the standardized incidence ratio was 5.34 (95% CI, 4.48 to 6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20). The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.

CONCLUSIONS

The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.

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After the emergency use authorization of the BNT162b2 messenger RNA (mRNA) vaccine (Pfizer–BioNTech) against coronavirus disease 2019 (Covid-19) by the Food and Drug Administration,[1] authorization was also granted for use in Israel. On December 20, 2020, a national vaccination campaign was initiated that was based on a two-dose regimen spaced 21 days apart.[2] The campaign initially targeted health care workers and persons who were 60 years of age or older, and later the vaccine was offered to all persons who were at least 16 years of age. By May 31, 2021, approximately 5.12 million Israeli residents had received two vaccine doses.

At the beginning of the vaccination campaign, a program of passive surveillance was initiated for the monitoring of adverse events within 21 days after the first dose of vaccine and within 30 days after the second dose. Health care providers reported these data to the Ministry of Health, as required by Israeli law. After receipt of reports of myocarditis, the Ministry of Health subsequently initiated active surveillance beginning in February 2021 by requesting that all hospitals report cases of myocarditis, including cases that had been diagnosed since December 2020, with or without pericardial effusion and regardless of vaccination status. Since persons with suspected myocarditis are almost always hospitalized in Israel, such surveillance data should approximate all cases of myocarditis during the period of active surveillance.

The aims of the current study were to present the clinical and epidemiologic characteristics and follow-up findings of cases of myocarditis that were diagnosed in temporal proximity to vaccination and to examine a possible causal relationship between the vaccine and myocarditis.

Methods

Data Source and Case Definition

We retrospectively reviewed data regarding presumptive cases of myocarditis, including clinical and laboratory data and discharge summaries, from medical records obtained from the Ministry of Health database. The focus of the study was the 6 months from December 2020 through May 2021, which included periods of both active and passive surveillance. We used the codes for myocarditis (422.0-9x and 429.0x) of the *International Classification of Diseases, 9th Revision* (ICD-9), for screening. Records were reviewed by one of four board-certified cardiologists, with advice from a board-certified rheumatologist for verification of the diagnosis of myocarditis. All the reviewers were aware of the vaccination status of the patients.

The diagnostic criteria for myocarditis and degree of certainty of diagnosis were adapted from the case definition and classification of the Brighton Collaboration (Pandemic Emergency Response Process).[3] Cases were classified as definitive, probable, possible, having insufficient data, or having an alternative diagnosis. Cases of pericarditis with myocarditis were included among these cases, although pericarditis alone was not included in case counts. We also compared the classification according to the Brighton Collaboration with classifications of myocarditis issued by the Centers for Disease Control and Prevention (CDC) for adverse events after smallpox vaccination.[4-6] Additional details regarding the two classification systems are provided in the Methods section and Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Since the study was conducted as part of ongoing clinical surveillance for side effects related to the BNT162b2 vaccine as required by national guidelines, it received a waiver for review by an institutional review board. Pfizer–BioNTech had no role in the collection or analysis of the data or in the reporting of the data in this study.

Statistical Analysis

We used descriptive frequencies, percentages, means, and standard deviations to characterize cases of myocarditis according to age, sex, time elapsed since vaccination, length of hospital stay, and clinical outcome. Incidence curves were examined for the occurrence of new cases of myocarditis during the first 21 days after the first dose of vaccine and 30 days after the second dose, since passive surveillance had usually been terminated at that point. The data were analyzed separately for males and females and according to age group (16 to 19 years, 20 to 24 years, 25 to 29 years, 30 to 39 years, 40 to 49 years, and 50 years or older). To assess the incidence of myocarditis among vaccine recipients, we calculated risk differences, observed-to-expected ratios, and rate ratios between vaccinated and unvaccinated persons.

To calculate the risk difference, we determined the risk of myocarditis per 100,000 persons after

Table 1. Reported Myocarditis Cases, According to Timing of First or Second Vaccine Dose.*

Timing	First Vaccine Dose			Second Vaccine Dose			Both Doses
	No. of Vaccinations	Myocarditis Cases	Males/ Females	No. of Vaccinations	Myocarditis Cases	Males/ Females	Myocarditis Cases
Six-month study period	5,442,696	19	17/2	5,125,635	117	101/16	136
December 2020	987,013	0	0/0	0	0	0/0	0
January 2021	2,109,854	4	3/1	1,844,896	13	12/1	17
February 2021	1,613,909	6	5/1	1,546,184	47	41/6	53
March 2021	528,069	7	7/0	1,397,609	44	38/6	51
April 2021	152,765	1	1/0	253,701	13	10/3	14
May 2021	51,086	1	1/0	83,245	0	0	1

* Data are from medical records, including clinical and laboratory data and discharge summaries, from the Ministry of Health database from December 2020 through May 2021, according to the codes for myocarditis used in the *International Classification of Diseases, 9th Revision*. Cases of myocarditis were reported within 21 days after the first dose of vaccine and 30 days after the second dose. All cases were clinically reviewed, and only definite or probable cases are shown.

the first and second doses of vaccine according to age group and sex. This analysis included only the probable or definite myocarditis cases. In the calculation of the risk differences between the second and first doses, we used the cumulative incidence for a follow-up period of 21 days for both vaccine doses; we computed 95% confidence intervals for the risk difference using the Jeffreys–Perks method. The percentage of the myocarditis risk that could be attributed to the second dose was calculated by dividing the risk difference between the two vaccine doses by the risk after the second dose and expressing the quotient as a percentage.

We compared the observed incidence of myocarditis with the expected incidence using data obtained during the period from 2017 through 2019 in the pre–Covid-19 pandemic era by calculating standardized incidence ratios (after adjustment for age and sex) for all reported cases of myocarditis. We performed this analysis in all myocarditis cases that had occurred in temporal proximity to the vaccination without accounting for the adjudicated category of certainty, because historical cases of myocarditis had not been adjudicated by a team of clinical experts. We calculated approximate 95% confidence intervals for the true standardized incidence ratio by applying the Wilson and Hilferty approximation for chi-square percentiles.[7] In addition, to determine whether the standardized incidence ratios could have been overestimated owing to the overreporting of myocarditis cases because of a higher index of clinical suspicion during the surveillance period, we performed a sensitivity analysis in which we determined the minimal number of observed cases that would be needed to produce a significant difference in the standardized incidence ratios for male recipients after the second vaccine dose. This subgroup was chosen post hoc according to the apparent increase in risk observed in male teenagers and young adults.

We compared the incidence of myocarditis among recipients 30 days after the second vaccine dose with the incidence among unvaccinated persons starting on January 11, 2021 (when second vaccine doses were first administered in Israel) up to May 31, 2021, with data reported according to age group and sex. We computed the rate ratio between vaccinated and unvaccinated persons and 95% confidence intervals for each stratum and for the overall study population after adjustment

Table 2. Classification of Myocarditis Cases Reported to the Ministry of Health.*

Timing of Myocarditis Diagnosis	Brighton Collaboration Classification of Myocarditis					
	Level 1	Level 2	Level 3	Level 4	Level 5	All Levels
	number of cases					
All cases	118	153	3	9	21	304
Vaccinated persons						
≤21 days after first dose and 30 days after second dose	55	81	1	5	9	151
>21 days after first dose and 30 days after second dose	15	23	0	2	5	45
Unvaccinated persons	48	49	2	2	7	108

* In the Brighton Collaboration classification system for the diagnosis of myocarditis, level 1 indicates definite, level 2 probable, level 3 possible, level 4 insufficient data, and level 5 ruled out. Included are data for persons who had a delayed second dose of vaccine and who received a diagnosis of myocarditis 22 days or longer after the first dose and those in whom myocarditis developed more than 30 days after the second dose, so the diagnosis was not considered to have been made in temporal proximity to vaccination.

for age and sex using a negative binomial regression model. This analysis included only definite or probable myocarditis cases (Fig. S1).

Since we had no prespecified plan for adjustment of the width of confidence intervals for multiple comparisons in any of these approaches, no definite conclusions can be drawn from these data. We also assessed our findings according to the Bradford Hill causality criteria.

RESULTS

CASES OF MYOCARDITIS

Among 9,289,765 Israeli residents who were included during the surveillance period, 5,442,696 received a first vaccine dose and 5,125,635 received two doses (Table 1 and Fig. S2). A total of 304 cases of myocarditis (as defined by the ICD-9 codes for myocarditis) were reported to the Ministry of Health (Table 2). These cases were diagnosed in 196 persons who had received two doses of the vaccine: 151 persons within 21 days after the first dose and 30 days after the second dose and 45 persons in the period after 21 days and 30 days, respectively. (Persons in whom myocarditis developed 22 days or more after the first dose of vaccine or more than 30 days after the second dose were considered to have myocarditis that was not in temporal proximity to the vaccine.) After a detailed review of the case histories, we ruled out 21 cases because of reasonable alternative diagnoses. Thus, the diagnosis of myocarditis was affirmed for 283 cases. These cases included 142 among vaccinated persons within 21 days after the first dose and 30 days after the second dose, 40 among vaccinated persons not in proximity to vaccination, and 101 among unvaccinated persons. Among the unvaccinated persons, 29 cases of myocarditis were diagnosed in those with confirmed Covid-19 and 72 in those without a confirmed diagnosis.

Of the 142 persons in whom myocarditis developed within 21 days after the first dose of vaccine or within 30 days after the second dose, 136 received a diagnosis of definite or probable myocarditis, 1 received a diagnosis of possible myocarditis, and 5 had insufficient data. Classification of cases according to the definition of myocarditis used by the CDC[4-6] is provided in Table S1.

Endomyocardial biopsy samples that were obtained from 2 persons showed foci of endointerstitial edema and neutrophils, along with mononuclear-cell infiltrates (monocytes or macrophages and lymphocytes) with no giant cells. No other patients underwent endomyocardial biopsy. The clinical features of myocarditis after vaccination are provided in Table S3.

In the 136 cases of definite or probable myocarditis, the clinical presentation in 129 was generally mild, with resolution of myocarditis in most cases, as judged by clinical symptoms and inflammatory markers and troponin elevation, electrocardiographic and echocardiographic normalization, and a relatively short length of hospital stay. However, one person with fulminant

myocarditis died. The ejection fraction was normal or mildly reduced in most persons and severely reduced in 4 persons. Magnetic resonance imaging that was performed in 48 persons showed findings that were consistent with myocarditis on the basis of at least one positive T2-based sequence and one positive T1-based sequence (including T2-weighted images, T1 and T2 parametric mapping, and late gadolinium enhancement). Follow-up data regarding the status of cases after hospital discharge and consistent measures of cardiac function were not available.

The peak number of cases with proximity to vaccination occurred in February and March 2021; the associations with vaccination status, age, and sex are provided in Table 1 and Figure 1. Of 136 persons with definite or probable myocarditis, 19 presented after the first dose of vaccine and 117 after the second dose. In the 21 days after the first dose, 19 persons with myocarditis were hospitalized, and hospital admission dates were approximately equally distributed over time. A total of 95 of 117 persons (81%) who presented after the second dose were hospitalized within 7 days after vaccination. Among 95 persons for whom data regarding age and sex were available, 86 (91%) were male and 72 (76%) were under the age of 30 years.

Figure 1 (facing page). Timing and Distribution of Myocarditis after Receipt of the BNT162b2 Vaccine.

Shown is the timing of the diagnosis of myocarditis among recipients of the first dose of vaccine (Panel A) and the second dose (Panel B), according to sex, and the distribution of cases among recipients according to both age and sex after the first dose (Panel C) and after the second dose (Panel D). Cases of myocarditis were reported within 21 days after the first dose and within 30 days after the second dose.

COMPARISON OF RISKS ACCORDING TO FIRST OR SECOND DOSE

A comparison of risks over equal time periods of 21 days after the first and second doses according to age and sex is provided in Table 3. Cases were clustered during the first few days after the second dose of vaccine, according to visual inspection of the data (Fig. 1B and 1D). The overall risk difference between the first and second doses was 1.76 per 100,000 persons (95% confidence interval [CI], 1.33 to 2.19); the overall risk difference was 3.19 (95% CI, 2.37 to 4.02) among male recipients and 0.39 (95% CI, 0.10 to 0.68) among female recipients. The highest difference was observed among male recipients between the ages of 16 and 19 years: 13.73 per 100,000 persons (95% CI, 8.11 to 19.46); in this age group, the percent attributable risk to the second dose was 91%. The difference in the risk among female recipients between the first and second doses in the same age group was 1.00 per 100,000 persons (95% CI, −0.63 to 2.72). Repeating these analyses with a shorter follow-up of 7 days owing to the presence of a cluster that was noted after the second vaccine dose disclosed similar differences in male recipients between the ages of 16 and 19 years (risk difference, 13.62 per 100,000 persons; 95% CI, 8.31 to 19.03). These findings pointed to the first week after the second vaccine dose as the main risk window.

OBSERVED VERSUS EXPECTED INCIDENCE

Table 4 shows the standardized incidence ratios for myocarditis according to vaccine dose, age group, and sex, as projected from the incidence during the prepandemic period from 2017 through 2019. Myocarditis after the second dose of vaccine had a standardized incidence ratio of 5.34 (95% CI, 4.48 to 6.40), which was driven mostly by the diagnosis of myocarditis in younger male recipients. Among boys and men, the standardized incidence ratio was 13.60 (95% CI, 9.30 to 19.20) for those 16 to 19 years of age, 8.53 (95% CI, 5.57 to 12.50) for those 20 to 24 years, 6.96 (95% CI, 4.25 to 10.75) for those 25 to 29 years, and 2.90 (95% CI, 1.98 to 4.09) for those 30 years of age or older. These substantially increased findings were not observed after the first dose. A sensitivity analysis showed that for male recipients between the ages of 16 and 24 years who had received a second vaccine dose, the observed standardized incidence ratios would have required overreporting of myocarditis by a factor of 4 to 5 on the assumption that the true incidence would not have differed from the expected incidence (Table S4).

RATE RATIO BETWEEN VACCINATED AND UNVACCINATED PERSONS

Within 30 days after receipt of the second vaccine dose in the general population, the rate ratio for the comparison of the incidence of myocarditis

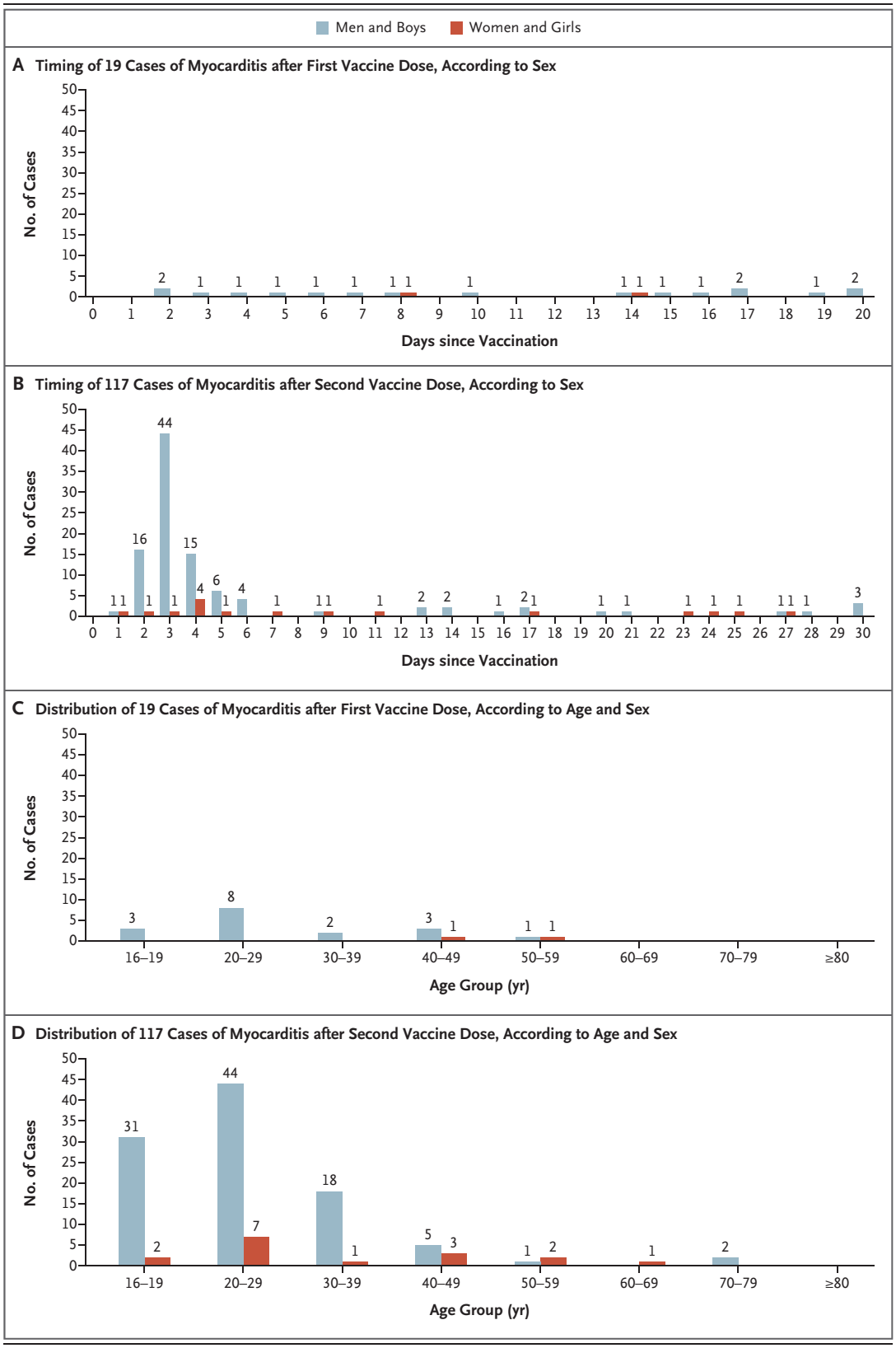

Table 3. Risk of Myocarditis within 21 Days after the First or Second Dose of Vaccine, According to Age and Sex.*

Age and Sex	First Dose			Second Dose			Risk Difference (95% CI)
	Recipients	Cases	Risk per 100,000 Persons	Recipients	Cases	Risk per 100,000 Persons	
	number			*number*			*no./100,000 persons*
Male recipients							
All ages	2,668,894	17	0.64	2,507,210	96	3.83	3.19 (2.37 to 4.02)
16–19 yr	224,518	3	1.34	199,115	30	15.07	13.73 (8.11 to 19.46)
20–24 yr	261,741	5	1.91	239,396	26	10.86	8.95 (4.42 to 13.55)
25–29 yr	246,638	3	1.22	228,988	16	6.99	5.77 (2.02 to 9.58)
30–39 yr	491,126	2	0.41	461,044	17	3.69	3.28 (1.41 to 5.18)
40–49 yr	458,268	3	0.65	433,069	5	1.15	0.50 (–0.82 to 1.84)
≥50 yr	986,603	1	0.10	945,598	2	0.21	0.11 (–0.29 to 0.52)
Female recipients							
All ages	2,773,802	2	0.07	2,618,425	12	0.46	0.39 (0.10 to 0.68)
16–19 yr	219,460	0	0	199,706	2	1.00	1.00 (–0.63 to 2.72)
20–24 yr	250,556	0	0	231,960	5	2.16	2.16 (0.13 to 4.24)
25–29 yr	235,575	0	0	219,113	0	0	0 (–0.83 to 0.89)
30–39 yr	481,045	0	0	451,791	1	0.22	0.22 (–0.37 to 0.84)
40–49 yr	472,083	1	0.21	444,916	2	0.45	0.24 (–0.61 to 1.11)
≥50 yr	1,115,083	1	0.09	1,070,939	2	0.19	0.10 (–0.26 to 0.46)

* Among vaccine recipients of all ages and both sexes, the overall difference in the incidence of myocarditis after the second dose as compared with the incidence after the first dose was 1.76 (95% confidence interval [CI], 1.33 to 2.19). The widths of the confidence intervals have not been adjusted for multiple testing.

Table 4. Standardized Incidence Ratios for 151 Cases of Myocarditis, According to Vaccine Dose, Age, and Sex.

Age and Sex	First Dose			Second Dose		
	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)	Observed Cases	Expected Cases per 2017–2019 Reference*	Standardized Incidence Ratio (95% CI)
	number			*number*		
All recipients†	25	17.55	1.42 (0.92–2.10)	126	23.43	5.34 (4.48–6.40)
16–19 yr						
Male	3	1.86	1.62 (0.32–4.72)	32	2.35	13.60 (9.30–19.20)
Female	0	0.23	0	2	0.30	6.74 (0.76–24.35)
20–24 yr						
Male	5	2.33	2.14 (0.69–5.00)	26	3.05	8.53 (5.57–12.50)
Female	1	0.42	2.37 (0.03–13.20)	6	0.56	10.76 (3.93–23.43)
25–29 yr						
Male	3	2.17	1.39 (0.28–4.05)	20	2.87	6.96 (4.25–10.75)
Female	0	0.30	0	1	0.39	2.54 (0.03–14.14)
≥30 yr						
Male	10	8.13	1.23 (0.59–2.26)	32	11.04	2.90 (1.98–4.09)
Female	3	2.11	1.42 (0.29–4.15)	7	2.87	2.44 (0.98–4.09)

* Reference data regarding the background incidence of myocarditis were extracted from the Israel National Hospital Discharge Database for the years 2017 through 2019.

† Data are listed for the 151 vaccine recipients in whom myocarditis was diagnosed at any level of certainty within 21 days after the first dose and 30 days after the second dose; data for all vaccine recipients have been weighted according to age and sex.

between vaccinated and unvaccinated persons was 2.35 (95% CI, 1.10 to 5.02) according to the Brighton Collaboration classification of definite and probable cases and after adjustment for age and sex. This result was driven mainly by the findings for males in younger age groups, with a rate ratio of 8.96 (95% CI, 4.50 to 17.83) for those between the ages of 16 and 19 years, 6.13 (95% CI, 3.16 to 11.88) for those 20 to 24 years, and 3.58 (95% CI, 1.82 to 7.01) for those 25 to 29 years (Table 5). When follow-up was restricted to 7 days after the second vaccine dose, the analysis results for male recipients between the ages of 16 and 19 years were even stronger than the findings within 30 days (rate ratio, 31.90; 95% CI, 15.88 to 64.08). Concordance of our findings with the Bradford Hill causality criteria is shown in Table S5.

DISCUSSION

During a nationwide vaccination campaign conducted from December 2020 through May 2021 involving more than 5 million residents, the Israeli Ministry of Health recorded 136 cases of definite or probable myocarditis that had occurred in temporal proximity to the receipt of two doses of the BNT162b2 mRNA vaccine — a risk that was more than twice that among unvaccinated persons. This association was highest in young male recipients within the first week after the second dose. In our study, definite or probable cases of myocarditis among persons between the ages of 16 and 19 years within 21 days after the second vaccine dose occurred in approximately 1 of 6637 male recipients and in 1 of 99,853 female recipients.

In most cases, symptoms of myocarditis developed within a few days after the second dose of vaccine. The incidence of myocarditis declined as the number of newly vaccinated persons decreased over time. This finding was suggestive of a possible causal relationship between two doses of the vaccine and the risk of myocarditis. Overall, we estimated that definite or probable cases of myocarditis occurred in the overall Israeli population at a rate of approximately 1 per 26,000 males and 1 per 218,000 females after the sec-

Table 5. Rate Ratios for a Diagnosis of Myocarditis within 30 Days after the Second Dose of Vaccine, as Compared with Unvaccinated Persons (January 11 to May 31, 2021).

Age and Sex	Vaccinated Group		Unvaccinated Group		Rate Ratio (95% CI)
	Person-Days of Follow-up	Cases	Person-Days of Follow-up	Cases	
	number				
All recipients*	149,786,065	117	296,377,727	98	2.35 (1.10–5.02)
16–19 yr					
Male	6,018,541	31	19,135,706	11	8.96 (4.50–17.83)
Female	6,033,192	2	17,768,696	2	2.95 (0.42–20.91)
20–24 yr					
Male	7,088,335	27	20,926,320	13	6.13 (3.16–11.88)
Female	6,889,399	5	20,832,407	2	7.56 (1.47–38.96)
25–29 yr					
Male	6,590,263	18	20,944,595	16	3.58 (1.82–7.01)
Female	6,417,564	1	20,943,920	0	0
≥30 yr					
Male	53,577,403	26	82,419,957	40	1.00 (0.61–1.64)
Female	57,171,368	7	93,406,126	14	0.82 (0.33–2.02)

* Data for all vaccine recipients have been weighted according to age and sex.

ond vaccine dose, with the highest risk again among young male recipients. This result may explain why a phase 3 trial of the vaccine, which included only 15,000 male and female recipients,[8] showed no cases of myocarditis. The mechanism of vaccine-induced myocarditis is not known but may be related to the active component of the vaccine, the mRNA sequence that codes for the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or to the immune response that follows vaccination.

Although selection bias in this study is possible, we consider it unlikely, since we used data from the entire nation. A major limitation of the study is that the calculation of rate ratios was based on individual patient data in the vaccinated group as compared with aggregated data in the unvaccinated group. In addition, the diagnosis of myocarditis was not validated by myocardial biopsy, and acquisition bias could be present, because clinical assessors were aware of vaccination status. Misclassification may have taken place during surveillance, which could have resulted in the underdiagnosis of myocarditis among young patients with chest pain or discomfort who were not referred for evaluation for myocarditis because of a low level of suspicion, despite notifications by the Ministry of Health to health care providers. There was also a possibility of overdiagnosis of cases of myocarditis owing to increased public and medical awareness of this possible side effect of vaccination. However, our sensitivity analysis did not support the occurrence of overreporting as an explanation for our findings. Our calculations of risk difference and rate ratios were confined to cases that had met strict criteria for definite or probable myocarditis, which would tend to reduce ascertainment bias. Another limitation may be the use of the Israel National Hospital Discharge Database for the years 2017 through 2019 as a reference for the background incidence of myocarditis in the analyses of standardized incidence ratios. Those years were different from the period between 2020 and 2021 with respect to viral circulation — including influenza outbreaks in 2017, 2018, and 2019 but not in 2020 and 2021 and Covid-19 morbidity in 2020 and 2021 but not in 2017 through 2019 — and to the lack of systematic reporting of myocarditis during the earlier period. However, hospitalization rates for myocarditis during the period from 2017 through 2019 were similar to those in 2020,

and the databases used for these denominators are representative of the unvaccinated population. We were unable to adjust for potential confounders other than age and sex.

Finally, the rates of myocarditis in our study can be compared with those in the Clalit Health Services database in the study by Witberg et al.,[9] as now reported in the *Journal*. That study showed a somewhat lower incidence of myocarditis, possibly because of the different methods that were used. In our study, each vaccination date was recorded to ensure accurate follow-up of 21 days after the first dose and 30 days after the second dose, whereas Witberg et al. followed vaccinees for 42 days after the first dose. The study design may have led to an underestimation of myocarditis cases owing to a shorter follow-up for the second dose. In our study, the rate of myocarditis in the general unvaccinated population was 1 per 10,857 and can be compared with findings indicating that myocarditis was more common after SARS-CoV-2 infection than after vaccination, as reported previously by Barda et al.[10]

On the basis of data from an Israeli national database, the incidence of myocarditis after two doses of the BNT162b2 mRNA vaccine was low but higher than the incidence among unvaccinated persons and among historical controls. The risk of myocarditis was driven primarily by the increased incidence after the second dose of vaccine and in young male recipients.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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The Ethics of Drug Research in Children

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Contents

Abstract

The obligation of society to improve the welfare of its members requires the conduct of paediatric drug trials. Nevertheless, research activities must satisfy obligations to individual participants.

The obligation to protect the welfare of children requires that nontherapeutic research procedures generally involve no more than minimal risk. It also requires that randomisation occurs only when the relative merits of therapeutic procedures remain unsettled among the relevant community of experts.

The duty to respect the developing autonomy of children requires that they be included in decision-making about research participation in a manner consistent with the level of their decision-making capacity. However, when children lack mature decision-making capacities, the duty of parents to protect their welfare may properly constrain their choices.

Justice requires that the benefits and burdens of research be distributed in a manner that assures equal opportunity for all children. Vulnerable children should receive special protection against the burdens of nontherapeutic research procedures. The benefits of participating in clinical trials should be available to all children with serious illnesses for which current treatment is unsatisfactory. Justice also requires that initiatives be undertaken to rectify current shortcomings in the scope of paediatric drug research.

Striking an appropriate balance between obligations to conduct research and to protect the interests of participants is essential to the moral integrity of paediatric drug research.

Childhood is characterised by dynamic processes of physical and psychosocial development. The distinctive features of physical development prevent the formulation of safe and effective drug therapies through simple extrapolation from research with adults. Some diseases afflict only children. Other diseases shared with adults have starkly different manifestations in children. The therapeutic action and toxicities of drugs may differ markedly in children. Additional variations in the pharmacokinetic and pharmacodynamic profile of drugs occur among children in different stages of physical development. These considerations underscore the essential role of clinical research in formulating paediatric drug therapies.

Similarly, the processes of psychosocial development suggest that ethical rules for research with adults cannot merely be grafted onto the paediatric enterprise. Developmental immaturity renders children susceptible to special physical and psychosocial harms. Slowly evolving capacities for self-determination generate complexities about the role and limits of decision-making by children regarding participation in research. These same vulnerabilities complicate the process of assuring fair distribution of the burdens and benefits of clinical research among children. Moreover, developmental differences introduce substantial variations among children in their susceptibility to harm and their capacity for making considered choices. These factors accentuate the difficulty of formulating moral rules for drug research with children.

Moral issues arising in paediatric research reflect the clash of important moral interests. On one hand, children as a group have an interest in drug research that expands generalisable knowledge useful in treating paediatric diseases. On the other hand, there are important interests of individuals that may be endangered by their participation in research. These are interests in protection of their welfare, respect for their developing autonomy, and fair treatment in the distribution of the benefits and burdens of research participation.

These interests suggest the basic moral issues regarding drug trials in children. First, does improved drug therapy for children constitute a merely desirable goal, or is there a moral obligation of society to foster its development? Secondly, what are the nature and limits of the moral obligations imposed on clinical investigators by the moral interests of child research participants?

1. The Research Imperative

Professional statements commonly ascertain that society has a moral obligation to conduct paediatric research. For example, the American Academy of Pediatrics maintains that '. . . it is unethical to deny children appropriate access to existing and new therapeutic agents'; therefore, it is '. . . the combined responsibility of the pediatric community, pharmaceutical industry, and regulatory agencies to conduct the necessary studies'.[1] Similarly, the British Medical Research Council insists that 'There is . . . a broad consensus, with which we concur, that a principled case can be made on ethical grounds for research on children'.[2]

Yet some philosophers have pointedly rejected the claim that society has a moral obligation to conduct medical research. On this view, the primary role of society is to protect its members from harm-causing practices. Improvement in the welfare of its members through increased medical knowledge is desirable, but not morally obligatory. For example, in his classic essay on the ethics of human research, Hans Jonas admits that 'Progress is an acknowledged interest of society' and that 'in medical science experimentation on human subjects is a necessary instrument . . .' of progress. However, he asserts that 'Unless the present state is intolerable, the melioristic goal is in a sense gratuitous . . . . Our descendants have a right to be left an unplundered planet; they do not have a right to new miracle cures'.[3]

This view reflects two mistaken assumptions.[4] One is that the obligation of society to protect persons from harm-causing activities does not require medical research. The widespread use of medical interventions later shown to be injurious suggests the crucial importance of medical research in eliminating harm-causing practices. For example, inad-

equate study of the pharmacokinetics of chloramphenicol in paediatric patients resulted in the occurrence of 'grey baby syndrome' and numerous deaths among infants. Subsequent investigation established that the immature livers of infants allowed toxic doses of the drug to accumulate in the body. Similarly, inadequate assessment of tetracycline use in children under 9 years of age resulted in severe enamel dysplasia in the developing teeth of many paediatric patients. Thus, even if we admit only the minimal obligation of society to limit harm-causing practices, there is an obligation to conduct paediatric drug research.

The other key assumption in Jonas's argument is that society does not have an obligation to improve the welfare of its members. Accordingly, he maintains that our descendants do not have a right to 'new miracle cures'. However, it is difficult to sustain the claim that society has an obligation to eliminate harm-causing medical practices, but that finding more effective treatments is morally optional. Both activities have precisely the same objective: minimising the extent of harm that may occur to persons.[5] Moreover, elimination of harm-causing medical practices and identification of new therapies require the same commitment of clinical research resources. These points are well illustrated in the context of paediatric research. Protocols evaluating new drug treatments or controversial standard therapies are both intended to minimise the harm that might occur to children. Furthermore, the same process must be used to identify improved treatments or inadequate standard therapies – their formal evaluation in well-designed clinical trials. Thus, if society has a role in reducing harm-causing practices, it has an obligation to identify more effective treatments as well.

Recognition of these societal obligations provides the basis for assigning moral priority to paediatric drug research. On one hand, disabling and life-threatening diseases may seriously undermine the ability of children to pursue opportunities and achieve personal goals over a lifetime. On the other hand, there are glaring shortcomings in the extent of paediatric drug research. As a result, most drugs are used in children without an adequate profile of toxicities or optimal administration regimens. According to the US Food and Drug Administration, only 33% of new medical entities with potential usefulness in paediatric patients and approved for marketing in 1997 had any labelling for paediatric indications.[6] More generally, 80% of drugs used in children do not have approved labelling for paediatric patients.[7] An analysis of data from 1994 assessed the frequency with which drugs are prescribed for children on an outpatient basis despite inadequate paediatric labelling. The 10 most frequently prescribed included asthma drugs, antibacterials and antidepressants, accounting for approximately 5 million paediatric prescriptions in 1 year.[8]

Thus, the research imperative in paediatric medicine reflects not merely a set of desirable goals, but a weighty obligation to improve drug therapy for children. At the same time, the endeavour to satisfy this imperative may conflict with obligations to protect the moral interests of this patient group.

2. The Welfare of Child Research Participants

An essential interest of children involves protection of their welfare. Adults with fiduciary relationships to children (such as parents and physicians) assume special moral obligations to secure their best interests. A critical moral issue concerns the conditions under which clinical research can be conducted with paediatric patients while satisfying these obligations.

Satisfactory analysis of this problem involves drawing an initial distinction between therapeutic and nontherapeutic research procedures.[9,10] Therapeutic research procedures are intended both to enhance the welfare of individual patients and to contribute to resolution of the research problem. By contrast, nontherapeutic research procedures are intended only to contribute to the achievement of study objectives. For example, a randomised clinical trial might compare the relative safety and efficacy of two chemotherapeutic regimens for neuroblastoma. Administration of the chemotherapy is a

therapeutic research procedure, because it is intended both to improve the welfare of patients and to evaluate the comparative worth of the treatments. By contrast, investigators might also undertake repeated blood samplings to profile the pharmacokinetics of one of the drugs. These procedures are nontherapeutic because they are intended solely to produce generalisable knowledge. As the examples suggest, a research protocol may include both therapeutic and nontherapeutic research procedures. These must undergo separate moral evaluation because of differences in the permissible limits of risk.

A crucial issue in paediatric research is to ensure that the conditions under which the use of nontherapeutic research procedures are implemented, are consistent with the moral obligation to protect the welfare of children. Some theorists have suggested that children ought never to undergo nontherapeutic research procedures if they are unable to give free and informed consent.[11] When they lack the capacity to give consent, the moral obligation of fiduciaries is to permit only interventions that promote their welfare. However, a critical problem with this view is that many interventions in the lives of children, particularly in the family context, are considered morally permissible even if they do not directly serve the welfare of children. A parent may properly insist that a child leave off watching a favourite TV programme in order to run an errand. Thus, some interventions which serve interests other than those of the child are morally permissible, provided that they are not seriously contrary to the child's welfare.

A more widely accepted view is that nontherapeutic research procedures involving children are morally permissible if they involve only minimal risk of harm.[12] One way of understanding minimal risk involves anchoring it in the risks of everyday life. For example, the US federal regulations and the guidelines of the British Medical Research Council specify that minimal or negligible risk exists when '. . . the probability and magnitude of harm or discomfort anticipated in the research are not greater in themselves than those ordinarily encountered in daily life'.[2,13] One way of interpreting this standard is to suppose that no matter how careful or safe we might be in daily life, there remains a residual risk of harm or discomfort that cannot be avoided. Harm or discomfort of this frequency and magnitude constitutes minimal risk.

The moral rationale for using this standard to delimit permissible interventions is that it identifies a level of risk that is substitutive rather than incremental.[14] Whatever the activities in which children engage in daily life, there is a certain residual risk of harm or discomfort that cannot be avoided. If they participate in nontherapeutic research procedures involving no more than minimal risk, then the risk to which they are exposed is not increased compared with other activities in which they might be engaged. Thus, inclusion of children for reasons other than the promotion of their own welfare is not incompatible with fiduciary obligations to protect their interests.

Although the moral rationale can be clearly elucidated, application of the standard in clinical research is fraught with difficulties. First, there are substantial variations among paediatricians in judging minimal risk. In a survey of departmental chairmen and clinical research centre directors, respondents rated procedures as minimal risk, minor increase over minimal risk, and greater than minor increase over minimal risk for children of different ages.[15] Virtual unanimity existed only with regard to the minimal risk of antecubital venipuncture in children 1 year of age and older. For procedures such as tympanocentesis, punch biopsy of the skin, gastrointestinal intubation and intramuscular placebo injection, no more than 35 to 77% of respondents selected the most frequently chosen risk category. Somewhat surprisingly, however, a majority of respondents rated the latter 3 procedures as minimal risk for children aged 7 years and older.

Secondly, research evaluating the risk of common paediatric procedures is difficult to design and much of it has yielded incompatible results. These problems are compounded when risk of harm is properly understood to consist in several dimensions, including '. . . causing physical disturbance, discomfort or pain, or psychological disturbance to the child . . .'.[16]

For example, Humphrey and colleagues[17] evaluated the emotional distress associated with venipuncture in 223 hospitalised children aged 2.5 to 18 years. Distress-related behaviours were assessed on a 5-point scale, with level 1 being calm, level 3 being serious but controlled distress, and level 5 being panic. The percentages experiencing level 3 distress or greater were 83% of children aged 2.5 to 6 years, 51% of those aged 7 to 12 years, and 28% of those older than 12 years. By contrast, Smith[18] evaluated the harmful effects of venipuncture in 92 healthy children between 6 and 8 years of age participating in a study of lead exposure. A survey of parents indicated that 75% of the children were not upset at the prospect of the procedure, 92% were not upset after the procedure and 93% of the children reported that the venipuncture hurt not at all or only a little.

Nevertheless, existing studies suggest several important guidelines for determining whether nontherapeutic procedures involve no more than minimal risk. One is that level of risk cannot be assessed with exclusive focus on physical harms, given the heavy emotional component of the reaction of children.[19] Another is that investigators must assess the risk of harm for individuals, given that pain and emotional distress may vary substantially among different children. This point is underscored in the new guidelines of the Royal College of Paediatrics and Child Health, which note that 'Children's responses are varied, often unpredictable, and alter as children develop'.[20] Moreover, the abovementioned studies clearly suggest that there is a small group of children who are highly distressed when undergoing minor procedures. For example, 8% of the parents interviewed by Smith considered their children mildly upset after venipuncture and 3% of the children reported that the procedure 'hurt a lot'.[18] In the study by Humphrey and co-workers,[17] 20% of 7- to 11-year-olds were assessed as very distressed by venipuncture. Investigators must sensitively seek to identify these children, because the extent of their reactions increases the risk of harm beyond minimal status. Lastly, investigators must be attentive to situational variables that may intensify or mitigate the stressful reactions of children.

A controversial issue concerns involvement of children in nontherapeutic research procedures involving greater than minimal risk. Unlike most national regulations and professional guidelines, the US federal rules and the guidelines of the Council for International Organizations of Medical Sciences (CIOMS) allow the use of such procedures under certain narrowly defined conditions.[21,22] There are two prominent moral difficulties with this practice. One is that it abandons the underlying moral rationale for considering the use of nontherapeutic procedures compatible with our duties to protect the welfare of children. When minimal risk procedures are employed, children are exposed only to a level of risk that they would otherwise encounter in daily life. Nontherapeutic procedures involving greater than minimal risk provide an increment to the risks of daily life rather than a substitute for them. Another problem is defining the conditions under which nontherapeutic procedures involving greater than minimal risk might be employed. For example, the US federal regulations and the CIOMS guidelines restrict the practice to procedures involving only 'a minor increase' or 'slight increase' over minimal risk. This provision suffers from terminal ambiguity, because it constructs the obscure notion of 'minor or slight increase' on the imprecise concept of 'minimal risk'.

Nevertheless, an exception to the minimal risk standard might be appropriate for older children with mature decision-making capacities. The minimal risk standard is grounded in our obligation to protect the welfare of children. As the decision-making capacity of children matures, the focus of our obligations shifts to respecting their own assessment of risks and benefits. For example, older adolescents with cancer might be invited to undergo an extra lumbar puncture or bone marrow aspiration to study drug pharmacokinetics.[23] International codes and regulations have failed to consider the appropriateness of nontherapeutic procedures involving greater than minimal risk in these circumstances.[12]

A different moral framework is pertinent to the assessment of therapeutic research procedures, such as the provision of drug therapies in a clinical trial. Justification for their use depends on evidence that they will promote the welfare of individual child patients. Specifically, available evidence must suggest that: (i) the risk of the procedures is justified by their anticipated benefits for the patient, and (ii) the risk-benefit ratio of the procedures is as favourable as that of any alternative procedures. These same conditions are applicable to the care of patients in the nonresearch setting.

However, interpretive complications arise in applying these requirements to the conduct of randomised clinical trials. Insofar as the latter involve the comparison of two or more treatments, each of the treatments evaluated must satisfy the above conditions. One interpretation of this situation would be to require that available evidence not favour one treatment arm over another as having a more favourable risk-benefit ratio for participants.[24] The problem with this interpretation is that often there is preliminary evidence that one treatment may be safer or more efficacious than another. This is especially the case when prior clinical trials have been conducted in adult populations. Indeed, preliminary evidence may be necessary to justify the effort and expense of a randomised clinical trial in children. Thus, if available evidence must be equally balanced, randomised clinical trials could rarely, if ever, be justified.

A more promising interpretation of our obligation to promote the welfare of research participants focuses on the comparative status of the treatments among the relevant community of experts. Provision of randomised treatment can be justified provided that the relevant community of experts are uncertain or disagree about whether scientific evidence establishes the superiority of one treatment over another – a condition Freedman has termed 'clinical equipoise'.[25] On this view, a precarious balance of preliminary evidence is not required to justify the conduct of a randomised clinical trial. Rather, the community standard of reasonable scientific practice must currently be unsettled. Moreover, this concept implies that an individual physician can both recommend randomisation to prospective participants and fulfil the duty to protect the patient's welfare, even when believing that preliminary evidence favours a particular treatment.

The difference in these interpretations is illustrated by the controversy regarding treatment of persistent pulmonary hypertension in neonates with extracorporeal membrane oxygen therapy (ECMO).[26] By 1980, ECMO achieved 70% survival versus 80% mortality in historical controls. However, the relevance of historical controls receded in the 1980s as conventional treatment with hyperventilation, paralysis and vasodilation became more sophisticated. By 1986, 90% of conventionally treated neonates in some series survived. Despite uncertainty about the most beneficial treatment, adequate controlled trials could not be mounted. Neonatologists believed that randomisation could not be recommended if they believed that the balance of evidence favoured one of the available treatments. However, if randomisation is justified when the relevant community of experts disagree about optimal therapy, then a clinical trial would be morally permissible even though individual neonatologists might favour ECMO or conventional therapy.

The clinical equipoise criterion is also helpful in clarifying our duty to protect the welfare of children in placebo-controlled clinical trials.[27,28] Justification for using placebo controls requires that the relevant community of experts are uncertain or disagree about the relative merits of placebo versus both the investigational agent and other drugs available for treating the children's disorder. Conversely, the use of placebo controls violates our duty to protect the welfare of child patients when the relevant community of experts agree that placebo is known to be inferior to other available treatments.

There are several situations in which the use of placebo controls is clearly acceptable.[29] There may be no treatment known to be safe and effective for treating the particular disorder. Sometimes the subpopulation of patients in which the study will be conducted is refractory to standard therapy. In other cases, standard therapy may possess limited effec-

tiveness but carry a substantial burden of unacceptable adverse effects. Finally, in some trial designs, the placebo or investigational agent is added on to the standard therapy received by all patients. For these situations, the duty to protect the welfare of individual children is not violated, because patients assigned to the placebo control group are not exposed to a treatment regimen known to be inferior.

It is considerably more difficult to justify the use of placebo controls when there is an established standard treatment for the disorder. Some commentators have suggested that placebo controls are unacceptable when established treatment reduces mortality or serious morbidity, but may be used if treatment is intended only to modify symptomatology.[30] However, there are clearly situations in which withholding treatment for symptoms may seriously compromise the welfare of patients. For example, a placebo-controlled trial of medication for the treatment of duodenal ulcer in children might involve considerably more epigastric distress in the placebo group compared with patients who might receive standard therapy, even if there is little evidence that serious adverse events such as haemorrhage or perforation would be more common without standard therapy.[31] In this case, patients receiving placebo would be provided a treatment known to be inferior in important respects. Because clinical equipoise does not hold, the duty to protect the welfare of patients in the placebo arm is violated.

A more promising approach is to ensure that elements of trial design are structured such that placebo recipients are not exposed to a treatment regimen that is disadvantageous compared with standard therapy. Several strategies might be employed to prevent harm to patients denied standard or investigational treatment. The duration of involvement in the trial might be comparatively brief. Frequent monitoring of patients might be implemented. Withdrawal criteria can be formulated to ensure that patients whose condition deteriorates are quickly withdrawn from the trial. In addition, inclusion and exclusion criteria can be stringently specified to assure that the most seriously ill patients are not eligible for involvement in the trial. For example, placebo-controlled trials examining the efficacy and safety of drug therapy for children with hypertension can be designed to incorporate these various design features. In these cases, it is arguable that patients receiving placebo are not exposed to a treatment regimen known to be inferior given the precise conditions of their involvement in the trial. Thus, even when standard therapy exists, carefully designed placebo-controlled trials may sometimes be consistent with the duty to protect the welfare of participants.

Placebo-controlled trials have some important advantages. They require smaller sample sizes than active-controlled trials. They avoid the need to make the (sometimes mistaken) assumption that the active-control drug actually works in the population being studied. Placebo controls serve as a measure of internal validity with regard to the ability of a trial to detect differences between treatment arms. Nevertheless, the duty to protect the welfare of child patients restricts the permissibility of such trials to circumstances in which the use of placebo is not known to constitute inferior treatment for paediatric patients under the conditions of their involvement in the trial.

3. The Developing Autonomy of Children

The principle of respect for personal autonomy acknowledges the basic interest of persons in exercising autonomous choice. It requires that we respect the capacity of persons to deliberate about, and act in accord with, their own values and goals. In the context of research, this moral obligation gives rise to the requirement for informed and voluntary consent of prospective participants. A crucial issue concerns the role and limits of decision-making by children about participation in research.

Analysis of the issue is complicated by two factors. One is that children's capacity for autonomous decision-making slowly evolves in conjunction with their cognitive and psychosocial development. As a result, the manner in which we acknowledge their autonomy must reflect the developmental stage of their decision-making capacity. The other com-

plication is that the decision-making of children may properly be constrained by the concern to protect their welfare. Parents and other fiduciaries sometimes have an obligation to override the wishes of children in order to secure their well-being. However, the degree to which the autonomy of children should be constrained depends on the importance of particular decisions for their welfare. Children may be given substantial freedom to choose extracurricular school activities, but might not be allowed to decline life-saving surgery. Both factors must be explored in setting guidelines for the role of children in decision-making about participation in research.

The capacity for autonomous decision-making involves several components.[32] First, persons must possess relatively stable values and goals to direct evaluation of their options. Secondly, they must possess the ability to understand information relevant to their decision. Thirdly, persons must have the capacity to reason and deliberate about the potential consequences of their options within the framework of their values and goals. Lastly, they must be able to make a decision that reflects their own values and goals rather than the desires or wishes of others.

Empirical research suggests that the capacity of children for autonomous decision-making is usefully conceptualised as involving three categories of competency.[33] Children 14 years of age and older exhibit decision-making capacities similar to those of adults. For example, Weithorn and Campbell[34] compared the decision-making competence of 4 groups of healthy individuals aged 9, 14, 18 and 21 years, using 4 hypothetical treatment decisions. The investigators found that 14-year-olds did not differ significantly from 18- and 21-year-olds in their understanding of key facts, the reasoning for their deliberation or the treatment option selected. Scherer[35] examined the capacity of adolescents for voluntary choice on three hypothetical treatment dilemmas involving varying degrees of parental pressure. He found that although adolescents 14 to 15 years of age were more likely to defer to parental wishes than adults aged 21 to 25 years, the difference did not reach statistical significance. Thus, empirical research supports full involvement of older adolescents in the decision-making process about participation in research.

Younger school-aged children exhibit more limited decision-making skills, but are able to formulate sensible choices. For example, Weithorn and Campbell[34] found that 9-year-olds had a poorer understanding of the facts and scored significantly less well than the other groups in considering multiple items of information and in performing abstract risk-benefit analysis. Nevertheless, the pattern of their choices did not differ significantly from those of the older groups. In Scherer's study[35] of voluntary choice, children aged 9 to 10 years were significantly more likely than adolescents and adults to defer to parental wishes regarding serious treatment decisions. However, in the absence of parental pressure, young children were able to express choices with a high level of conviction.

These results, typical of studies of younger school-aged children, support a more limited role for younger children in decisions about participation. When addressed in language that is age-appropriate, younger children can understand that the researcher is attempting to learn something about their illness or its treatment. They are also able to comprehend basic information about what procedures will be done and how they may be affected. Moreover, they are able to understand that they are being invited to participate and may decline involvement. Although the sophistication of understanding and deliberation does not approach adult levels, younger children are able to consider options relative to their values and goals and to make sensible choices. Although they may still require adult protection, their capacity for autonomous choice is sufficiently well developed to require their inclusion in the decision-making process. In the literature of research ethics, this level of decision-making is frequently called 'child assent', in order to distinguish it from informed and voluntary consent by fully competent persons.[36]

A third level of decision-making capacity characterises younger children who are not capable of

assent. At this level, children are not able to understand the purpose of the research or key items of factual information. Their deliberative skills are undeveloped. Nevertheless, they are able to understand what intervention is proposed and to express their objection to undergoing the procedure. When children know what they do not want to do, respect for their developing autonomy requires consideration of their objection to undergoing specific procedures. This level of decision-making capacity may be called 'child dissent'.

As noted above, the second complicating factor in clarifying the decision-making role of children concerns the constraints properly imposed on their choices by the moral obligation of parents and others to protect their welfare. The importance of this duty depends on the relevance of research participation to the welfare of children. With respect to nontherapeutic research procedures, the obligation to protect the welfare of children provides no grounds for constraining their choices to decline participation. As a result, the agreement of school-aged children and adolescents should be considered a necessary condition of their participation and their refusal sufficient for excluding them. For children who are capable only of dissent, their objection to undergoing nontherapeutic procedures should also be considered sufficient to exclude them. Although the latter requirement is ignored in the US federal regulations, more recent guidelines emphasise the moral significance of dissent by young children.[2,20,22] For example, the British Medical Research Council guidelines specify that children should be excluded from involvement in nontherapeutic research procedures when they 'object or appear to object in either word or action'.[2]

The situation is more complex with regard to therapeutic research procedures. The latter are justifiable only when the risk is justified by the anticipated benefit and the risk-benefit ratio is at least as favourable as other therapeutic options. Under these conditions, concern for their welfare may properly constrain the choices of children who might decline participation in research. Nevertheless, there are two notable exceptions to this rule. When the risk-benefit ratio of therapeutic research procedures is not more favourable than interventions available outside the research context, careful consideration should be given to the wishes of children for treatment in the nonresearch setting. Furthermore, when older adolescents are judged fully competent to make choices regarding participation in therapeutic research procedures, their informed and voluntary agreement should be a necessary condition of their involvement. This exception receives only very limited recognition in international guidelines.[12]

This analysis also suggests the appropriate role and limits of permission by parents or guardians regarding the participation of children in clinical research. Permission of parents or guardians is usually a necessary condition for the involvement of children in nontherapeutic and therapeutic research procedures, because in both cases inclusion may adversely affect the welfare of children. It is also often a sufficient condition for involvement of children in therapeutic research procedures that offer potential benefits unavailable in the nonresearch setting, because exclusion of children may be detrimental to their interests. The primary exception to these conditions involves adolescents with mature decision-making capacities. Moreover, even when children have the appropriate capacities to accept or decline participation in research activities, the guidance and support of parents or guardians in the decision-making process is compatible with respect for their developing autonomy. It is essential, however, that this assistance facilitates a choice that reflects the emerging values and goals of the child. Otherwise, there is a risk that the choices expressed by children will be less than voluntary. Thus, the obligation of parents or guardians to protect the welfare of their children must be exercised in a manner that essentially complements respect for their developing autonomy.

4. Fair Treatment of Children in Research

Persons have a basic interest in being treated fairly *vis à vis* one another. One aspect of justice

concerns fair distribution of the benefits and burdens of cooperative social endeavours such as clinical research.[37] According to a common view, fairness requires that the benefits and burdens of cooperative social activities be distributed in a manner that provides all persons with equal opportunity to pursue their life plans. This principle has several implications for the conduct of paediatric drug trials.

One aspect of the principle concerns fair distribution of the burdens of research participation. This component focuses on the use of nontherapeutic research procedures in vulnerable groups of patients. Vulnerable individuals are persons whose limited decision-making capacity or impaired physical, psychological or social condition renders them especially susceptible to harm when participating in research.[38] These burdens occur primarily with nontherapeutic procedures, because these pose a risk of harm without offsetting medical benefits. Fair treatment requires preservation of the equal opportunity of vulnerable individuals to pursue their life plans *vis à vis* other persons. Given their increased susceptibility to harm when undergoing nontherapeutic procedures, greater protection must be afforded to vulnerable individuals.

This interpretation has implications regarding selection of research participants. In general, more vulnerable groups of children should not be involved as participants when the use of less vulnerable children permits the research question to be adequately addressed.[39] More vulnerable children include those who are younger, psychologically immature, suffering from serious disease, or institutionalised. For example, safety testing of a new paediatric drug formulation should not occur in institutionalised children when the research question can be adequately answered using children in the general population. Because their social situation poses greater burdens in achieving a good life, institutionalised children should bear an additional burden only if the research problem has special relevance to their status as institutionalised.

The requirement of fair distribution of burdens also has important implications regarding risk assessment. As suggested in section 2, children may experience heightened pain, discomfort and anxiety compared with adults when undergoing nontherapeutic procedures such as venipuncture. If children are to be exposed to no greater burden in research participation than older patients, greater protections against potential harm must be implemented when nontherapeutic interventions are proposed.[40] These include avoiding more invasive interventions, limiting repetition of procedures, using topical anaesthetics, and allowing the presence of parents.

These features of fair distribution of burdens highlight the controversial character of specific provisions of the US federal regulations on research with children. These regulations allow the use of nontherapeutic procedures involving more than minimal risk when the risk is only a minor increase over minimal risk, the experiences are familiar to the children, and the research offers the prospect of securing vitally important knowledge about the disorder from which the children suffer.[21] These regulations permit only sick children to be exposed to greater than minimal risk in nontherapeutic procedures. In doing so, they violate the requirement of justice that lesser burdens be imposed on more vulnerable persons.[41] Moreover, they fail to acknowledge that the reactions of children might result in a greater burden than experienced by adults. Thus, rather than offering greater protections for children who are sick, the regulations permit an additional risk of harm.

A second component of justice focuses on the fair distribution of the benefits of research participation.[42] This feature is pertinent to the use of therapeutic research procedures. Involvement of children in these procedures is justified only when the risk-benefit ratio is at least as favourable as any alternative treatments available outside the research context. However, when current treatment does not possess satisfactory safety and/or efficacy, participation in research may secure a more beneficial treatment outcome than provided by standard therapy. In addition, research centres for serious childhood diseases often offer access to multidis-

ciplinary specialty care for the complex medical and psychosocial needs of patients. More comprehensive nursing care, monitoring and follow-up of child patients are also typically provided. Under these circumstances, justice requires that all children have equal opportunity to participate in clinical trials. Otherwise, those without access are less able to achieve their life plans than children with the opportunity to receive treatment in clinical trials.

These points are illustrated in the context of research on drug therapies for paediatric cancers. Studies have established that children treated in clinical trials have more favourable outcomes in achieving long term, disease-free survival than those who are treated outside the research setting.[43] However, at present, the proportion of adolescents with paediatric cancers represented in clinical trials is much lower than the proportion of younger children with similar diagnoses.[44] Thus, justice requires enhanced efforts to accrue adolescent patients in order to improve their opportunity *vis à vis* other children. Similarly, the number of infants with HIV infection is rapidly increasing in the developing world, yet their opportunity to participate in clinical trials is frequently constrained by poverty, maternal HIV disease or their status as wards of the state. If infected infants are to have equal opportunity *vis à vis* adult patients to benefit from participation in clinical trials, social services must be structured in ways that facilitate their inclusion.[45]

A final component of justice concerns the fair distribution of societal resources to research on the health problems of different age groups. If children are to have equal opportunity to pursue their life plans *vis à vis* other age groups, appropriate resources must be devoted to ameliorating the medical problems that afflict children. Indeed, fairness as equal opportunity may require that children receive special priority in the distribution of resources for medical research. Medical disabilities that arise in childhood may afflict persons over the full course of a lifetime, unlike health problems with adult onset. These medical problems may have deleterious and pervasive consequences for the socialisation, education and employment prospects of children. As a result, paediatric illnesses may undermine opportunities to pursue life plans much more severely than adult-onset diseases.

These considerations provide the moral rationale for recent initiatives to rectify the glaring shortcomings in the scope of paediatric drug research. For example, the US Food and Drug Administration recently established the requirement that all new drugs and biologicals that may present meaningful therapeutic advantages for paediatric patients or are likely to be used in a substantial number of children must undergo proper evaluation in paediatric trials prior to marketing. Paediatric studies of marketed drugs may also be required under the same conditions if the absence of clinical trials might pose significant risks to children.[6] Similarly, all clinical research conducted or supported by the National Institutes of Health must now include children, unless there are valid scientific or ethical reasons for excluding them.[46] These policies are intended to enhance equal opportunity by altering current inequities in the distribution of the benefits of research to children as a group.

Some moral issues in paediatric drug research reflect disputes about the relative weight of these different requirements of justice. An example involves the controversy about the timing of drug evaluation in children who suffer from catastrophic diseases, such as AIDS, that also afflict adults. One rule of justice requires that more vulnerable individuals such as children receive added protections against the burdens of research participation. Initial testing in adults may rule out inefficacious or excessively toxic drug therapies without exposing children to these harms. By contrast, the other rules of justice require that the benefits of research participation and of the knowledge accrued be available to children. Simultaneous testing of new agents in adults and children provides earlier opportunity for beneficial new drugs to be distributed to children as well as adults. In weighing these different requirements of justice, the added risks of simultaneous testing in children must be compared with the possible benefits of earlier availability of potentially superior therapy. In general, the grounds for simul-

taneous paediatric testing are most compelling when the disease being studied involves considerable morbidity or mortality, existing drug therapies are inefficacious or excessively toxic and preliminary evidence suggests probable advantages of the investigational agent.

5. Conclusions

The dynamic processes of physical and psychosocial development in childhood underscore the necessity of paediatric drug research and the complexity of formulating moral rules for its conduct. The obligation of society to eliminate harm-causing practices and to improve the welfare of its members establishes the imperative to conduct paediatric research. Nevertheless, the conduct of paediatric trials must be constrained by duties to child participants derived from concern for their welfare, respect for their developing autonomy and fair treatment. Striking an appropriate balance between the obligations to conduct research and to protect the moral interests of child participants is essential to the moral integrity of paediatric drug research.

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Prashant Bhushan
(TRUE COPY)

2019 SCC OnLine Del 11929

In the High Court of Delhi at New Delhi
(BEFORE VIBHU BAKHRU, J.)

W.P. (C) 343/2019 & CM Nos. 1604-1605/2019

Master Haridaan Kumar and Others ... Petitioners;

Versus

Union of India and Another ... Respondents.

And

W.P. (C) 350/2019 & CM Nos. 1642-1644/2019

Baby Veda Kalaan and Others ... Petitioners;

Versus

Directorate of Education and Others ... Respondents.

W.P. (C) 343/2019, CM Nos. 1604-1605/2019, W.P. (C) 350/2019 and CM Nos. 1642-1644/2019

Decided on January 22, 2019

Advocates who appeared in this case:

Mr. Anubhav Kumar and Mr. Abhinav Mukherji, Advocates.

Mr. Ramesh Singh, Standing Counsel, GNCTD with Mr. Chirayu Jain and Ms. Nikita Goyal, Advocates for GNCTD.

Mr. Sushil Kumar Pandey, Senior Panel Counsel with Ms. Neha Sharma, Advocates for UOI with Dr. Pradeep Haldar (Deputy Commissioner (IMM) Incharge).

Ms. Diya Kapur, Ms. Shyel Trehan and Mr. Rishabh Sharma, Advocates.

Mr. Ramesh Singh, Standing Counsel, GNCTD with Mr. Santosh Kumar Tiwari, ASC, Mr. Chirayu Jain and Ms. Nikita Goyal, Advocates for GNCTD.

Ms. Monika Arora, CGSC for R-2/UOI with Mr. Harsh Ahuja and Mr. Praveen Singh, Advocate for UOI.

The Order of the Court was delivered by

VIBHU BAKHRU, J.:— The petitioners have filed the above-captioned petitions, *inter alia*, impugning the notification No. DE.23 (386)/Sch.Br./2018 dated 19.12.2018 (hereafter 'the impugned notification') issued by the Directorate of Education (DoE), Government of National Capital Territory of Delhi. By the impugned notification, the Directorate of Education (DoE) has directed the Chairman/Manager/Principal to direct all schools (whether Government, Government Aided and Private Unaided Recognised schools) to comply with certain guidelines relating to implementation of the Measles and Rubella (MR) vaccination campaign. Under the said campaign, MR vaccines are to be administered to all children aged between nine months and fifteen years (the beneficiaries). The said guidelines, *inter alia*, provide that no consent would be required from the beneficiaries/their parents for implementing the MR Campaign.

2. The petitioners are, essentially, aggrieved by the decision of the respondents to forcibly administer MR vaccination without the consent of the parents/guardians or family members of the beneficiaries (children aged between nine months to fifteen years). The petitioners in W.P. (C) 350/2019 pray that the impugned notification be set aside and further directions be issued that no vaccination be administered in cases where there is parental objection to such vaccination. The petitioners in W.P. (C) 343/2019, *inter alia*, pray that an order be issued to the respondents restraining them from forcibly administering vaccinations to children without the consent of their

parents/guardians.

3. On 15.01.2019, this Court had observed that the contention of the petitioners, that children cannot be administered vaccination forcibly and without the parental consent, is merited. Mr. Singh, learned counsel appearing for DoE and Government of NCT of Delhi (respondent nos. 1 and 2) did not dispute the said proposition that readily accepted that vaccination cannot be administered forcibly and without the consent of the parents.

4. He, however, submitted that an express affirmative consent from parents/guardians of the beneficiaries ought not to be a pre-condition for administering the said vaccine. He contended that such consent of the parents/guardians should be inferred unless they expressly state in the negative. He referred to the same as "*opt-out consent*".

5. Plainly, in order for any parent or guardian to give his/her consent (whether expressly or by inference), it would be necessary for such parent or guardian to have complete information with regard to the proposed vaccination campaign. Clearly, for any parent or guardian to take an informed decision, it would be necessary for such parent to be aware of (a) the vaccine proposed to be administered; (b) contraindications or side effects of such vaccine; (c) the date on which such vaccine administered to the ward/children; and (d) the personnel who would administer the same.

6. Mr. Raj Shekhar Rao and Ms. Diya Kapur, learned counsel advanced arguments on behalf of the petitioners and Mr. Ramesh Singh advanced arguments on behalf of respondent nos. 1 and 2. It was apparent from the said arguments that learned counsel for both the sides were *ad idem* that vaccination could not be administered to children without consent of their parents/guardians. Mr. Pandey, learned counsel appearing for the Union of India, did not advance any submissions apart from stating that the MR Campaign was successfully implemented in twenty-six states of the country.

7. In view of the above, impugned notification, to the extent it provides that no consent is required for the beneficiaries and/or their parents, is quashed.

8. Mr. Singh, also readily agreed, on instructions, that information with regard to MR. campaign would require to be disseminated. He also handed over a tabular statement indicating the names of daily newspapers in English, Hindi, Urdu and Punjabi, which would carry the advertisements. It was also submitted that advertisements would be of a quarter page and would indicate the material information. It was also agreed that the said information would be put up on the website of DoE.

9. In view of the above, the controversy between the parties was narrowed down, essentially, on two issues, (a) whether an express consent of the parents/guardians was necessary or whether the same could be inferred by silence on the part of the concerned parents/guardians; and (b) whether the respondents were required to indicate the contraindications and the side effects of the vaccines in the newspaper advertisements as well as in other literature to be provided to parents/guardians of the beneficiaries.

10. Insofar as the first issue is concerned - that is, whether an express consent from parents/guardians is necessary - Mr. Singh contended that the vaccination campaign is required to cover at least 95% of the beneficiaries within a short span of time for the same to be successful and, therefore, there would not be enough time for respondents to elicit a positive express response from the parents/guardians. He had further submitted that there are a large number of students from EWS categories and it would be very difficult to ensure a response from the parents of such students. He further submitted that the respondents would also have no opportunity to counsel

such parents.

11. Ms. Diya Kapur countered the aforesaid submissions. She submitted that she had contacted certain schools and the data indicated that parents of EWS students, in most cases, had responded to the consent forms sent by the concerned schools. She referred to the case of one such school (Bal Bharti), where consent forms were sent to 856 students from the EWS category and 812 such consent forms were received back. Out of the aforesaid, 394 had not agreed for administration of the MR vaccine. She further contended that the contention of the respondents, that it is difficult to contact students from EWS category, is without basis. She further referred to various newspaper reports, which had reported incidents where the children had fallen sick after administration of the MR vaccine. She contended that it was, thus, necessary for parents to take an informed decision.

12. Mr. Singh, countered the aforesaid submissions and submitted that vaccination was a necessary measure for eradication of the diseases in question and those children, who are not vaccinated, may act as a disease vector putting the general health of others at risk. He contended that in larger public interest, it was necessary that the MR campaign be supported by all measures.

13. Undisputedly, there is an urgent need to disseminate information regarding the MR campaign and the assumption that children could be vaccinated forcibly or without consent is unsustainable. This Court is of the view that all efforts are required to be made to obtain the decision of the parents before proceeding with the MR campaign. In this regard, it would be apposite to ensure that the consent forms/slips are sent to each and every student. Since the time period for implementing the campaign is short, the response period should be reduced and parents/guardians of students must be requested to respond immediately and, in any case, in not more than three working days. If the consent forms/slips are not returned by the concerned parent, the class teacher must ensure that the said parents are contacted telephonically and the decision of such parent is taken on phone. The concerned teacher ought to keep full records of such decisions received telephonically. In respect of those parents/guardians that neither return the consent slips nor are available telephonically despite efforts by the concerned teacher, their consent can be presumed provided respondent nos. 1 and 2 ensure that full information regarding the commission is provided to all parents.

14. The contention that indication of the side effects and contraindications in the advertisement would discourage parents or guardians from consenting to the MR campaign and, therefore, the same should be avoided, is unmerited. The entire object of issuing advertisements is to ensure that necessary information is available to all parents/guardians in order that they can take an informed decision. The respondents are not only required to indicate the benefits of the MR vaccine but also indicate the side effects or contraindications so that the parents/guardians can take an informed decision whether the vaccine is to be administered to their wards/children.

15. In view of the above, it is directed as under:

(1) Directorate of Family Welfare shall issue quarter page advisements in various newspapers as indicated by the respondents, namely, The Hindustan Times, The Times of India, The Hindu, The Pioneer, The Indian Express, Delhi Tribune, Mail Today, The Asian Age, Navbharat Times, Dainik Jagran, Punjab Kesari, Hindustan, Amar Ujala, Navodaya Times, Hamara Samaj, Pratap, Daur-e-Jadeed, Jathedar, Jan Ekta. The advertisements shall also indicate that the vaccination shall be administered with Auto Disable Syringes to the eligible children by Auxiliary Nurse Midwifery. The advertisement shall also clearly indicate the side effects and contraindications as may be finalised by the Department of Preventive Medicine, All India Institute of Medical Sciences.

(2) The Head of Department of Preventive Medicine, All India Institute of Medical Sciences is directed to finalise the list of contraindications and risks associated with the vaccine being included in the aforesaid advertisements. Advertisements in two of the newspapers (one in English and the other in Hindi language) will also indicate the dates on which MR vaccine will be administered in respective schools. The website of DoE shall also clearly set out the above information.

(3) The School shall issue consent forms to parents of all students admitted in their schools up to Class X with instructions that the forms be returned to the school within a period of two working days. The class teacher/nodal teacher shall contact parents/guardians of students who have not returned the consent forms within a period of one working day thereafter and elicit their consent or objection to administration of such vaccines. The class teacher/nodal teacher shall keep a record of the decision of the parents so contacted. In the event the class teacher/nodal teacher is unable to reach parents despite best efforts, the record of the efforts made shall be duly noted by her.

(4) MR vaccines will not be administered to those students whose parents/guardians have declined to give their consent. The said vaccination will be administered only to those students whose parents have given their consent either by returning the consent forms or by conforming the same directly to the class teacher/nodal teacher and also to students whose parents/guardians cannot be contacted despite best efforts by the class teacher/nodal teacher and who have otherwise not indicated to the contrary.

16. It will be open for the DoE/Department of Health to approach the parents directly to inform them and educate them regarding the MR vaccine campaign in order to elicit their consent.

17. Mr. Singh had submitted that under the present MR Vaccination campaign, DoE is targeting 55 lakh children in the age group of nine months to fifteen years. of these 55 lakh children, approximately 34 lakh children are attending recognised schools; approximately 10-11 lakh children are attending unrecognised private/pre-nursery schools; and the remaining 10-11 lakh children are either not attending any school or are below the age of 3 years and are living with their parents/guardians.

18. It is made clear that the directions set out above relate only to students attending recognized schools. In respect of the remaining children, the respondents seek time of two to three weeks to submit the modalities of obtaining consent. Once these have been submitted, the court shall consider the conditions on which the MR campaign in respect of the remaining unrecognised private/pre-nursery schools and children not attending school shall proceed.

19. List for further proceedings on 01.02.2019.

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* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

\+ **W.P.(C) 343/2019 & CM No. 1604/2019 & 1605/2019**

MASTER HRIDAAN KUMAR MINOR
THROUGH AND ORS. ..... Petitioners

Through: Mr Raj Shekhar Rao, Mr Abhinav Mukerji and Mr Arijit Mazumdar, Advocates.

versus

UNION OF INDIA AND ANR. ..... Respondents

Through: Mr Sushil Kumar Pandey, Senior Panel Counsel, Ms Neha Sharma, Mr Anurudh Sukla, Advocates for R-1 with Dr Aggrwal, Health and Family Department.
Mr Ramesh Singh, Standing Counsel, GNCTD with Ms Nikira Goyal and Mr Chirayu Jain, Advocates for DOE.
Mr S. K. Tripathi, ASC, GNCTD for R-2.

AND

50.

\+ **W.P.(C) 350/2019 & CM Nos. 1642/2019, 1643/2019 & 1644/2019**

BABY VEDA KALAAN AND ORS. ..... Petitioners

Through: Ms Diya Kapur, Ms Shyel Trehan and Mr Rishabh Sharma, Advocates.

versus

DIRECTORATE OF EDUCATION AND ORS. ..... Respondents

Through: Mr Ramesh Singh, Standing Counsel, GNCTD with Ms Nikira Goyal and Mr Chirayu Jain, Advocates for DOE.

Ms Monika Arora, CGSC with Mr Kushal Kumar, Advocate for UOI. Mr S. K. Tripathi, ASC, GNCTD for R-1& 2.

CORAM:
HON'BLE MR. JUSTICE VIBHU BAKHRU

O R D E R

% 15.01.2019

1. The petitioners have filed the present petitions, *inter alia*, impugning a notification dated 19.12.2018 issued by the Directorate of Education, Government of National Capital Territory of Delhi (hereafter 'DoE'). By the said notification, the Chairman/Manger/Principal of all schools (Government, Government Aided, Private and Unaided Recognised Schools) have been informed that the Measles and Rubella Vaccine (MR) Campaign would be held, and all children aged between 9 months to 15 years will be provided an additional dose of MR vaccine, regardless of previous vaccination status or history of Measles /Rubella like illness.

2. The said notification also indicates that the vaccination would be administered without obtaining any consent from the beneficiaries or their parents. The petitioners are particularly, aggrieved by the said notification, inasmuch as, it compels them to be vaccinated under the Measles and Rubella Campaign without their consent. The learned counsel appearing for the petitioners have cited instances where the vaccination proposed to be administered has had certain adverse reactions. It is their case that the direction of the respondent to administer vaccines without obtaining consent of the beneficiaries/their parents violated their fundamental rights under the Constitution of India. The said contention is merited. This Court is also of

the view that the vaccination cannot be forcibly administered to any minor without the consent of his or her parents.

3. Mr Ramesh Singh, learned counsel appearing for the DoE does not dispute the aforesaid proposition.

4. The only question that remains to be addressed is whether an express positive consent from the parents/guardians ought to be a pre-condition for administering the said vaccine. Mr Singh contends that the vaccine be administered to all students unless parents of any of the students expressly objects to the same. He refers to the same as *opt out consent*.

5. Before proceeding to examine whether consent in this manner can be obtained. It is clear that all parents must have full information as to (a) the particulars of the vaccine proposed to be administered; (b) contra indications and side effects of such a vaccine; (c) the date on which such vaccine would be administered to their wards/children; and (d) the personnel who would administer the same.

6. The learned counsel appearing for the parties seeks time to address arguments as to how this information can be provided to the parents and whether it would be permissible to proceed on an assumption that they have consented to vaccination of their children/wards, unless they do not expressly object to such vaccination.

7. At their request, list on 21.01.2019.

8. Since, it is apparent that the consent of the parents/beneficiaries has not been obtained, and the respondents are proceeding on the basis that such a consent is not necessary, it is directed that the MR Campaign be deferred till further orders from this Court.

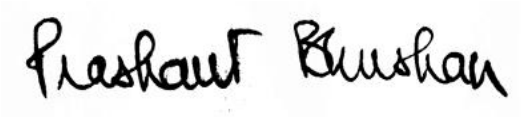
9. The Directorate of Education shall also contact the principals of some

of the schools with the object of eliciting information as to whether the parents of the students (including students from the EWS category) can be contacted on telephone by their respective class teachers for eliciting their consent to the vaccination.

10. Order *dasti* under signatures of the Court Master.

VIBHU BAKHRU, J

JANUARY 15, 2019
MK



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ANNEXURE: P20

Charter of Patients' Rights for adoption by NHRC

Patients' rights are Human rights!

Preamble

The Universal Declaration of Human Rights (1948) emphasizes the fundamental dignity and equality of all human beings. Based on this concept, the notion of Patient Rights has been developed across the globe in the last few decades. There is a growing consensus at international level that all patients must enjoy certain basic rights. In other words, the patient is entitled to certain amount of protection to be ensured by physicians, healthcare providers and the State, which have been codified in various societies and countries in the form of Charters of Patient's Rights. In India, there are various legal provisions related to Patient's Rights which are scattered across different legal documents e.g. The Constitution of India, Article 21, Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations 2002; The Consumer Protection Act 1986; Drugs and Cosmetic Act 1940, Clinical Establishment Act 2010 and rules and standards framed therein; various judgments given by Hon'ble Supreme Court of India and decisions of the National Consumer Disputes Redressal Commission.

This Charter of Patient's Rights adopted by the National Human Rights Commission draws upon all relevant provisions, inspired by international charters and guided by national level provisions, with the objective of consolidating these into a single document, thereby making them publicly known in a coherent manner. There is an expectation that this document will act as a guidance document for the Union Government and State Governments to formulate concrete mechanisms so that Patient's Rights are given adequate protection and operational mechanisms are set up

to make these rights functional and enforceable by law. This is especially important and an urgent need at the present juncture because India does not have a dedicated regulator like other countries and the existing regulations in the interest of patients, governing the healthcare delivery system is on the anvil, some States have adopted the national Clinical Establishments Act 2010, certain other States have enacted their own State level legislations like the Nursing Homes Act to regulate hospitals, while a few other States are in the process of adopting / developing such regulation. The Charter of Patient's Rights has been drafted with the hope that it shall be incorporated by policy makers in all existing and emerging regulatory legislations concerning the health care sector. This charter would also enable various kinds of health care providers to actively engage with this framework of patients' rights to ensure their observance, while also benefiting from the formal codification of patients responsibilities.

Another objective of this Charter is to generate widespread public awareness and educate citizens regarding what they should expect from their governments and health care providers—about the kind of treatment they deserve as patients and human beings, in health care settings. NHRC firmly believes that informed and aware citizens can play a vital role in elevating the standard of health care, when they have guidance provided by codified rights, as well as awareness of their responsibilities.

NHRC believes that this Charter of Patients' Rights will be an enabling document to ensure the protection and promotion of Human rights of those who are among some of the most vulnerable sections of society – ordinary patients and citizens seeking health care across India.

	Rights of patients	Description of rights and associated duty bearers	Reference
1	**Right to information**	Every patient has a right to adequate relevant information about the nature, cause of illness, provisional / confirmed diagnosis, proposed investigations and management, and possible complications To be explained at their level of understanding in language known to them. The treating physician has a duty to ensure that this information is provided in simple and intelligible language to the patient to be communicated either personally by the physician, or by means of his / her qualified assistants. Every patient and his/her designated caretaker have the right to factual information regarding the expected cost of treatment based on evidence. The hospital management has a duty to communicate this information in writing to the patient and his/her designated caretaker. They should also be informed about any additional cost to be incurred due to change in the physical condition	1) Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 2) MCI Code of Ethics 3) Patients Charter by National Accreditation Board for Hospitals (NABH) 4) The Consumer Protection Act, 1986

		of the patient or line of treatment in writing. On completion of treatment, the patient has the right to receive an itemized bill, to receive an explanation for the bill(s) regardless of the source of payment or the mode of payment, and receive payment receipt(s) for any payment made. Patients and their caretakers also have a right to know the identity and professional status of various care providers who are providing service to him / her and to know which Doctor / Consultant is primarily responsible for his / her care. The hospital management has a duty to provide this information routinely to all patients and their caregivers in writing with an acknowledgement.	
2	**Right to records and reports**	Every patient or his caregiver has the right to access originals / copies of case papers, indoor patient records, investigation reports (during period of admission, preferably within 24 hours and after discharge, within 72 hours). This may be made available wherever applicable after paying appropriate fees for photocopying or allowed to be photocopied by patients at their cost.	**1)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 **2)** MCI Code of Ethics section1.3.2 **3)** Central Information Commission

		The relatives / caregivers of the patient have a right to get discharge summary or in case of death, death summary along with original copies of investigations. The hospital management has a duty to provide these records and reports and to instruct the responsible hospital staff to ensure provision of the same are strictly followed without fail.	judgment, Nisha Priya Bhatia Vs. Institute of HB&AS, GNCTD, 2014 **4)** The Consumer Protection Act, 1986
3	**Right to Emergency Medical Care**	As per Supreme Court, all hospitals both in the government and in the private sector are duty bound to provide basic Emergency Medical Care, and injured persons have a right to get Emergency Medical Care. Such care must be initiated without demanding payment / advance and basic care should be provided to the patient irrespective of paying capacity. It is the duty of the hospital management to ensure provision of such emergency care through its doctors and staff, rendered promptly without compromising on the quality and safety of the patients.	**1)** Supreme court judgment Parmanand Katara v. Union of India (1989) **2)** Judgment of National Consumer Disputes Redressal Commission Pravat Kumar Mukherjee v. Ruby General Hospital & Others (2005) **3)** MCI Code of Ethics sections 2.1 and 2.4 **4)** Article 21 of the Constitution 'Right to Life'

4	**Right to informed consent**	Every patient has a right that informed consent must be sought prior to any potentially hazardous test/treatment (e.g. invasive investigation / surgery / chemotherapy) which carries certain risks. It is the duty of the hospital management to ensure that all concerned doctors are properly instructed to seek informed consent, that an appropriate policy is adopted and that consent forms with protocol for seeking informed consent are provided for patients in an obligatory manner. It is the duty of the primary treating doctor administering the potentially hazardous test / treatment to explain to the patient and caregivers the main risks that are involved in the procedure, and after giving this information, the doctor may proceed only if consent has been given in writing by the patient / caregiver or in the manner explained under Drugs and Cosmetic Act Rules 2016 on informed consent.	**1)** MCI Code of Ethics section 7.16 **2)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 **3)** The Consumer Protection Act, 1986 **4)** Drugs and Cosmetic Act 1940, Rules 2016 on Informed Consent
5	**Right to confidentiality,**	All patients have a right to privacy, and doctors have a duty to hold information about their health condition and treatment plan in strict confidentiality, unless	**1)** MCI Code of Ethics sections 2.2**,** 7.14 and 7.17.

	human dignity and privacy	it is essential in specific circumstances to communicate such information in the interest of protecting other or due to public health considerations. Female patients have the right to presence of another female person during physical examination by a male practitioner. It is the duty of the hospital management to ensure presence of such female attendants in case of female patients. The hospital management has a duty to ensure that its staff upholds the human dignity of every patient in all situations. All data concerning the patient should be kept under secured safe custody and insulated from data theft and leakage.	**2)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010
6	**Right to second opinion**	Every patient has the right to seek second opinion from an appropriate clinician of patients' / caregivers' choice. The hospital management has a duty to respect the patient's right to second opinion, and should provide to the patients caregivers all necessary records and information required for seeking such opinion without any extra cost or delay. The hospital management has a duty to ensure that any decision to seek such	**1)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 **2)** The Consumer Protection Act, 1986

		second opinion by the patient / caregivers must not adversely influence the quality of care being provided by the treating hospital as long as the patient is under care of that hospital. Any kind discriminatory practice adopted by the hospital or the service providers will be deemed as Human Rights' violation.	
7	**Right to transparency in rates, and care according to prescribed rates wherever relevant**	Every patient and their caregivers have a right to information on the rates to be charged by the hospital for each type of service provided and facilities available on a prominent display board and a brochure. They have a right to receive an itemized detailed bill at the time of payment. It would be the duty of the Hospital / Clinical Establishment to display key rates at a conspicuous place in local as well as English language, and to make available the detailed schedule of rates in a booklet form to all patients / caregivers. Every patient has a right to obtain essential medicines as per India Pharmacopeia, devices and implants at rates fixed by the National Pharmaceutical Pricing Authority (NPPA) and other relevant authorities. Every patient has a right to receive health care services within the range of rates for procedures and services prescribed by Central and State Governments from	**1)** MCI Code of Ethics section 1.8 regarding Payment of Professional Services **2)** Section 9(i) and 9(ii) of Clinical establishments (Central Government) Rules 2012 **3)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 **4)** Various Drug price control orders **5)** The Consumer Protection Act, 1986

		time to time, wherever relevant. However, no patient can be denied choice in terms of medicines, devices and standard treatment guidelines based on the affordability of the patients' right to choice. Every hospital and clinical establishment has a duty to ensure that essential medicines under NLEM as per Government of India and World Health Organisation, devices, implants and services are provided to patients at rates that are not higher than the prescribed rates or the maximum retail price marked on the packaging.	**6)** Drugs Price Control Order (DPCO) section 3 of the Essential Commodities Act, 1955
8	**Right to non-discrimination**	Every patient has the right to receive treatment without any discrimination based on his or her illnesses or conditions, including HIV status or other health condition, religion, caste, ethnicity, gender, age, sexual orientation, linguistic or geographical /social origins. The hospital management has a duty to ensure that no form of discriminatory behaviour or treatment takes place with any person under the hospital's care. The hospital management must regularly orient and instruct all its doctors and	**1)** Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010

		staff regarding the same.	
9	**Right to safety and quality care according to standards**	Patients have a right to safety and security in the hospital premises. They have a right to be provided with care in an environment having requisite cleanliness, infection control measures, safe drinking water as per BIS/FSSAI Standards and sanitation facilities. The hospital management has a duty to ensure safety of all patients in its premises including clean premises and provision for infection control. Patients have a right to receive quality health care according to currently accepted standards, norms and standard guidelines as per National Accreditation Board for Hospitals (NABH) or similar. They have a right to be attended to, treated and cared for with due skill, and in a professional manner in complete consonance with the principles of medical ethics. Patients and caretakers have a right to seek redressal in case of perceived medical negligence or damaged caused due to deliberate deficiency in service delivery. The hospital management and treating doctors have a duty to provide quality health care in accordance with current standards of care and standard treatment guidelines and to avoid medical negligence or deficiency in service	**1)** Clinical establishments (Central Government) Rules 2012 **2)** The Consumer Protection Act, 1986

		delivery system in any form.	
10	**Right to choose alternative treatment options if available**	Patients and their caregivers have a right to choose between alternative treatment / management options, if these are available, after considering all aspects of the situation. This includes the option of the patient refusing care after considering all available options, with responsibility for consequences being borne by the patient and his/her caregivers. In case a patient leaves a healthcare facility against medical advice on his / her own responsibility, then notwithstanding the impact that this may have on the patient's further treatment and condition, this decision itself should not affect the observance of various rights mentioned in this charter. The hospital management has a duty to provide information about such options to the patient as well as to respect the informed choice of the patient and caregivers in a proper recorded manner with due acknowledgement from the patient or the caregivers on the communication and the mode.	1) Annexure 8 of standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical Establishment Act 2010 2) The Consumer Protection Act, 1986
11	**Right to choose source for**	When any medicine is prescribed by a doctor or a hospital, the patients and their caregivers have the right to choose any registered pharmacy of their	1) Various judgments by the National Consumer Dispute Redressal

	obtaining medicines or tests	choice to purchase them. Similarly when a particular investigation is advised by a doctor or a hospital, the patient and his caregiver have a right to obtain this investigation from any registered diagnostic centre/laboratory having qualified personnel and accredited by National Accreditation Board for Laboratories (NABL). It is the duty of every treating physician / hospital management to inform the patient and his caregivers that they are free to access prescribed medicines / investigations from the pharmacy / diagnostic centre of their choice. The decision by the patient / caregiver to access pharmacy / diagnostic centre of their choice must not in any ways adversely influence the care being provided by the treating physician or hospital.	Commission 2) The Consumer Protection Act, 1986
12	**Right to proper referral and transfer, which is free from perverse commercial**	A patient has the right to continuity of care, and the right to be duly registered at the first healthcare facility where treatment has been sought, as well as at any subsequent facilities where care is sought. When being transferred from one healthcare facility to another, the patient / caregiver must receive a complete explanation of the justification for the transfer, the alternative options	1) Medical Council of India code of ethics section 3.6 2) World Health Organisation – Referral Notes 3) Various IPHS documents

	influences	for a transfer and it must be confirmed that the transfer is acceptable to the receiving facility. The patient and caregivers have the right to be informed by the hospital about any continuing healthcare requirements following discharge from the hospital. The hospital management has a duty to ensure proper referral and transfer of patients regarding such a shift in care. In regard to all referrals of patients, including referrals to other hospitals, specialists, laboratories or imaging services, the decision regarding facility to which referral is made must be guided entirely by the best interest of the patient. The referral process must not be influenced by any commercial consideration such as kickbacks, commissions, incentives, or other perverse business practices.	
13	**Right to protection for patients involved in clinical trials**	Every person / patient who is approached to participate in a clinical trial has a right to due protection in this context. All clinical trials must be conducted in compliance with the protocols and Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organisation, Directorate General of Health	1) Protocols and Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organisation, Directorate General

		Services, Govt. of India as well as all applicable statutory provisions of Amended Drugs and Cosmetics Act, 1940 and Rules, 1945, including observance of the following provisions related to patients rights: a) Participation of patients in clinical trials must always be based on informed consent, given after provision of all relevant information. The patient must be given a copy of the signed informed consent form, which provides him / her with a record containing basic information about the trial and also becomes documentary evidence to prove their participation in the trial. b) A participant's right to agree or decline consent to take part in a clinical trial must be respected and her/his refusal should not affect routine care. c) The patient should also be informed in writing about the name of the drug / intervention that is undergoing trial along with dates, dose and	of Health Services, Govt. of India 2) Amended Drugs and Cosmetics Act, 1940 and Rules, 1945 especially schedule Y 3) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, Indian Council of Medical Research, New Delhi, 2017 4) World Medical Assembly Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects available at www.wma.net/en/30publications/10policies/b3/17c.pdf

		duration of administration. d) At all times, the privacy of a trial participant must be maintained and any information gathered from the participant must be kept strictly confidential. e) Trial participants who suffer any adverse impact during their participation in a trial are entitled to free medical management of adverse events, irrespective of relatedness to the clinical trial, which should be given for as long as required or till such time as it is established that the injury is not related to the clinical trial. In addition, financial or other assistance must be given to compensate them for any impairment or disability. In case of death, their dependents have the right to compensation. f) Ancillary care may be provided to clinical trial participants for non-study/trial related illnesses arising during the period of the trial. This could be in the form of medical care or reference to facilities, as may be	

		appropriate. g) Institutional mechanisms must be established to allow for insurance coverage of trial related or unrelated illnesses (ancillary care) and award of compensation wherever deemed necessary by the concerned Ethics Committee. h) After the trial, participants should be assured of access to the best treatment methods that may have been proven by the study. Any doctor or hospital who is involved in a clinical trial has a duty to ensure that all these guidelines are followed in case of any persons / patients involved in such a trial.	
14	**Right to protection of participants involved in biomedical and**	Every patient who is taking part in biomedical research shall be referred to as research participant and every research participant has a right to due protection in this context. Any research involving such participants should follow the National Ethical Guidelines for Biomedical and Health Research Involving Human	1) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, Indian Council of Medical Research,

	health research	Participants, 2017 laid down by Indian council for Medical Research and should be carried out with prior approval of the Ethics Committee. Documented informed consent of the research participants should be taken. Additional safeguards should be taken in research involving vulnerable population. Right to dignity, right to privacy and confidentiality of individuals and communities should be protected. Research participants who suffer any direct physical, psychological, social, legal or economic harm as a result of their participation are entitled, after due assessment, to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. The benefits accruing from research should be made accessible to individuals, communities and populations whenever relevant.	New Delhi, 2017 2) World Medical Assembly Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects available at www.wma.net/en/30publications/10policies/b3/17c.pdf 3) Drugs & Cosmetic Act, Rules 2016 on Clinical Trails

		Any doctor or hospital who is involved in biomedical and health research involving patients has a duty to ensure that all these guidelines are followed in case of any persons / patients involved in such research.	
15	**Right to take discharge of patient, or receive body of deceased from hospital**	A patient has the right to take discharge and cannot be detained in a hospital, on procedural grounds such as dispute in payment of hospital charges. Similarly, caretakers have the right to the dead body of a patient who had been treated in a hospital and the dead body cannot be detailed on procedural grounds, including nonpayment/dispute regarding payment of hospital charges against wishes of the caretakers. The hospital management has a duty to observe these rights and not to indulge in wrongful confinement of any patient, or dead body of patient, treated in the hospital under any circumstances.	1) Prohibition of wrongful confinement under Sec. 340-342 of IPC. Statements of Mumbai High Court. 2) Consumer Protection Act 1986
16	**Right to Patient Education**	Patients have the right to receive education about major facts relevant to his/her condition and healthy living practices, their rights and responsibilities, officially supported health insurance schemes relevant to the patient, relevant entitlements in case of charitable hospitals, and how to seek redressal of	1) The Consumer Protection Act, 1986 2) Standards for Hospital level 1 by National Clinical Establishments Council set up as per Clinical

		grievances in the language the patients understand or seek the education. The hospital management and treating physician have a duty to provide such education to each patient according to standard procedure in the language the patients understand and communicate in a simple and easy to understand manner.	Establishment Act 2010
17	**Right to be heard and seek redressal**	Every patient and their caregivers have the right to give feedback, make comments, or lodge complaints about the health care they are receiving or had received from a doctor or hospital. This includes the right to be given information and advice on how to give feedback, make comments, or make a complaint in a simple and user-friendly manner. Patients and caregivers have the right to seek redressal in case they are aggrieved, on account of infringement of any of the above mentioned rights in this charter. This may be done by lodging a complaint with an official designated for this purpose by the hospital / healthcare provider and further with an official mechanism constituted by the government such as Patients'	1) The Consumer Protection Act, 1986 2) NHS - Charter of Patient Rights and Responsibilities

		rights Tribunal Forum or Clinical establishments regulatory authority as the case may be. All complaints must be registered by providing a registration number and there should be a robust tracking and tracing mechanism to ascertain the status of the complaint resolution. The patient and caregivers have the right to a fair and prompt redressal of their grievances. Further, they have the right to receive in writing the outcome of the complaint within 15 days from the date of the receipt of the complaint. Every hospital and clinical establishment has the duty to set up an internal redressal mechanism as well as to fully comply and cooperate with official redressal mechanisms including making available all relevant information and taking action in full accordance with orders of the redressal body as per the Patient's Right Charter or as per the applicable existing laws.	

Responsibilities of patients and caretakers

Along with promoting their rights, patients and caretakers should follow their responsibilities so that hospitals and doctors can perform their work satisfactorily.

1) Patients should provide all required health related information to their doctor, in response to the doctor's queries without concealing any relevant information, so that diagnosis and treatment can be facilitated.

2) Patients should cooperate with the doctor during examination, diagnostic tests and treatment, and should follow doctor's advice, while keeping in view their right to participate in decision making related to treatment.

3) Patients should follow all instructions regarding appointment time, cooperate with hospital staff and fellow patients, avoid creating disturbance to other patients, and maintain cleanliness in the hospital.

4) Patients should respect the dignity of the doctor and other hospital staff as human beings and as professionals. Whatever the grievance may be, patient / caregivers should not resort to violence in any form and damage or destroy any property of the hospital or the service provider**.**

5) The Patients should take responsibility for their actions based on choices made regarding treatment options, and in case they refuse treatment (not clear???).

Recommended mechanism for implementation of Charter of Patient's Rights and Grievance redressal mechanism

NHRC recommends to the Government of India, all State Governments and Administration of all the Union Territories that they should seriously consider the adoption of the charter and incorporate this Charter of Patients' Rights in the entire range of existing and emerging regulatory frameworks concerning the health care sector, under their jurisdiction.

Further NHRC recommends that all State Human Rights Commissions should adopt the Charter of Patients' Rights to be treated as a reference document in all cases related to human rights violations concerning patients and all users of health care services.

NHRC further recommends that all administrative and regulatory authorities completely or partially related with the healthcare sector, including but not limited to the following should incorporate and promote implementation of the Charter of Patient's Rights within their jurisdiction wherever applicable.

1. Ministry of Health and Family Welfare, Government of India
2. Public Health and Family Welfare Departments in all States and UTs
3. Medical Education Department of States and UTs, wherever they exist
4. Executive/Managing authorities of all publicly funded healthcare insurance schemes and Public-Private-Partnership arrangements in healthcare by Government of India, all State Governments and administrations in all UTs
5. National Council for Clinical Establishments
6. State Councils for Clinical Establishments, wherever applicable

7. Authorities established under State Nursing Home Acts or equivalent acts, wherever applicable
8. Medical Council of India / National Medical Commission or equivalent body
9. State Medical Councils in all States and UTs
10. Central Council of Indian Medicine
11. State Councils for Indian Medicine in all States and UTs
12. Any other healthcare related statutory councils established in all States and UTs
13. Central Consumer Protection Council, all State and District consumer protection councils
14. Registrar of Societies in all States and UTs, in the context of non-profit clinical establishments
15. Charity Commissioner in those States wherever applicable, in the context of non-profit clinical establishments
16. Department of Religious and Charitable Endowments in those States wherever applicable, in the context of non-profit clinical establishments
17. Registrar of Companies, in the context of for-profit hospitals run by companies and non-profit clinical establishments run by companies registered under Section 25
18. Central Drugs and Standard Control Organisation, Ministry of Health & Family Welfare, Government of India

19. Quality Council of India, New Delhi

20. Department of Consumer Affairs, Ministry of Consumer Affairs, Food & Public Distribution, Government of India

Once the Patients' Rights Charter has been adopted by the Govt. of India, State Governments and the Administration of the Union Territories, they may stipulate/ensure that all types of Clinical Establishments (both therapeutic and diagnostic) display this Charter prominently within their premises, orient all their staff and consultants regarding the Charter, and observe the Charter of Patients' Rights in letter and spirit irrespective of whether such clinical establishment is owned, controlled or managed by-

i. the Government or a department of the Government;
ii. a trust, whether public or private;
iii. a corporation (including a society) registered under a Central, Provincial or State Act, whether or not owned by the Government;
iv. a privately owned enterprise;
v. a local authority

Further, NHRC recommends to the Government of India, all State Governments and administration of Union Territories to ensure the setting up of a grievance redressal mechanism for patients, as a component of their existing or emerging regulatory frameworks for clinical establishments, by making required modifications in rules, regulations and acts where required. Observance of patients' rights and setting up of grievance

redressal mechanism for protection of these Rights should be made an integral component of the implementation of Clinical Establishment (Registration and Regulation) Act 2010 in those states who have adopted it, or as a component of state specific regulatory frameworks for clinical establishments in other states, which have equivalent state specific legislations, or are planning to enact state specific legislations to regulate clinical establishments.

NHRC recommends that Patients' rights grievance redressal mechanisms should have the following components-

1. Every clinical establishment should set up an internal grievance redressal mechanism. First, patients may file a complaint with an authorized representative who can be named 'Internal Grievance Redressal Officer' of the clinical establishment, either individually in person through an authorized representative or collectively through a consumer group or civil society organization. The clinical establishment's Internal Grievance Redressal Officer shall consider the complaint and try to find an appropriate solution, keeping in view the provisions of the Patients' Rights Charter and promptly acknowledge the receipt of the complaint within 24 hours by assigning a registration number for tracking and tracing the status of the complaint.

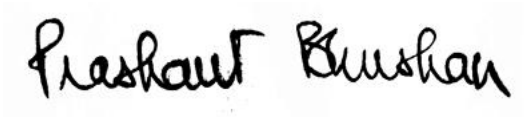
2. If a solution acceptable to the patient is not found at the level of the clinical establishment and the patient/representative is not satisfied, then he/she may approach the office of the district level registering authority set up under Clinical Establishment (Registration and Regulation) Act 2010 in those States who have adopted it, or equivalent district level authorities created under the State specific clinical establishments act or similar regulatory frameworks for clinical establishments in other states which have other State specific legislations. The district level registering authority shall verify the facts of the matter, and where there is clear violation of patient's

rights as brought out facts, the registering authority may issue necessary executive orders to the clinical establishment for rectification. If there is any dispute over interpretation of Charter of Patient's Rights and provisions in the regulatory framework, the registering authority may clarify the procedure, rules, regulations and attempt to resolve the complaint through mediation between both parties within 30 days from the date of receipt of the appeal.

3. In case of any particular complaint, if even after completing the above mentioned procedure, the patient or his/her representative is not satisfied, then he/she can file appeal before the State Council of Clinical Establishments under Clinical Establishment (Registration and Regulation) Act 2010 in those states who have adopted the Act. Section 8(5)(e) empowers the 'State Council for Clinical Establishments' to hear appeals against the orders of the District Registering Authority set up under CEA 2010. 'State Council of Clinical Establishment' can set up a three or five member sub-committee / cell (with multi-stakeholder participation) which can be named as 'Healthcare Grievance Redressal Authority' for resolution of patient's grievances, and pass rectification orders or disciplinary orders or punitive orders which would be binding upon the clinical establishments within the framework of CEA within 30 days from the date of receipt of the appeal. The complaints procedure to be set up under the State Council of Clinical Establishments should explicitly state that it is not intended as a means of achieving monetary compensation.

4. Apart from the above mentioned grievance redressal mechanisms, patients/representatives would always be free to approach the State Medical Council to seek disciplinary action against unethical conduct of any specific doctor, and also free to approach Consumer Forums at

various levels to seek financial compensation, or approach Civil/Criminal Courts keeping in view the nature of the complaint i.e., creation of a separate grievance redressal machinery to deal with violations of Patients' Rights Charter shall in no way either extinguish or affect adversely the existing legal remedies both civil and criminal available to patients and their caregivers under the existing legal framework.



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Government of Haryana
Haryana State Disaster Management Authority

No. DMC-SPO-2020/14198 Dated: 01.01.2022

ORDER

Whereas vide order No. DMC-SPO-2020/5215 dated 02.05.2021, the State Executive Committee had initially declared a lockdown from 03.05.2021 (05:00 am onwards) to 10.05.2021 (till 05:00 am) and subsequently the same was extended from time to time, till 05.01.2022 in the State of Haryana.

However, keeping in view the emergence of Omicron variant and persistent rise in COVID-19 cases in the State, in exercise of the powers conferred under Section 22(2)(h) of the Disaster Management Act, 2005, the undersigned in my capacity as Chairperson, State Executive Committee do hereby direct to impose the guidelines of **Mahamari Alert–Surakshit Haryana**'महामारी अलर्ट–सुरक्षित हरियाणा' from 02.01.2022 (05:00 am onwards) to 12.01.2022 (till 05:00 am) in the State of Haryana, as follows:-

I. On the basis of daily positive cases, the following restrictions are imposed in the **Group A** districts with the highest daily infection rates viz., Gurugram, Faridabad, Ambala, Panchkula and Sonipat:-

- All cinema halls, theaters, multiplexes shall remain closed.
- All Sports complexes, stadia, swimming pools shall remain closed (except being used for training of sports persons for participation in National/International sports events as well as for organizing National/International sports events). No Spectators or visitors are to be allowed.
- All entertainment parks and B2B exhibitions are prohibited
- Offices (Government and Private), except for emergency/essential services, are advised to function with 50% staff attendance.
- Malls and Markets are allowed to open up to 05:00 PM.
- Bars and Restaurants are allowed to operate with 50% seating capacity

II. COVID-19 vaccination

- Only fully vaccinated persons are allowed to enter at places like sabzi mandi, grain markets, public Transport (Bus Stand and Railway stations), parks, religious places, bars, restaurants, hotels, departmental stores, ration shops, liquor and wine shops, malls, shopping complexes, cinema hall, haats, local markets, petrol and CNG Stations, LPG gas cylinder collection centers, sugar mills, milk booths, yogshalas, gym, fitness centers, all Government/Board/Corporation offices, private and Government Sector banks. The onus of ensuring this will be on the owners/management of these institutions.
- Truck and auto rickshaw unions shall allow only fully vaccinated persons.
- COVID-19 Vaccination of eligible persons (more than 15 Years) is mandatory.
- Citizens, who have received the 1st dose but the 2nd dose is not due, shall not come under above mentioned restrictions for mandatory 2nd dose (in case

COVISHIELD beneficiary will be eligible for second dose after 84 days from first dose and in case of COVAXIN beneficiary will be eligible for second dose after 28 days from first dose). The following means may be considered for verifying the vaccination status:-

1.Downloaded certificates of 2nd dose (Hard/soft copies)

2.1st dose certificate to check if 2nd dose is due or not.

3.Person not having smart phones, text message sent via COWIN portal (NHPSMS) may be considered for successful vaccination.

4.Arogya Setu app to check vaccination status.

- Adequate publicity of all above mentioned measures to be done by districts to ensure awareness among general public regarding making COVID-19 vaccination mandatory. Vaccination camps shall be arranged by the Deputy Commissioners. Health Department shall depute vaccination teams where and whenever demanded by the Deputy Commissioners for on spot vaccination or for regular vaccination camps at places of gatherings.

III. In **non-group A** districts, the followings restrictions are imposed:-

- For gatherings more than 100, prior permission of concerned Deputy Commissioners should be solicited.
- Cinema Halls (in malls and stand alone), Restaurants, bars (including in hotels and in malls), gyms, spas and club houses/ restaurants/ bars of the Golf Courses are allowed to open with 50% seating capacity with adherence to requisite social distancing, other COVID-19 appropriate safety norms and regular sanitisation of the premises.

IV. School, Colleges, Polytechnics, ITIs, Coaching institutions, Libraries and Training Institutes (whether Government or private), Anganwadi Centers and Creches under Woman and Child development Department shall remain closed in the State.

V. In funeral and marriages, gatherings shall not be more than 50 and 100 persons, respectively, subject to strict observance of COVID-19 appropriate behavioural norms and social distancing.

VI. NGOs and Urban Local Bodies Department are advised to distribute masks in the public.

VII. "No Mask-No Service" will be strictly observed in the State.

VIII. The violators of COVID-19 appropriate behavior including wearing of masks, social distancing and persons(adults) who have not received any COVID-19 vaccination dose or due for 2nd COVID-19 vaccination dose, shall be imposed a fine of Rs. 500/- by issuing a Challan. Institutional violators shall be imposed a fine of Rs. 5000/-, similarly. Non-payment of fine and major violations will attract proceedings under the provisions of Section 51 to 60 of the Disaster Management Act, 2005, besides legal action under Section 188 of the IPC, and other legal provisions as applicable.

IX.Night movement restrictions shall be continued from 11:00 PM to 05:00 AM in the State strictly.

However, the following guidelines shall continue in the districts, except where specific restrictions have been imposed, as released vide earlier orders dated 24.12.2021:-

a. Conduct of entrance and recruitment examinations by different Universities/Institutes/ Government Departments and Recruitment Agencies are allowed in the State with strict implementation of "Revised SOP issued by Ministry of Health and Family Welfare, GOI dated 10.09.2020 regarding preventive measures to contain spread of COVID-19" as well as guidelines released by Central/State Government/Departments time to time.

b. Swimming Pools are allowed to open after adopting requisite social distancing norms, regular sanitisation and Covid appropriate behavioural norms. All swimmers/ practioners/eligible visitors and staff to preferably get vaccinated with both doses of COVID-19 vaccine.

c. Sports Complexes, Stadia are permitted to open for sports activities including for outdoor sports activities except contact sports. Sports Authorities shall ensure adherence to requisite social distancing norms, regular sanitisation of the premises and COVID-19 appropriate behavioural norms.

d. Religious places are allowed to open with 50 persons at one time with the condition that they shall follow requisite social distancing norms, regular sanitisation and COVID-19 appropriate behavioural norms.

e. Corporate Offices are permitted to open with full attendance subject to strict observance of social distancing, COVID-19 appropriate behavioural norms and regular sanitisation.

f. All production units, establishments, Industries are permitted to function. However they shall strictly adhere to COVID-19 appropriate and prescribed guidelines, behavioural norms and Social distancing.

There will be continuous focus on the fivefold strategy for effective management of COVID-19 i.e. Test-Trace-Track-Vaccination and adherence of COVID-19 appropriate behaviour.

The Deputy Commissioners of the concerned districts are hereby directed/authorised to implement the above mentioned guidelines strictly. Department of Information, Public Relations and Langugaes, Haryana shall release advertisements for awareness of general public.

(SANJEEV KAUSHAL)
Chief Secretary-cum-Chairperson
Haryana State Executive Committee

To

1. All Administrative Secretaries in the State of Haryana.
2. The Director General of Police.
3. All Deputy Commissioners in the State of Haryana.

Note: - HSDMA orders can be seen at our website https://revenueharyana.gov.in/. Any message not on the website may be treated as fake.

Prashant Bhushan

(TRUE COPY)

PROCEEDINGS OF THE DISTRICT EDUCATIONAL OFFICER : : YSR DISTRICT, KADAPA
Present : Smt. P. Sailaja, M.Sc., B.Ed.,

Rc.No.1Spl /A6/2022 Dated:01.01.2022

Sub: School Education - Covid - 19 - Complete vaccination to all the students in the age group of 15-18 from 03.01.2022 to 10.01.2022 in the respective Sachivalams - Instructions - Issued - Regarding.

Ref: Telephonic instructions of the Joint Collector (V,WS & D), YSR District on 01.01.2022.

oOo

In pursuance of the instructions issued by the Joint Collector (V, WS & D), YSR District in the reference cited, all the Deputy Educational Officers and Mandal Educational Officers in the district are requested to inform all the Headmasters of High Schools and Principals of Junior Colleges/AP Model Schools and Special Officers of KGBVs under their jurisdiction to complete vaccination (Covid-19) to all the students in the age group of 15-18 from 03.01.2022 to 10.01.2022 in their respective Sachivalams and see that all students are vaccinated.

Further, they are informed that it is the responsibility of the Principals / Headmasters concerned to do vaccination of each and every student of their institutions within the schedule time and they are personally held responsible if any complaints received for non-vaccination of any student in this regard. Therefore, they are once again requested to complete the vaccination to all the students in the age group of 15-18 within the time schedule without fail.

Top most priority should be given to this item of work.

Sd/- P. Sailaja
District Educational Officer
YSR District, Kadapa.

To
All the Deputy Educational Officers & Mandal Educational Officers in the district.
Copy to the District Vocational Educational Officer, O/o Regional Inspection Officer, Kadapa for information.
Copy transmitted to the Regional Inspection Officer, Kadapa for information.
Copy submitted to the Regional Joint Director of Intermediate Education with a request to issue instructions to the Principals of Junior Colleges in this regard.
Copy submitted to the Joint Collector (V,WS &D), YSR District for favour of kind information.
Copy to file.

Prashant Bhushan

(TRUE COPY)

ANNEXURE: A23

Deccan Herald

Parents fume after some Karnataka schools make Covid-19 vaccinations mandatory

Several schools made vaccination mandatory and sent out warning messages as the vaccination programme kicked off

Rashmi Belur, Bengaluru, JAN 04 2022, 00:32 IST | UPDATED: JAN 04 2022, 12:25 IST

As kids in the 15-18 age group began getting jabbed against Covid-19 on Monday, parents began receiving messages.

"Vaccination done for 10 A girls. Those who were absent must be vaccinated at whichever place you prefer. Submission of certificates is a must by this week itself. It is compulsory, take it seriously," read one message that was sent by a CBSE school and shared with DH by a parent.

The message spooked the parents. "We were really shocked with the communication from school saying children will not be allowed to write board exams if they are not vaccinated," said the parent. "What kind of rule is this?"

"It is for parents to decide and we demand that concerned authorities should instruct schools about the same."

Such sentiments were also echoed by other parents that DH met after several schools made vaccination mandatory and sent out warning

messages as the vaccination programme kicked off amid a Covid-19 surge. Parents revealed that some of the private unaided schools sent out messages on Sunday evening itself, mandating offline attendance for children on Monday following the vaccination session.

"My daughter's school has made vaccination compulsory," said a parent. "They have been given the option to get it done outside or at the camp to be organised at the school. But we need to submit a vaccination certificate if the child has to attend offline or online classes from January second week."

While several parents disapproved of schools making vaccination mandatory, at least one school batted for "caution" over the jabs that has triggered anxiety.

"Vaccination for children is a government advisory. However, parental consent is required to facilitate the same on our campus. The schools will also need to gauge the current scenario and proceed with caution," said Aloysius D'mello, principal of Greenwood High International School, Bengaluru.

On the other hand, government schools had a different kind of problem. At some schools, despite requests, most of the parents and kids did not turn up, with the former citing several issues.

School principals asked parents to get their wards jabbed whenever and wherever it is convenient for them.

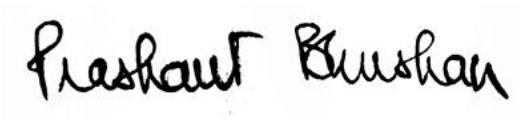
Dr Vishal R, Commissioner, Department of Public Instruction, sought to allay fears of parents.

"Vaccination is not mandatory, but parents should take it on a positive note," he told DH.

But the private schools' management association advised parents to consider vaccination as a responsibility.

"All these days parents said they were waiting for vaccines for children. Now, instead of blaming schools for making it mandatory, let them take it as a responsibility and get the kids vaccinated," said D Shashi Kumar, general secretary of Associated Managements of Primary and Secondary Schools in Karnataka.

Link: https://www.deccanherald.com/state/top-karnataka-stories/parents-fume-after-some-karnataka-schools-make-covid-19-vaccinations-mandatory-1067706.html



(TRUE COPY)

Government of India
Ministry of Women and Child Development
(Child Welfare-II Section)

Room No.640, A-Wing,
Shastri Bhawan, New Delhi
Dated: 04th January, 2022

To,

The Principal Secretaries / Secretaries
WCD/SJE (All States/UTs)

Subject: Preventive measures to contain spread of COVID 19 & new variant Omicron - Vaccination of Children in CCIs - Reg

Madam/Sir,

Please refer to the Order of Ministry of Home Affairs No. 40-3/2020-DM-I (A) dated 27th December 2021, whereby States/UTs have been directed in view of the initial surge in cases of COVID-19 as well as detection of the Variant of Concern (VoC), Omicron in different parts of the country, to consider implementation of the normative framework to contain spread of COVID-19. MoHFW vide D.O letter No. Z.28015/318/21-EMR, dated 21st December, 2021 has issued an advisory to all States/UTs, prescribing a framework for taking evidence based containment measures at district/local level.

2. In continuation of the advisories/guidelines issued by Ministry of Women and Child Development requesting the States/UTs to ensure care and protection of Children adversely impacted by COVID especially Children living in Child Care Institutions (CCIs), while following the protocol as mandated under Juvenile Justice (Care and Protection of Children) Act, 2015; it is stated that while number of actions have been taken by the States/UTs, it is necessary to continue the efforts relentlessly, to bring all children under the safety net provided under the Government Schemes and programmes.

3. Further, it is brought to the notice that in light of the compulsory vaccination of children against COVID-19 falling in the **15-18 age group**, it is requested that all District Magistrates may be directed to make appropriate arrangements on for vaccination of the Children living in CCIs as well, on priority basis.

4. An update on Children vaccinated in CCIs may be shared on a fortnightly basis with MWCD. The Person In-charge of CCI/Superintendent shall keep record of the vaccination administered to these Children along with vaccination teams in the following format:

Date	No. of eligible Children	No. of Children Vaccinated	Percentage of Vaccination

5. It is further requested to ensure that report for first fortnight from 1st January 2022 - 15th January 2022 is sent to the Ministry in the above format at email **cw2section-mwcd@gov.in** on the next working day. The regular progress of vaccination may be mailed for every fortnight thereafter, till completion of vaccination process.

Encl. : As above.

Yours faithfully,

04.01.202

(Navendra Singh)
Director to the Govt. of India
e-mail: navendra.singh@nic.in

Copy for information to:

1. Principal Secretary (H&FW), Health and Family Welfare Department (All States/UTs).
2. MD, NHM, All States/UTs.
3. Member Secretary, National Disaster Management Authority.

Prashant Bhushan

(TRUE COPY)

COUNCIL FOR THE INDIAN SCHOOL CERTIFICATE EXAMINATIONS

PRAGATI HOUSE, 3RD FLOOR, 47-48, NEHRU PLACE, NEW DELHI - 110019

TELEPHONES: 29564831, 29564833, 26411706, 26413620 E-mail : council@cisce.org FAX: 91-11-29564735

Chief Executive & Secretary
GERRY ARATHOON
M.A., B.Ed.

PV/CIR/2022
4th January 2022

To: All Heads of affiliated Schools

Dear Principal,

Subject: Advisory on Covid-19 Vaccination of children in the age group of 15 – 18 years

As per the Ministry of Health & Family Welfare, Government of India guidelines dated 27th December 2021, under the National COVID Vaccination Program, **all children in the age group of 15 – 18 years are eligible to take the Covid-19 vaccination from 3rd January 2022 onwards.**

This is indeed heartening and a positive step in the right direction, for the students in the examination Classes of X & XII. It will ensure their safety and protection while leaving the safe confines of their homes to travel to school, either to attend Classes, do the Practical work or to appear for the Semester 2 Examinations.

Considering the above, **the CISCE would like to advise you to encourage all your parents and guardians to get their children in the age group of 15-18 years vaccinated at the earliest**. Vaccination against the Covid-19 virus is the best protection which can be given to children at this stage. **All candidates for the ICSE & ISC Year 2022 Examinations should be vaccinated before the start of the said examinations.**

This advisory has been issued in the best interest of our students, parents, guardians, and our affiliated schools.

Kindly treat this on a priority basis. Your cooperation in this matter is solicited.

With warm regards,

Yours sincerely,

Gerry Arathoon

Chief Executive & Secretary

(TRUE COPY)

LAWRANCE PUBLIC SR. SEC. SCHOOL, SEC-51, MOHALI

Date: 08/01/2022

Dear Parents,

Punjab Health Dept is organizing a vaccine camp in school campus for students of classes IX, X, XI, XII, that is age group 15-18 yrs on **Sunday, 9th January 2022**. The vaccine is free of cost. Please read the following directions carefully and abide by them:

1. Every student must be accompanied by atleast one parent as children will be under medical observation after the vaccine for 20 minutes.
2. Students must be warmly clad, wear a proper mask and carry their School ID card, water bottle, a small sanitizer bottle and a light snack.
3. It is mandatory for every student to be vaccinated against Covid / Omicron virus. It is our parents & teachers sacred duty to see to the welfare of our students both health and academic.
4. Time schedule for vaccination will be as follows:

Class	**Time**
Class XII	10:00 AM
Class XI	11:00 AM
Class X	12:00 noon
Class IX	01:00 pm

5. No unvaccinated student will be allowed in offline classes . As board exams are round the corner , we are very keen to start offline classes as soon as we can.

Principal
Lawrance Public Sr Sec School

(TRUE COPY)

Gmail **Bhushan Offices <thebhushanoffice@gmail.com>**

Re- IA For Direction in Writ Petition (Civil) No. 607 of 2021 Jacob Puliyel Vs. Union of India & Ors.

1 message

Bhushan Offices <thebhushanoffice@gmail.com> Mon, Jan 10, 2022 at 9:41 PM
To: gs.makkar@gov.in, nairvipin73@gmail.com, malvikakapila84@gmail.com, shaktirazdan82@gmail.com, patilsachin286@gmail.com, aristotleaor@gmail.com, cmshroff.associates@gmail.com

Dear Sir/Madam

I, on behalf of the Petitioner have filed attached copy of the application in Writ petition (Civil) no. 607 of 2021 titled Jacob Puliyel Vs. Union of India & Ors.
Thank You.

Regards

Dol Raj Bhandari
Clerk of Mr. Prashant Bhushan, AOR
Mobile No. 9868255076

Final Application (Vaccine).pdf
8429K