Washington State Board of Health

Technical Advisory Group meeting: COVID-19 vaccines

Matthew Kronman, MD MSCE
Pediatric Infectious Diseases
University of Washington | Seattle Children's Hospital
February 17, 2022

Seattle Children's®
HOSPITAL • RESEARCH • FOUNDATION

Disclosures

- I have no actual or potential conflict of interest in relation to this presentation.
- Data presented are current as of 2/7/22 to facilitate translation of slides prior to the meeting

Objectives

Discussion of the following criteria:

- #2 The vaccine containing this antigen is effective as measured by immunogenicity[2] and population-based prevention data in Washington State, as available.

- #4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

[2]*Immunogenicity means the ability of an antigen or vaccine to stimulate the body to produce an immune response. Vaccines often include antigens that stimulate an immune response to a particular disease but are not necessarily the same as the organism that would cause the disease.*

Definitions

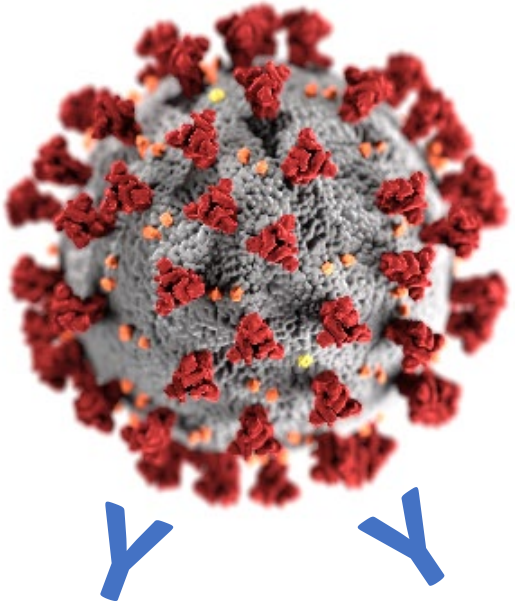
- **Coronavirus**: a family of viruses that can cause disease in humans and animals

- **SARS-CoV-2**: the specific coronavirus identified in 2019 that causes COVID-19 illness

- **COVID-19**: the clinical illness caused by SARS-CoV-2, which can cause acute symptoms (fever, cough, loss of smell or taste, etc), late symptoms (multisystem inflammatory syndrome in children [MIS-C]), or no symptoms

Definitions

Antigen: the **molecular structure** of the germ that triggers the immune response



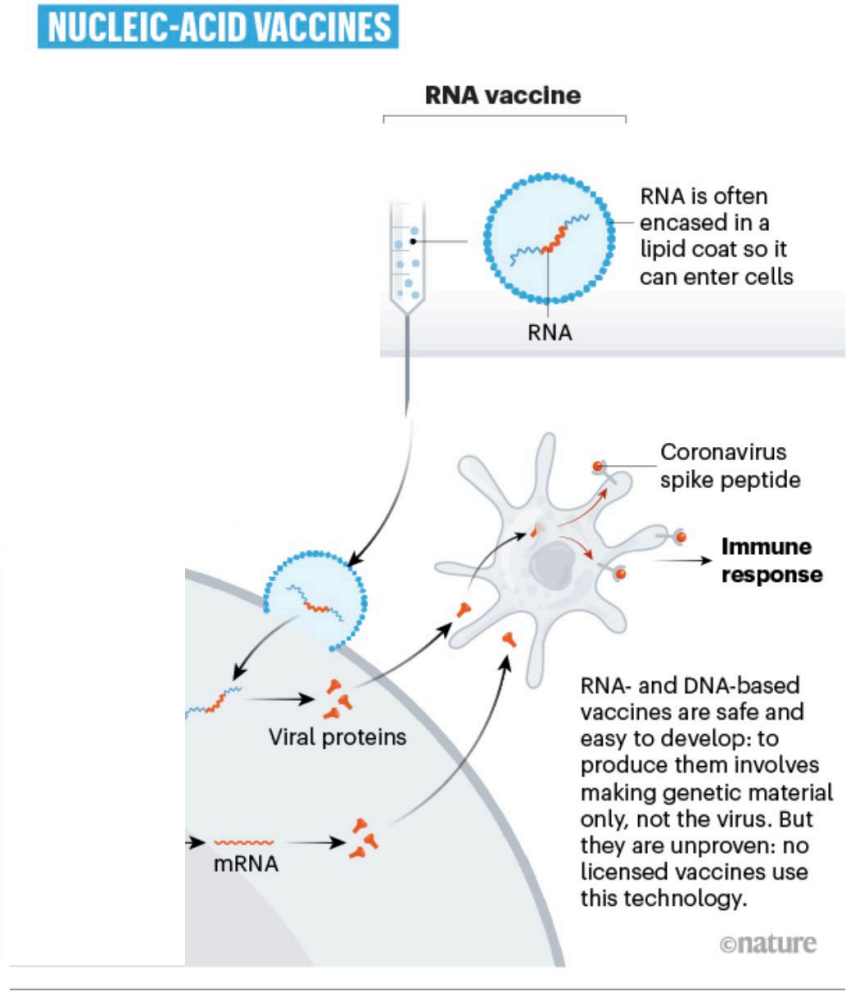
Antibody: the **measurable protein** made by the body in response to an infection, and which helps prevent or clear infection

mRNA (messenger Ribonucleic Acid): the genetic code that tells a human cell to make a certain protein

Vaccine efficacy: Disease risk in the unvaccinated group minus the risk in the vaccinated group, divided by the risk among unvaccinated

Definitions

- After injection, the mRNA vaccine teaches our cells how to make the spike protein
- The mRNA is then quickly destroyed by the cell
- Our body recognizes spike protein as foreign, and starts making antibodies in response.
- The mRNA vaccine **DOES NOT** cause COVID-19 infection
- The mRNA vaccine **DOES NOT** interact with or change our genes (DNA)



Callaway, Nature | Vol 580 | 30 April 2020

BNT-162b2 (Pfizer-BioNTech) vaccine

Contains:

- mRNA (30µg for children ≥12 years and 10µg for children 5-11 years)
- Lipids, sucrose
- potassium chloride, monobasic potassium phosphate, dibasic sodium phosphate dihydrate (purple cap)
- sodium chloride (purple and orange cap)
- tromethamine, tromethamine hydrochloride (grey and orange cap)
- Purple needs to be diluted; grey does not; both are for ≥12 years
- Orange is for 5-11 years

BNT-162b2 vaccine timeline

12/11/2020 FDA Emergency Use Authorization (EUA) for ≥16 yrs

5/10/2021 FDA EUA for 12-15 yrs

8/23/2021 FDA full approval for ≥16 yrs

9/22/2021 EUA for boosters for high risk

10/29/2021 EUA for 5-11 yrs

11/19/2021 EUA for boosters for ≥18 yrs

12/08/2021 EUA for boosters for 16-17 yrs

1/3/2022 FDA EUA for boosters for ≥ 12yrs

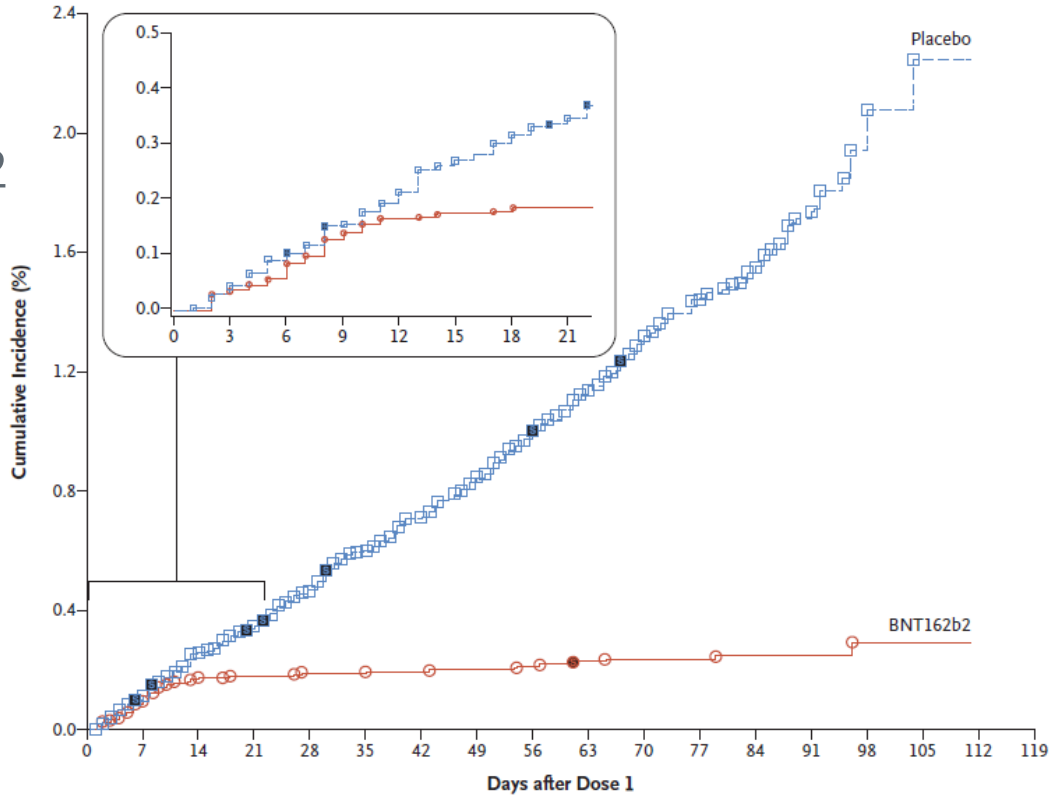
Dec 2020 Jun 2021 Dec 2021

#2 The vaccine containing this antigen is effective as measured by immunogenicity[2] and population-based prevention data in Washington State, as available.

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Initial randomized trial of those **≥16 years old**
- 21,720 given 30µg BNT-162b2 and 21,728 given placebo
- 2 doses, 21 days apart
- Primary end point was efficacy against confirmed COVID ≥7 days after the second dose in participants without prior infection
- Vaccine efficacy **95.0%**

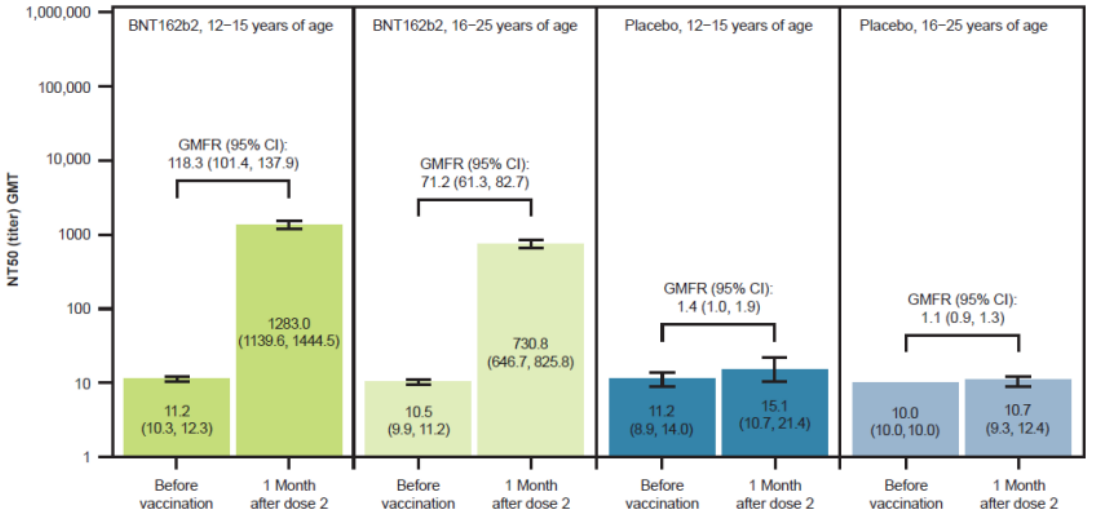


Polack, NEJM Dec 2020, DOI: 10.1056/NEJMoa2034577

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Randomized trial in US
- **12 to 15 year-olds**
- 1,131 given 30µg BNT-162b2 and 1,129 given placebo
- 2 doses, 21 days apart
- Primary end point was comparing immune responses between groups 1 mo. after dose 2
- Vaccine efficacy **100.0%**

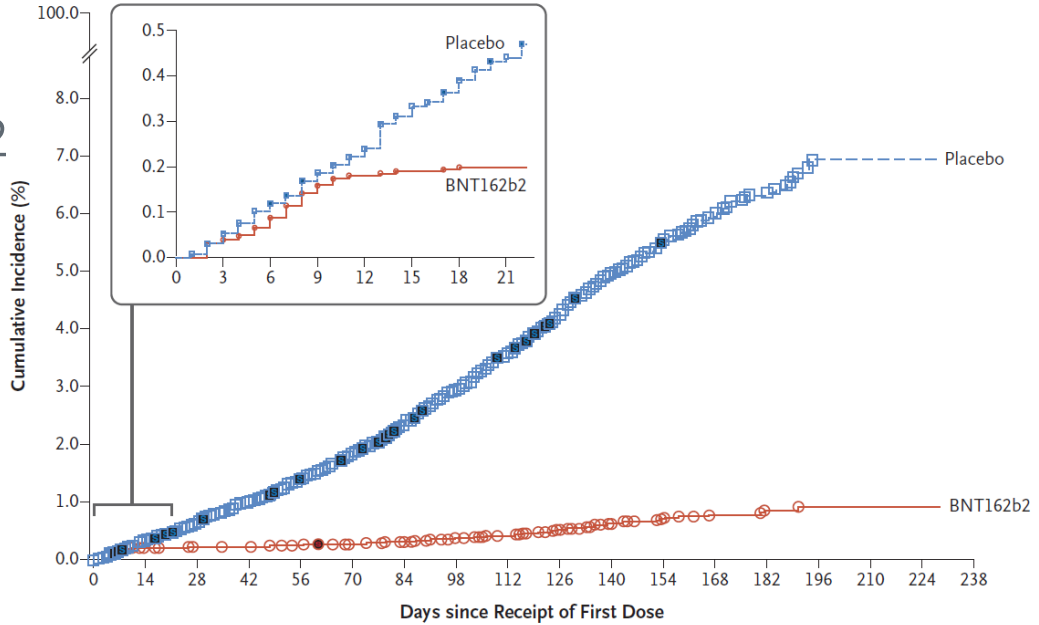


Frenck, NEJM May 2021, DOI: 10.1056/NEJMoa2107456

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- 6 month follow up of initial randomized trial
- 20,998 given 30µg BNT-162b2 and 21,096 given placebo
- End point was efficacy against confirmed COVID ≥7 days after the second dose
- Vaccine efficacy **91.3%** overall
- In 16 to 17 year-olds, vaccine efficacy **100%**

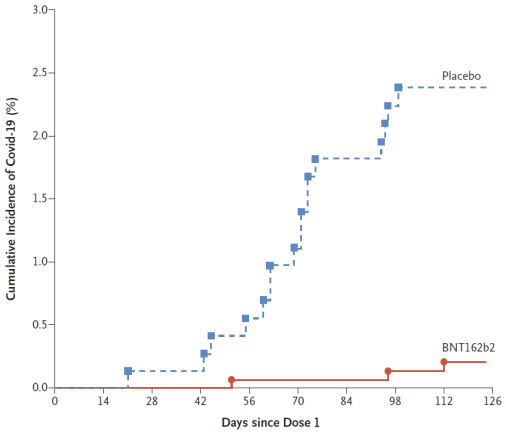


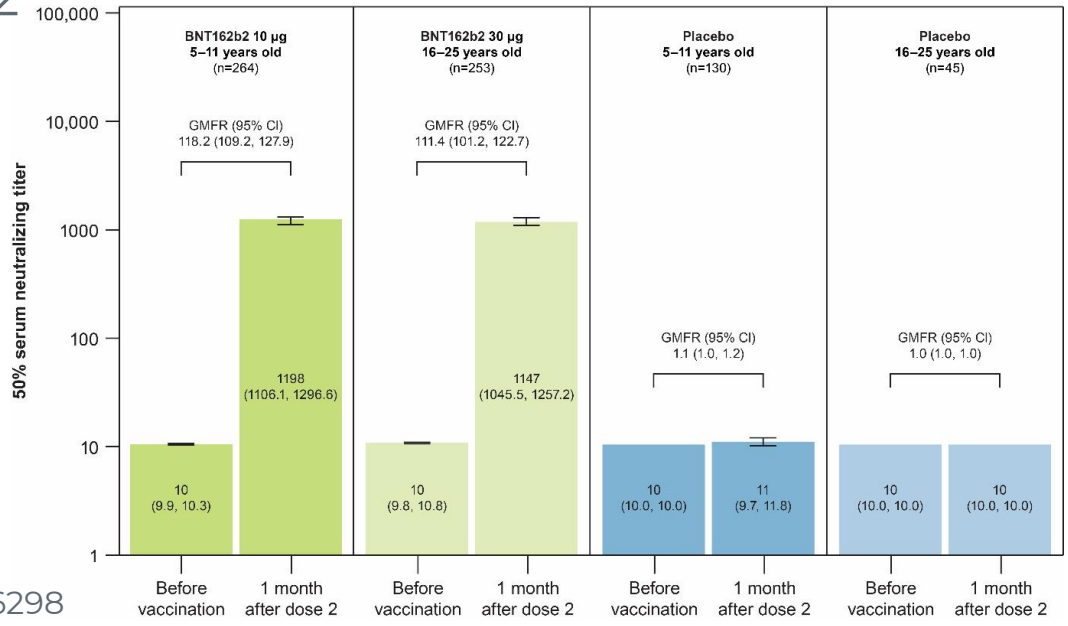
Thomas, NEJM Sep 2021, DOI: 10.1056/NEJMoa2110345

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Randomized trial
- **5 to 11 year-olds**
- 1,517 given 10µg BNT-162b2 and 751 given placebo
- End point was efficacy against confirmed COVID ≥7 days after the second dose and immune response
- Vaccine efficacy **90.7%**





Walter, NEJM Nov 2021, DOI: 10.1056/NEJMoa2116298

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Observational study in Israel during **Delta variant** predominance
- **12 to 18 year-olds**
- 94,354 vaccinated with BNT-162b2 vs. 94,354 unvaccinated
- Vaccine efficacy **90%** against documented infection; **93%** against symptomatic COVID

Reis, NEJM Dec 2021, DOI: 10.1056/NEJMc2114290

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Prospective observational study in Arizona during **Delta variant** predominance
- **12 to 17 year-olds**
- 194 vaccinated with BNT-162b2 vs. 49 unvaccinated
- Collected weekly nasal swabs
- Adjusting for likelihood of being vaccinated, vaccine efficacy **92%** against documented infection

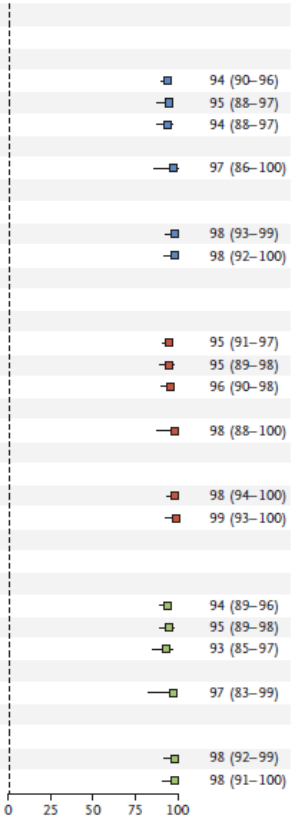
Lutrick, MMWR / December 31, 2021 / Vol. 70 / No. 51-52

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Observational case-control study in **12-18 year-olds**
- 445 case patients hospitalized with COVID-19; 777 controls without COVID
- Evaluated both groups for prior full receipt of BNT-162b2
- Vaccine effectiveness **94%** against hospitalization, **98%** against ICU admission, **98%** against need for life support

Subgroup	Vaccinated Case Patients	Vaccinated Control Patients	Vaccine Effectiveness (95% CI)
	no. of patients with event/total no. (%)		
Both control groups combined			
Any Covid-19 hospitalization			
Fully vaccinated			
12–18 yr	17/444 (4)	282/723 (39)	94 (90–96)
12–15 yr	8/251 (3)	156/427 (37)	95 (88–97)
16–18 yr	9/193 (5)	126/296 (43)	94 (88–97)
Partially vaccinated			
12–18 yr	1/428 (<1)	54/495 (11)	97 (86–100)
Severity of disease, 12–18 yr			
Fully vaccinated			
ICU admission for Covid-19	2/196 (1)	282/723 (39)	98 (93–99)
Life support for Covid-19	1/127 (<1)	282/723 (39)	98 (92–100)
Test-negative control group			
Any Covid-19 hospitalization			
Fully vaccinated			
12–18 yr	17/444 (4)	139/351 (40)	95 (91–97)
12–15 yr	8/251 (3)	74/202 (37)	95 (89–98)
16–18 yr	9/193 (5)	65/149 (44)	96 (90–98)
Partially vaccinated			
12–18 yr	1/428 (<1)	32/244 (13)	98 (88–100)
Severity of disease, 12–18 yr			
Fully vaccinated			
ICU admission for Covid-19	2/196 (1)	139/351 (40)	98 (94–100)
Life support for Covid-19	1/127 (<1)	139/351 (40)	99 (93–100)
Syndrome-negative control group			
Any Covid-19 hospitalization			
Fully vaccinated			
12–18 yr	17/444 (4)	143/372 (38)	94 (89–96)
12–15 yr	8/251 (3)	82/225 (36)	95 (89–98)
16–18 yr	9/193 (5)	61/147 (41)	93 (85–97)
Partially vaccinated			
12–18 yr	1/428 (<1)	22/251 (9)	97 (83–99)
Severity of disease, 12–18 yr			
Fully vaccinated			
ICU admission for Covid-19	2/196 (1)	143/372 (38)	98 (92–99)
Life support for Covid-19	1/127 (<1)	143/372 (38)	98 (91–100)



Olson, NEJM Jan 2022, DOI: 10.1056/NEJMoa2117995

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Observational case-control study in **12-18 year-olds** in July-Dec 2021
- 102 case patients hospitalized with MIS-C; 181 controls without MIS-C
- Evaluated both groups for prior full receipt of BNT-162b2 ≥28 days prior
- Vaccine effectiveness **91%** against hospitalization for MIS-C

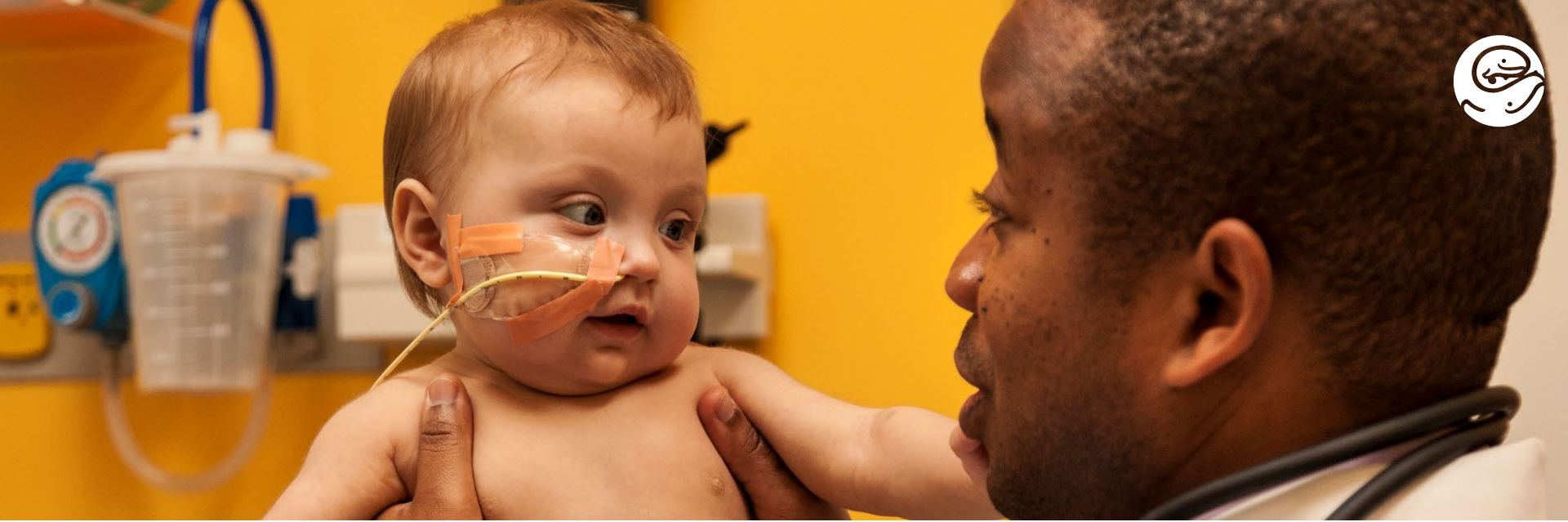
Zambrano, MMWR / January 14, 2022 / Vol. 71 / No. 2

Review of the evidence

#2 The vaccine containing this antigen is effective as measured by immunogenicity and population-based prevention data…

- Cohort study July-Oct 2021 in Israel
- Evaluated age groups including **16-29 year-olds**
- Compared group who received booster BNT-162b2 ≥12 days prior vs. booster-eligible subjects with no booster
- 8.4 COVID infections per 10,000 days at risk among non-boosted vs 0.33 among boosted, a **17.2-fold** adjusted increase in COVID risk among the non-boosted

Bar-On, NEJM Dec 2021, DOI: 10.1056/NEJMoa2115926



Summary of vaccine efficacy

- **Efficacy >90%** of BNT-162b2 vaccine against **infection, hospitalization, severe disease, MIS-C** in
- ≥16 year-olds, 12-15 year-olds, 5-11 year-olds

- Data for added protection against infection with booster BNT-162b2 vaccine dose in
- ≥16 year-olds

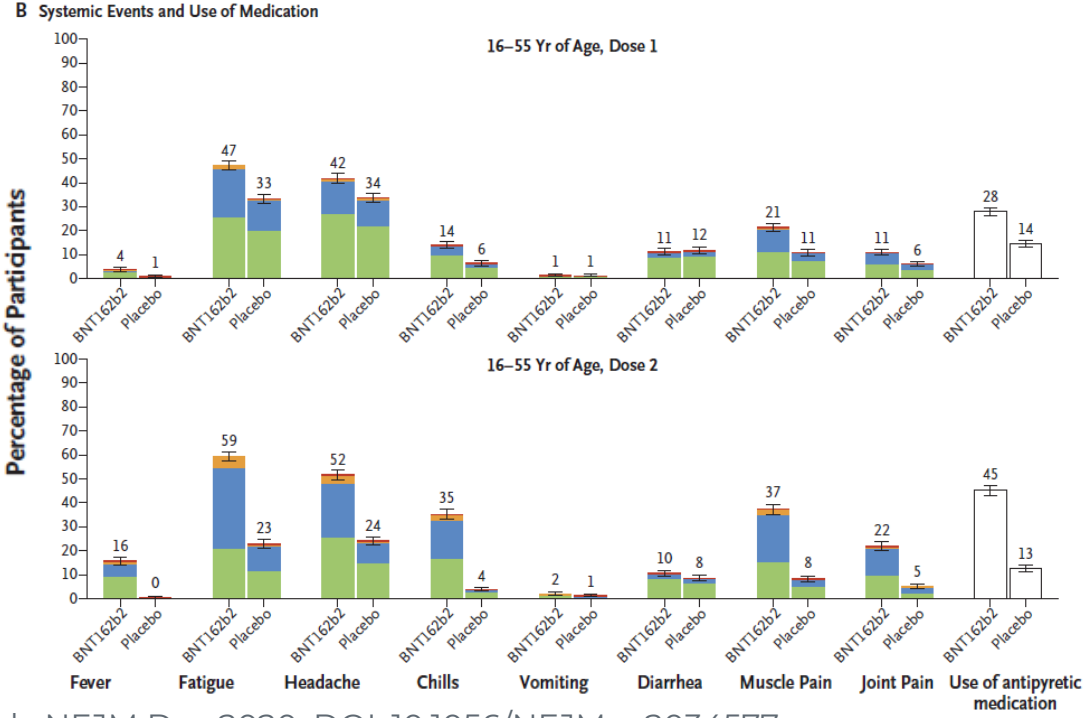
Ashton

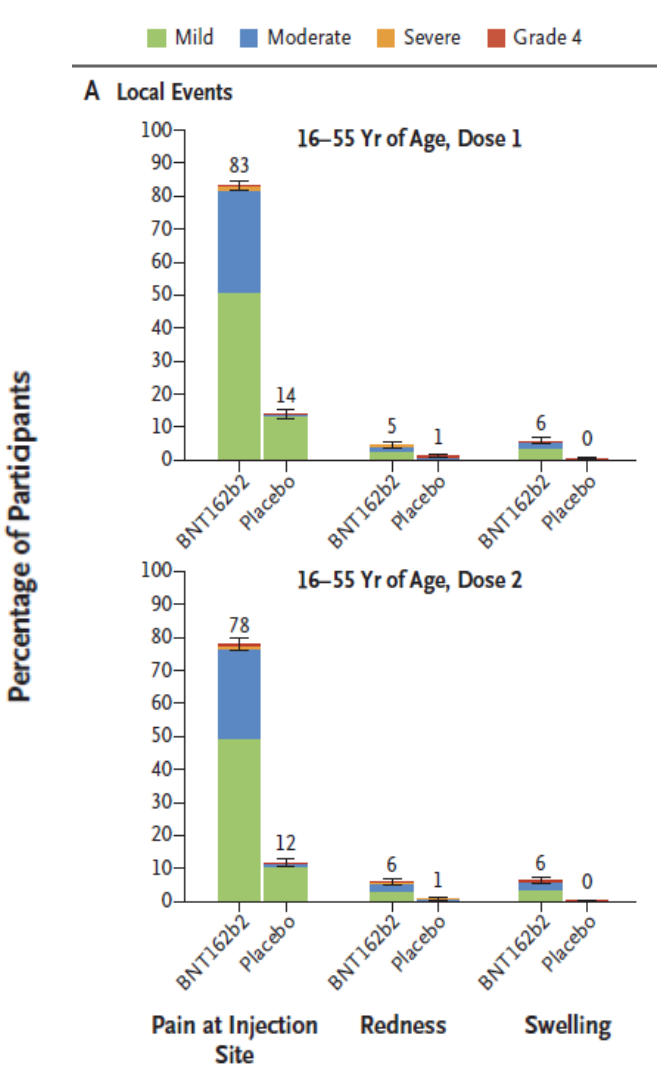
#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial randomized trial of those **≥16 years**



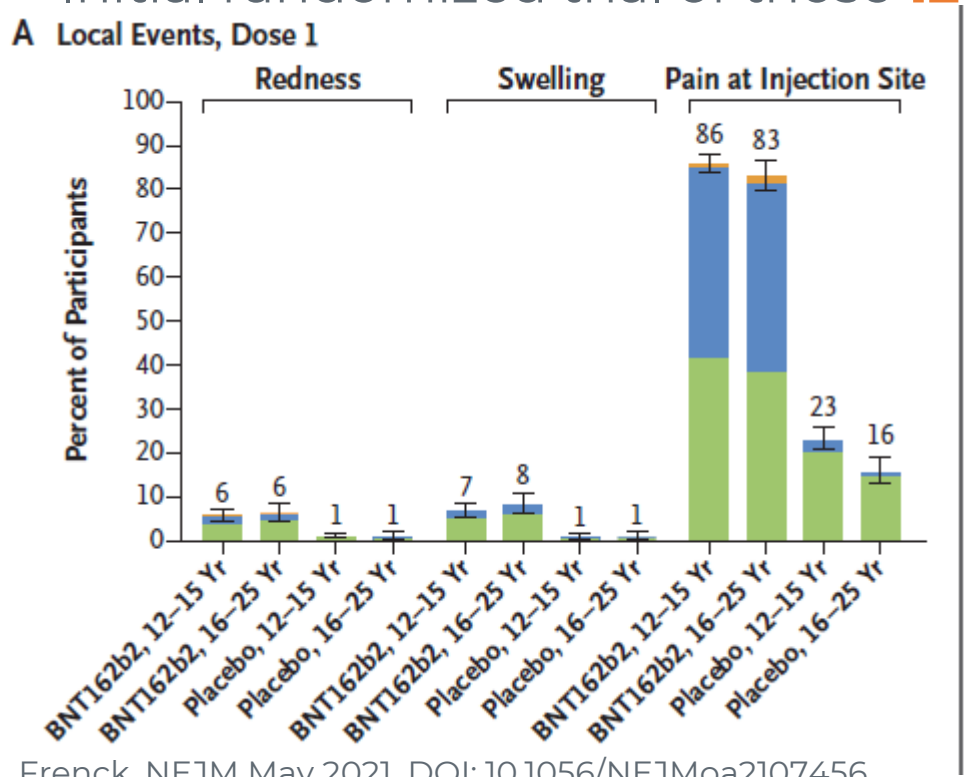


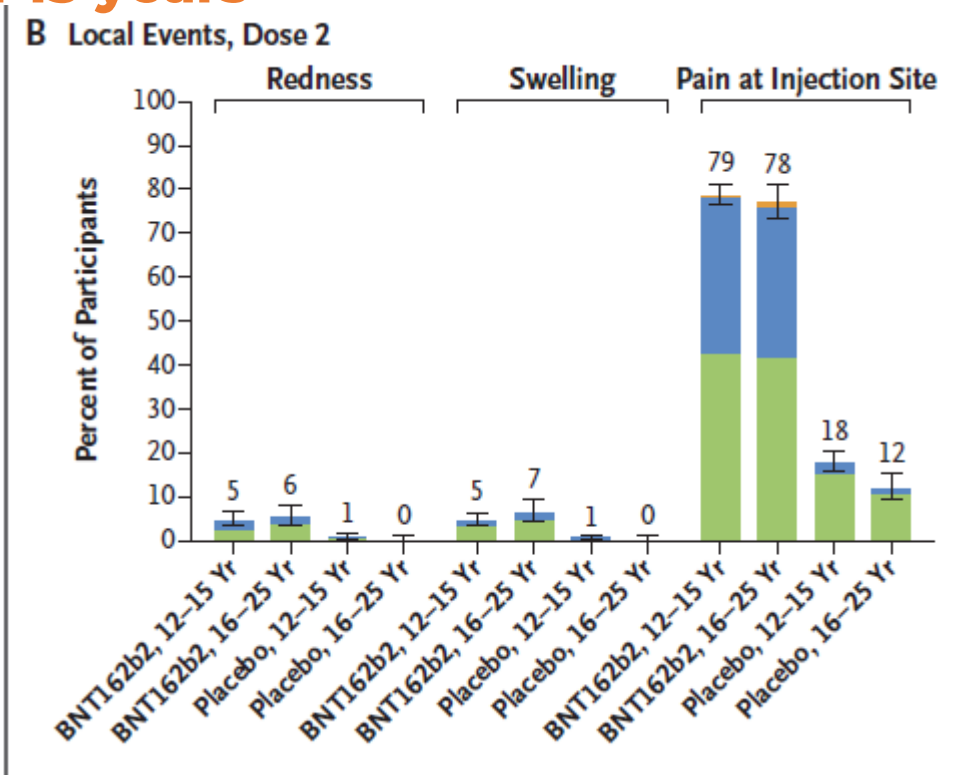
Polack, NEJM Dec 2020, DOI: 10.1056/NEJMoa2034577

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial randomized trial of those **12-15 years**



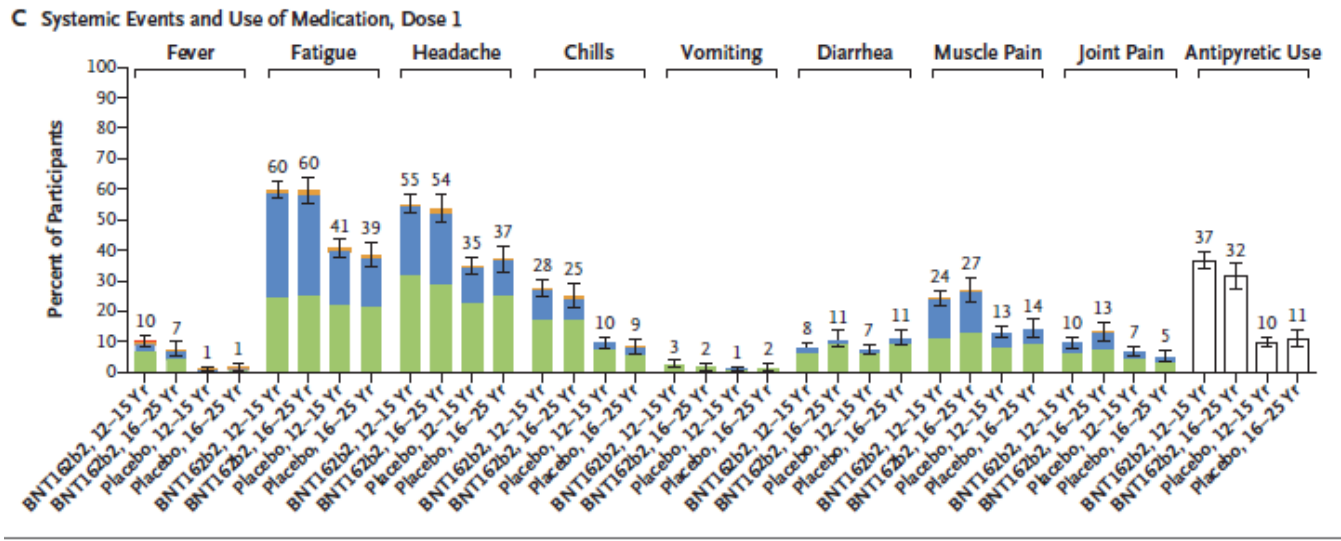


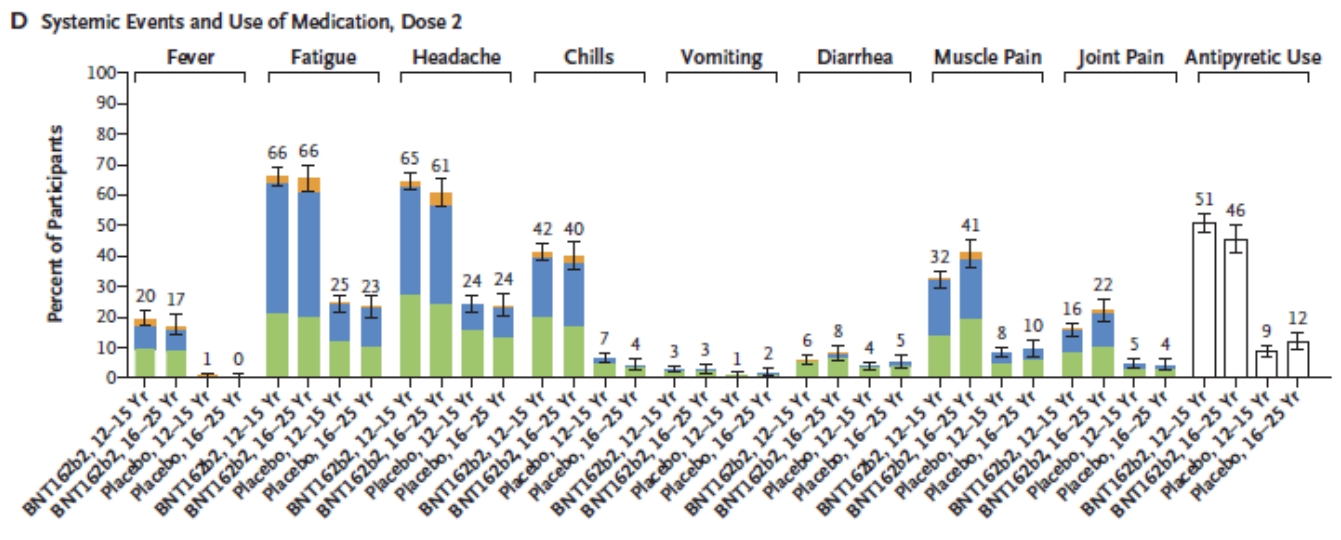
Frenck, NEJM May 2021, DOI: 10.1056/NEJMoa2107456

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial randomized trial of those **12-15 years**



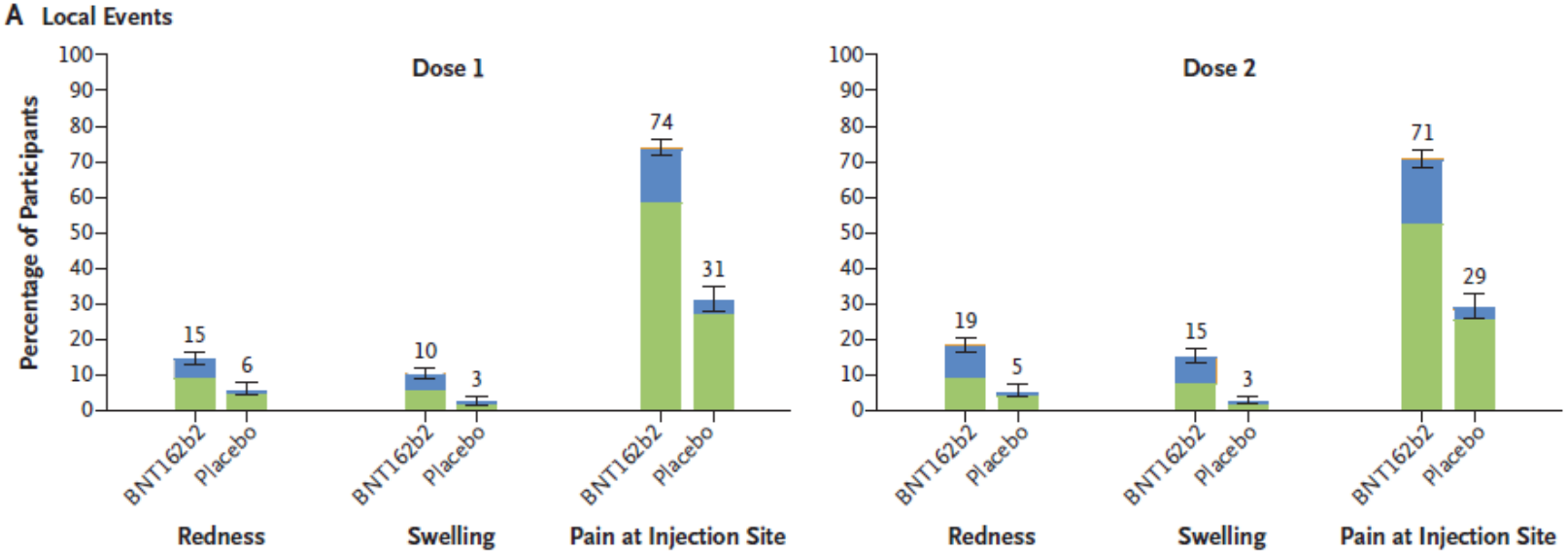


Frenck, NEJM May 2021

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial randomized trial of those **5-11 years**

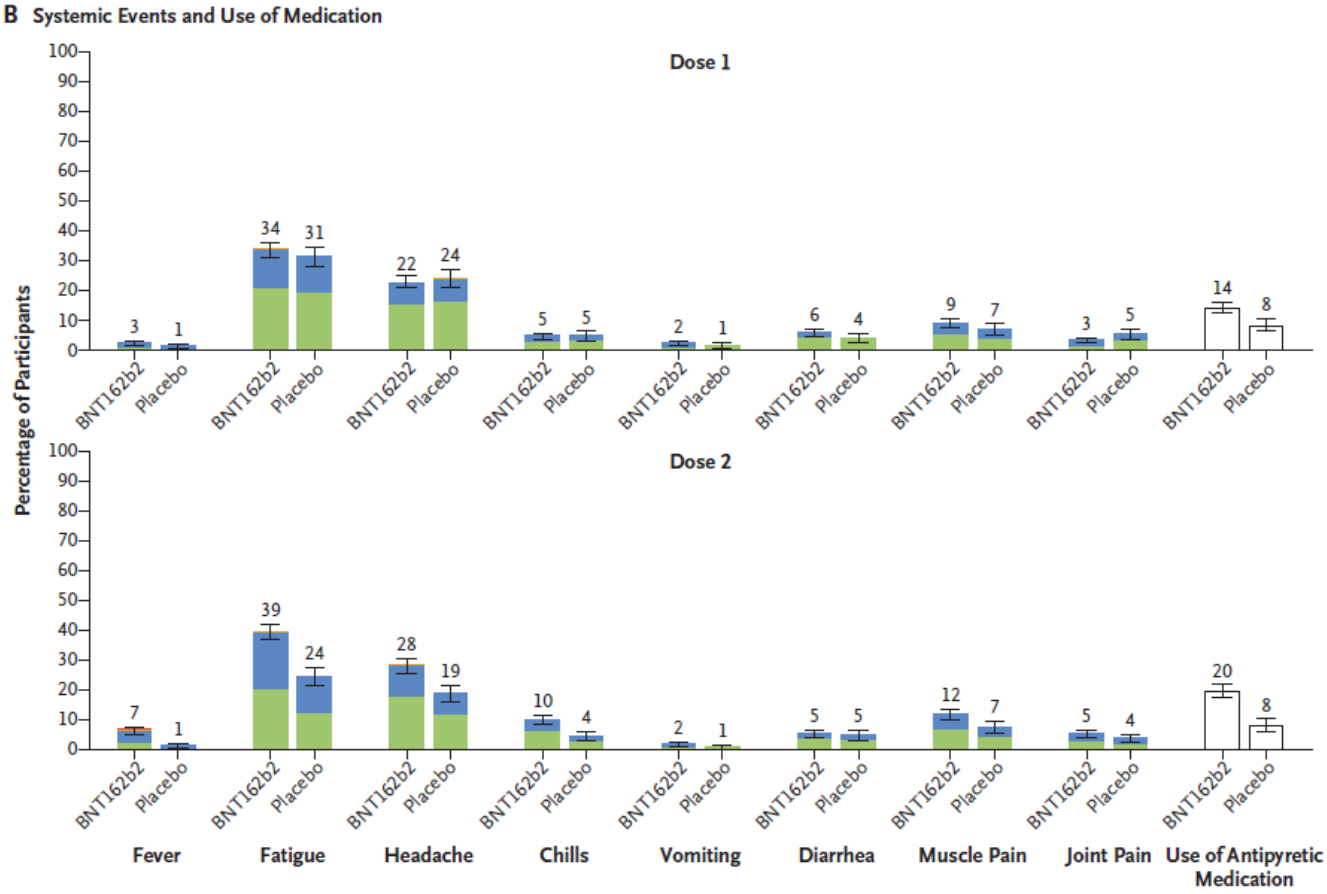


Walter, NEJM Nov 2021, DOI: 10.1056/NEJMoa2116298

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial randomized trial of those **5-11 years**

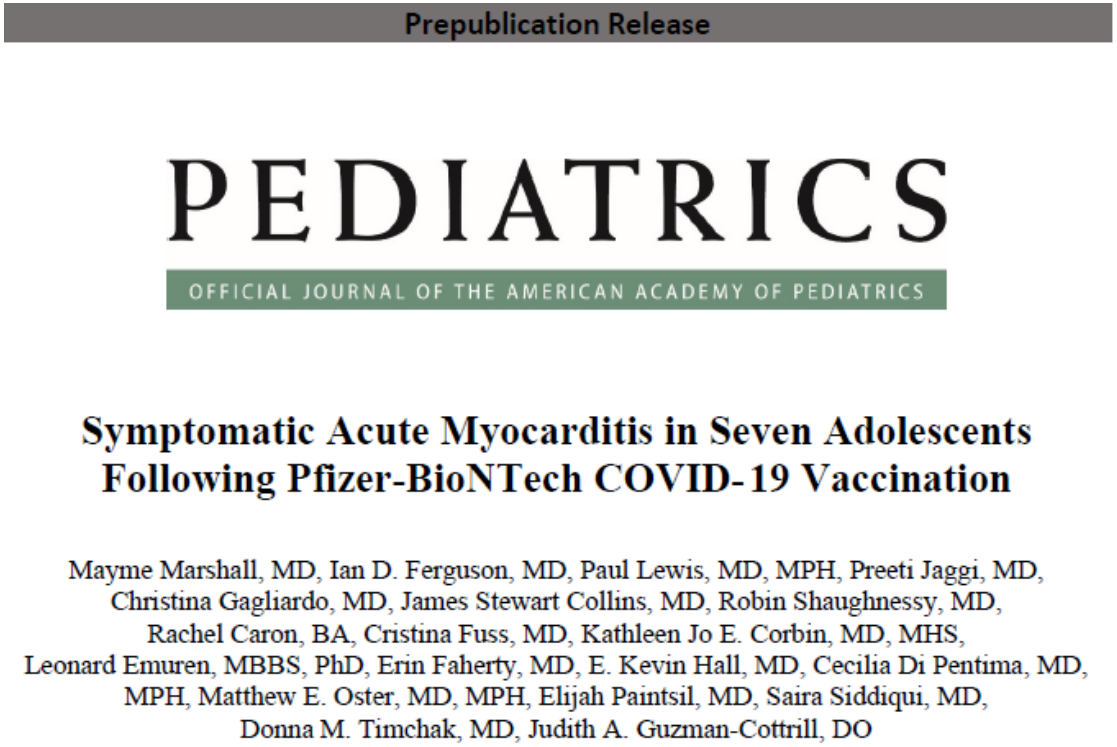


Walter, NEJM Nov 2021, DOI: 10.1056/NEJMoa2116298

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Initial report of myocarditis in adolescents accepted May 28, 2021



Prepublication Release

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Symptomatic Acute Myocarditis in Seven Adolescents Following Pfizer-BioNTech COVID-19 Vaccination

Mayme Marshall, MD, Ian D. Ferguson, MD, Paul Lewis, MD, MPH, Preeti Jaggi, MD, Christina Gagliardo, MD, James Stewart Collins, MD, Robin Shaughnessy, MD, Rachel Caron, BA, Cristina Fuss, MD, Kathleen Jo E. Corbin, MD, MHS, Leonard Emuren, MBBS, PhD, Erin Faherty, MD, E. Kevin Hall, MD, Cecilia Di Pentima, MD, MPH, Matthew E. Oster, MD, MPH, Elijah Paintsil, MD, Saira Siddiqui, MD, Donna M. Timchak, MD, Judith A. Guzman-Cottrill, DO

Marshall, Pediatrics Jun 7 2021, DOI: 10.1542/peds.2021-052478

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Benefits of vaccine vs. risks of myocarditis in those **12-17 years**
- VAERS data: requires providers to submit information

TABLE 2. Individual-level estimated number of COVID-19 cases and COVID-19–associated hospitalizations, intensive care unit admissions, and deaths prevented after use of 2-dose mRNA COVID-19 vaccine for 120 days and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group* — United States, 2021

	No. per million vaccine doses administered in each age group (yrs)†				
Sex/Benefits and harms from mRNA vaccination	**12–29**	**12–17**	**18–24**	**25–29**	**≥30**
Male					
Benefit					
COVID-19 cases prevented§	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected¶	39–47	56–69	45–56	15–18	3–4
Female					
Benefit					
COVID-19 cases prevented§	12,500	8,500	14,300	14,700	14,900
Hospitalizations prevented	922	183	1,127	1,459	3,484
ICU admissions prevented	73	38	93	87	707
Deaths prevented	6	1	13	4	347
Harm					
Myocarditis cases expected¶	4–5	8–10	4–5	2	1

Abbreviations: ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.

* This analysis evaluated direct benefits and harms, per million second doses of mRNA COVID-19 vaccine given in each age group, over 120 days. The numbers of events per million persons aged 12–29 years are the averages of numbers per million persons aged 12–17 years, 18–24 years, and 25–29 years.

† Receipt of 2 doses of mRNA COVID-19 vaccine, compared with no vaccination.

§ Case numbers have been rounded to the nearest hundred.

¶ Ranges calculated as ±10% of crude VAERS reporting rates. Estimates include cases of myocarditis, pericarditis, and myopericarditis.

Gargano, MMWR, July 6, 2021 / Vol. 70

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Report of adverse events in those **12-17 years** after BNT-162b2 vaccine
- ~8.9 million doses given at this time
- Used 2 sources:
  - VAERS (90.7% non-serious)
  - V-Safe, a smartphone app from CDC where people need to sign up and complete surveys

TABLE 2. Most frequent symptoms, signs, diagnostic results, and conditions* reported to the Vaccine Adverse Event Reporting System for adolescents aged 12–17 years after receipt of the Pfizer-BioNTech COVID-19 vaccine (N = 9,246) — United States, December 14, 2020–July 16, 2021

Symptom, sign, diagnostic result, or condition	% Reporting
Nonserious reports (n = 8,383)	
Dizziness	21.2
Syncope	14.4
Nausea	10.4
Headache	10.0
Fever	8.3
Loss of consciousness	7.5
Excessive sweating	7.4
Fatigue	7.2
Pallor	7.1
Product administered to patient outside of indicated age range	7.0
Product storage error	6.4
Vomiting	6.4
Difficulty breathing	5.3
Chest pain	4.9
Pain	4.6
Serious reports, including reports of death† (n = 863)	
Chest pain	56.4
Increased troponin	41.7
Myocarditis	40.3
Increased c-reactive protein	30.6
Negative SARS-CoV-2 test result	29.4
Fever	28.3
Normal echocardiogram	26.9
Abnormal electrocardiogram	25.6
Headache	22.2
Difficulty breathing	21.4
Elevated electrocardiogram ST segment	20.5
Normal chest radiograph	19.7
Intensive care	18.1
Vomiting	17.0
Nausea	16.6

Hause, MMWR / August 6, 2021 / 70(31);1053-1058

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Adverse events in those **12-17 years**
- V-Safe data shown here

TABLE 3. Reactions reported by adolescents aged 12–17 years (N = 129,059) who completed at least one v-safe health check-in survey on days 0–7 after receiving Pfizer BioNTech COVID-19 vaccine — United States, December 14, 2020–July 16, 2021

	% of v-safe enrollees reporting reaction or health impact*			
	Age 16–17 yrs, dose (no.)		Age 12–15 yrs, dose (no.)	
Event	Dose 1 (66,350)	Dose 2 (41,040)	Dose 1 (62,709)	Dose 2 (38,817)
Any injection site reaction	62.7	64.4	63.9	62.4
Itching	5.7	6.3	5.8	5.5
Pain	60.2	62.0	61.2	59.9
Redness	3.4	4.9	4.1	5.3
Swelling	7.7	9.9	7.5	8.9
Any systemic reaction	**55.7**	**69.9**	**48.9**	**63.4**
Abdominal pain	4.7	8.5	4.1	7.0
Myalgia	25.4	40.7	21.4	31.4
Chills	8.3	26.2	6.8	21.1
Diarrhea	4.2	4.9	3.1	3.3
Fatigue	34.1	52.3	27.4	44.6
Fever	9.9	31.0	9.3	29.9
Headache	29.8	50.6	25.2	43.7
Joint pain	7.9	18.2	6.3	12.4
Nausea	10.2	19.8	7.5	14.8
Rash	1.2	1.1	1.2	1.2
Vomiting	1.1	2.3	1.0	2.6
Any health impact	**11.0**	**28.6**	**10.6**	**25.4**
Unable to perform normal daily activities	9.0	24.7	9.3	23.1
Unable to work or attend school	3.7	11.6	2.4	6.1
Needed medical care	0.5	0.6	0.5	0.8
Telehealth	0.1	0.2	0.1	0.2
Clinic	0.2	0.2	0.2	0.3
Emergency department visit	0.1	0.2	0.1	0.2
Hospitalization	0.02	0.03	0.02	0.04

* Percentage of enrollees who reported a reaction or health impact at least once during days 0–7 post-vaccination.

Hause, MMWR Aug 2021

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Adverse events in those **5-11 years**
- VAERS and V-Safe data
- Among ~8.7 million doses, with **97.6% for non-serious** events

Hause, MMWR December 31, 2021 / Vol. 70 / No. 51-52

TABLE 2. Most frequent symptoms, signs, diagnostic results, and conditions by MedDRA preferred term* reported to the Vaccine Adverse Event Reporting System among children aged 5–11 years after receipt of Pfizer-BioNTech COVID-19 vaccine (N = 4,249) — United States, November 3–December 19, 2021

Symptom, sign, diagnostic result, or condition (MedDRA PT)	No. reporting	% Reporting
Nonserious reports (n = 4,149)		
No adverse event†	1,157	27.9
Product preparation issue	925	22.3
Incorrect dose administered	675	16.3
Underdose	324	7.8
Vomiting	316	7.6
Fever	291	7.0
Headache	255	6.2
Syncope	255	6.2
Dizziness	244	5.9
Fatigue	201	4.8
Nausea	192	4.6
Urticaria	186	4.5
Rash	166	4.0
Pallor	151	3.6
Product storage error	146	3.5
Serious reports§ (n = 100)		
Fever	29	29.0
Vomiting	21	21.0
Troponin increased	15	15.0
Chest pain	12	12.0
Echocardiogram normal	12	12.0
Blood test	11	11.0
C-reactive protein increased	11	11.0
SARS-CoV-2 test negative	11	11.0
Appendicitis	10	10.0
Electrocardiogram normal	10	10.0
Headache	10	10.0
Rash	10	10.0
Seizure	10	10.0
Intensive care	9	9.0
Full blood count normal	8	8.0

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Adverse events in those **5-11 years**
- VAERS and V-Safe data
- Among ~8.7 million doses, with **97.6% for non-serious** events

TABLE 3. Reactions reported for children aged 5–11 years (N = 42,504) who completed at least one v-safe health check-in survey on days 0–7 after receiving Pfizer-BioNTech COVID-19 vaccine — United States, November 3–December 19, 2021

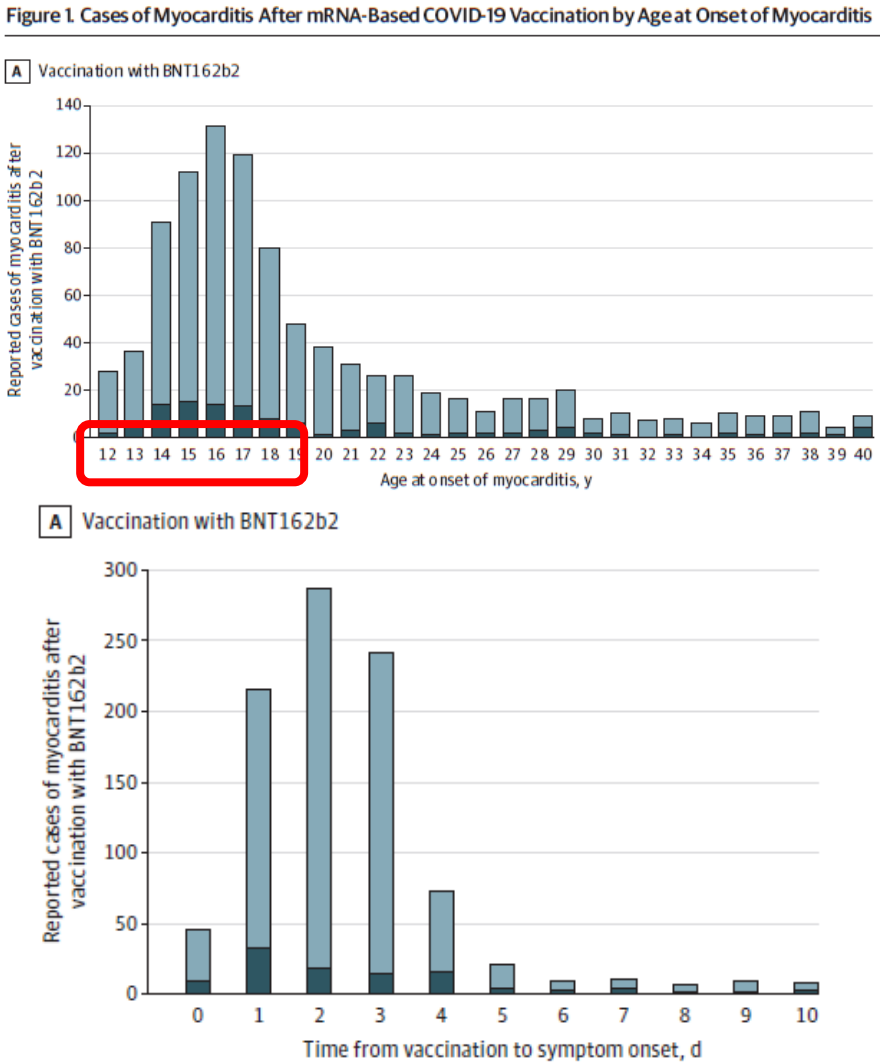
	% of v-safe enrollees reporting reaction or health impact*	
Event	**Dose 1 (N = 42,504)**	**Dose 2 (n = 29,899)**
Any injection site reaction	54.8	57.5
Itching	3.8	3.7
Pain	52.7	55.8
Redness	3.7	4.4
Swelling	3.9	4.9
Any systemic reaction	34.7	40.9
Abdominal pain	5.1	6.4
Myalgia	7.1	10.2
Chills	3.9	6.8
Diarrhea	2.6	2.2
Fatigue	20.1	25.9
Fever	7.9	13.4
Headache	13.9	19.8
Joint pain	2.1	2.9
Nausea	5.0	6.9
Rash	1.2	1.0
Vomiting	2.3	2.7
Any health impact	10.9	15.1
Unable to perform normal daily activities	5.1	7.4
Unable to attend school	7.9	10.9
Needed medical care	1.2	1.1
Telehealth	0.3	0.2
Clinic	0.6	0.6
Emergency visit	0.1	0.1
Hospitalization	0.02	0.02

Hause, MMWR December 31, 2021 / Vol. 70 / No. 51-52

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Myocarditis reports in VAERS from December 2020 – August 20201
- Among over 200 million doses of BNT-162b2 received
- Overall 82% occurred in males and 82% after second dose of vaccine



Oster, JAMA. 2022;327(4):331-340. doi:10.1001/jama.2021.24110

Review of the evidence

#4 Experience to date with the vaccine containing this antigen demonstrates that it is safe and has an acceptable level of side effects.

- Among people <30 years old:
- 96% were hospitalized
- Need for intensive therapy was rare (2%)
- Overall 98% were discharged, and **87% had resolved symptoms at discharge**

Reported cases of myocarditis within a 7-d risk interval per million doses of vaccine administered (95% CI)[a]

	Vaccination with BNT162b2	
	First dose	Second dose
Males		
Age group, y		
12-15	7.06 (4.88-10.23)	70.73 (61.68-81.11)
16-17	7.26 (4.45-11.86)	105.86 (91.65-122.27)
Females		
Age group, y		
12-15	0.49 (0.12-1.98)	6.35 (4.05-9.96)
16-17	0.84 (0.21-3.37)	10.98 (7.16-16.84)

Outcome among those who were hospitalized	
Discharged from the hospital	747/762 (98.0)
Still hospitalized at time of review	15/762 (2.0)
Died	0
Resolution of presenting symptoms by hospital discharge	577/661 (87.3)

Oster, JAMA. 2022;327(4):331-340. doi:10.1001/jama.2021.24110

Summary of vaccine side effects

- Local and systemic reactions occur in children given BNT-162b2 at rates similar to adults
- Myocarditis is associated with vaccination, more so among teen males and after the second dose
- Myocarditis symptoms typically resolved quickly and without long term consequences
- Benefits of vaccination outnumber myocarditis harms ~100 to 1 in males and ~1000 to 1 in females

Upcoming activities

- EUA submitted for BNT-162b2 for children 6 months to 4 years
- FDA discussion of those data anticipated on 2/15/22
- ACIP discussion of those data anticipated on 2/17/22

Thank you!