

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Thomas SJ, Moreira ED Jr, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months. *N Engl J Med* 2021;385:1761-73. DOI: [10.1056/NEJMoa2110345](https://doi.org/10.1056/NEJMoa2110345)

## SUPPLEMENTARY APPENDIX

List of Investigators .....	2
Ethical Conduct of the Study .....	6
Study Responsibilities.....	6
Testing for SARS-CoV-2 Virus and Antibodies.....	6
Determination of SARS-CoV-2 Lineage .....	6
Definitions of Confirmed and Severe COVID-19 Cases .....	7
Table S1   Explanation of the Changes in Denominator Numbers in Various Analyses. ....	8
Table S2   Baseline Comorbidities in Participants $\geq 16$ Years of Age.....	9
Table S3   Participants Reporting at Least 1 Adverse Event from Dose 1 to 1 Month After Dose 2 During the Blinded Follow-up Period. ....	10
Table S4   Causes of Death from Dose 1 to Unblinding (Safety Population, $\geq 16$ Years Old).....	11
Table S5   Vaccine Efficacy Overall and by Subgroup after Dose 1 During the Blinded Placebo Controlled Follow-up Period (All-Available Population).....	13
Table S6   Vaccine Efficacy against Severe COVID-19 Occurrence after Dose 1 (All-Available Population).....	14
Table S7   Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities (Risk Status) among Participants Without Evidence of Infection Prior to 7 Days after Dose 2 (Evaluable Efficacy Population) .....	15
Figure S1   Local Reactions and Systemic Events Reported within 7 Days after Receipt of BNT162b2 or Placebo by Baseline SARS-CoV-2 Status. ....	16

## List of Investigators

Name	Institute	Location
Aberg, Judith	Icahn School of Medicine at Mount Sinai	New York, NY, USA
Addo, Marylyn	Universitätsklinikum Hamburg-Eppendorf	Hamburg, Germany
Akhan, Sila	Kocaeli University Med	Kocaeli, Turkey
Albertson, Timothy	University of California, Davis	Sacramento, CA, USA
Al-Ibrahim, Mohamed	SNBL Clinical Pharmacology Center	Baltimore, MD, USA
Altın, Sedat	Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital	Istanbul, Turkey
Anderson, Corey	Clinical Research Consortium	Tempe, AZ, USA
Andrews, Charles	Diagnostics Research Group	San Antonio, TX, USA
Arora, Samir	Aventiv Research	Columbus, OH, USA
Balik, Ismail	Ankara University Medical School	Ankara, Turkey
Barnett, Elizabeth	Boston Medical Center	Boston, MA, USA
Bauer, George	Benchmark Research	Metairie, LA, USA
Baumann-Noss, Sybille	CRS Clinical Research Services Berlin	Berlin, Germany
Berhe, Mezgebe	North Texas Infectious Diseases Consultants	Dallas, TX, USA
Bradley, Paul	Meridian Clinical Research	Savannah, GA, USA
Brandon, Donald	California Research Foundation	San Diego, CA, USA
Brune, Daniel	Optimal Research	Peoria, IL, USA
Burgher, Abram	The Pain Center of Arizona	Peoria, AZ, USA
Butcher, Bain	Sterling Research Group	Cincinnati, OH, USA
Butuk, David	Solaris Clinical Research	Meridian, ID, USA
Cannon, Kevin	PMG Research of Wilmington	Wilmington, NC, USA
Cardona, Jose	Indago Research and Health Center	Hialeah, FL, USA
Cavelli, Rachael	State University of New York Upstate Medical University	Syracuse, NY, USA
Chalhoub, Fadi	CNS Healthcare	Jacksonville, FL, USA
Christensen, Shane	J. Lewis Research	Salt Lake City, UT, USA
Christensen, Tom	Waterway Family Medicine	Little River, SC, USA
Chu, Laurence	Benchmark Research	Austin, TX, USA
Cox, Steven	Lynn Institute of Norman	Norman, OK, USA
Crook, Gretchen	Austin Regional Clinic: ARC Wilson Parke	Austin, TX, USA
Davis, Matthew	Rochester Clinical Research	Rochester, NY, USA
Davit, Rajesh	Sterling Research Group	Cincinnati, OH, USA
Denham, Douglas	Clinical Trials of Texas (CTT)	San Antonio, TX, USA
Dever, Michael	Clinical Neuroscience Solutions	Orlando, FL, USA
Donskey, Curtis	Louis Stokes Cleveland VA Medical Center	Cleveland, OH, USA
Doust, Matthew	Hope Research Institute	Phoenix, AZ, USA
Dunn, Michael	Quality Clinical Research	Omaha, NE, USA
Earl, John	PMG Research of Hickory	Hickory, NC, USA
Eder, Frank	United Medical Associates - Meridian Clinical Research	Binghamton, NY, USA
Eich, Andreas	IKF Pneumologie	Frankfurt, Germany
Ensz, David	Meridian Clinical Research	Dakota Dunes, SD, USA
Essink, Brandon	Meridian Clinical Research	Omaha, NE, USA
Falcone, Robert	Amici Clinical Research	Raritan, NJ, USA
Falsey, Ann	University of Rochester/Rochester General Hospital	Rochester, NY, USA
Farrington, Cecil	PMG Research of Salisbury	Salisbury, NC, USA

Finberg, Robert	University of Massachusetts Medical School	Worcester, MA, USA
Finn, Daniel	Kentucky Pediatric/Adult Research	Bardstown, KY, USA
Fitz-Patrick, David	East-West Medical Research Institute	Honolulu, HI, USA
Fortmann, Stephen	Kaiser Permanente Center for Health Research	Portland, OR, USA
Fouche, Leon	Tambotie Medical Centre	Thabazimbi, South Africa
Fragoso, Veronica	Texas Center for Drug Development	Houston, TX, USA
Frenck, Robert	Cincinnati Children's Hospital	Cincinnati, OH, USA
Fried, David	Omega Medical Research	Warwick, RI, USA
Fuller, Gregory	Ventavia Research Group	Keller, TX, USA
Fussell, Suzanne	Long Beach Clinical Trials Services	Long Beach, CA, USA
Garcia-Diaz, Julia	Ochsner Health	New Orleans, LA, USA
Gentry, Andrew	Bozeman Health Clinical Research	Bozeman, MT, USA
Glover, Richard	Alliance for Multispecialty Research	Newton, KS, USA
Greenbaum, Carla	Benaroya Research Institute at Virginia Mason	Seattle, WA, USA
Grubb, Stephen	Main Street Physicians	Little River, SC, USA
Hammitt, Laura	Johns Hopkins Center for American Indian Health	Whiteriver, AZ, USA
	Johns Hopkins Center for American Indian Health	Chinle, AZ, USA
	Johns Hopkins Center for American Indian Health	Shiprock, NM, USA
	Johns Hopkins Center for American Indian Health	Gallup, NM, USA
Harper, Charles	Meridian Clinical Research	Norfolk, NE, USA
Harper, Wayne	Wake Research	Raleigh, NC, USA
Hartman, Aaron	Virginia Research Center	Midlothian, VA, USA
Heller, Robert	Bayview Research Group	Valley Village, CA, USA
Hendrix, Ernest	North Alabama Research Center	Athens, AL, USA
Herrington, Darrell	Benchmark Research	San Angelo, TX, USA
Jennings, Timothy	Clinical Research Professionals	Chesterfield, MO, USA
Karabay, Oğuz	Sakarya University Faculty of Medicine	Sakarya, Turkey
Kaster, Steven	Confluence Health/Wenatchee Valley Hospital & Clinics	Wenatchee, WA, USA
Katzman, Steven	Michigan Center for Medical Research	Farmington Hills, MI, USA
Kingsley, Jeffrey	Columbus Regional Research Institute	Columbus, GA, USA
Klein, Nicola	Kaiser Permanente, Northern California	Santa Clara, CA, USA
		Sacramento, CA, USA
Klein, Tracy	Heartland Research Associates	Wichita, KS, USA
Koch, Mark	Ventavia Research Group	Fort Worth, TX, USA
Köksal, İftahar	Acibadem University Hospital Atakent	Istanbul, Turkey
Koren, Michael	Jacksonville Center for Clinical Research	Jacksonville, FL, USA
Kutner, Mark	Suncoast Research Group	Miami, FL, USA
Lee, Marcus	Trinity Clinical Research	Tullahoma, TN, USA
Leibowitz, Mark	National Research Institute	Huntingdon Park, CA, USA
Levin, Michael	Clinical Research Center of Nevada	Las Vegas, NV, USA
Libster, Romina	Fundacion INFANT	Buenos Aires, Argentina
Lillestol, Michael	Lillestol Research	Fargo, ND, USA
Lucasti, Christopher	South Jersey Infectious Disease	Somers Point, NJ, USA
Luttermann, Matthias	Studienzentrum Brinkum Dr. Lars Pohlmeier und Torsten Drescher	Stuhr, Germany
Manning, Mary Beth	Velocity Clinical Research	Cleveland, OH, USA
Martin, Earl	Martin Diagnostic Clinic	Tomball, TX, USA
Matherne, Paul	MedPharmics	Gulfport, MS, USA

McMurray, James	Medical Affiliated Research Center (MARC)	Huntsville, AL, USA
Mert, Ali	Medipol University Hospital	Istanbul, Turkey
Middleton, Randle	Optimal Research	Huntsville, AL, USA
Mitha, Essack	Newtown Clinical Research	Johannesburg, South Africa
Morawski, Emily	Holston Medical Group	Kingsport, TN, USA
Moreira, Edson	Associação Obras Sociais Irmã Dulce and Oswaldo Cruz Foundation	Bahia, Brazil
Murray, Alexander	PharmQuest	Greensboro, NC, USA
Mussaji, Murtaza	LinQ Research	Houston, TX, USA
Musungaie, Dany	Jongaie Research	Pretoria, South Africa
Nell, Haylene	Tiervlei Trial Centre, Karl Bremer Hospital	Cape Town, South Africa
Odekirk, Larry	Lynn Institute of Denver	Denver, CO, USA
Ogbuagu, Onyema	Yale University School of Medicine	New Haven, CT, USA
Paolino, Kristopher	State University of New York, Upstate Medical University	Syracuse, NY, USA
Patel, Suchet	Regional Clinical Research	Endwell, NY, USA
Peterson, James	J. Lewis Research	Salt Lake City, UT, USA
Pickrell, Paul	Tekton Research	Austin, TX, USA
Polack, Fernando	Fundacion INFANT	Buenos Aires, Argentina
Poretz, Donald	Clinical Alliance for Research and Education	Annandale, VA, USA
Raad, George	PMG Research of Charlotte	Charlotte, NC, USA
Randall, William	PriMed Clinical Research	Dayton, OH, USA
Rankin, Bruce	Accel Research Sites - DeLand Clinical Research Unit	DeLand, FL, USA
Reynolds, Steven	Collaborative Neuroscience Network	Long Beach, CA, USA
Riesenberg, Robert	Atlanta Center for Medical Research	Atlanta, GA, USA
Rodriguez, Hector	Acevedo Clinical Research Associates	Miami, FL, USA
Rosen, Jeffrey	Clinical Research of South Florida	Coral Gables, FL, USA
Rubino, John	Raleigh Medical Group, PA	Raleigh, NC, USA
Rupp, Richard	University of Texas	Galveston, TX, USA
Saiger, Salma	Research Across America	Mesquite, TX, USA
Salata, Robert	University Hospitals Cleveland Medical Center	Cleveland, OH, USA
Saleh, Jamshid	Northern California Neurological Surgery	Redding, CA, USA
Schaefer, Axel	Medizentrum Essen Borbeck	Essen, Germany
Shear, Martin	Dayton Clinical Research	Dayton, OH, USA
Schultz, Armin	CRS Clinical Research Services Mannheim	Mannheim, Germany
Schwartz, Howard	Research Centers of America	Hollywood, FL, USA
Segall, Nathan	Clinical Research Atlanta	Stockbridge, GA, USA
Seger, William	HealthFirst Medical Group	Fort Worth, TX, USA
Senders, Shelly	Senders Pediatrics	South Euclid, OH, USA
Sharp, Stephan	Clinical Research Associates	Nashville, TN, USA
Shoffner, Sylvia	PMG Research of Cary	Cary, NC, USA
Simsek Yavuz, Serap	Istanbul Faculty of Medicine, Istanbul University	Istanbul, Turkey
Sligh, Teresa	Providence Clinical Research	North Hollywood, CA, USA
Smith, William	New Orleans Center for Clinical Research	New Orleans, LA, USA
Stacey, Helen	Diablo Clinical Research	Walnut Creek, CA, USA
Stephens, Michael	Fleming Island Center for Clinical Research	Fleming Island, FL, USA
Studdard, Harry	Coastal Clinical Research	Mobile, AL, USA
Tabak, Fehmi	Istanbul University Cerrahpaşa Medical School	Istanbul, Turkey
Talaat, Kawsar	Johns Hopkins School of Medicine	Baltimore, MD, USA

Thomas, Stephen	State University of New York, Upstate Medical University	Syracuse, NY, USA
Towner, William	Kaiser Permanente	Los Angeles, CA, USA
Tran, Van	Ventavia Research Group	Houston, TX, USA
Ünal, Serhat	Hacettepe University	Ankara, Turkey
Usdan, Lisa	CNS Healthcare	Memphis, TN, USA
Vanchiere, John	Louisiana State University Health Shreveport	Shreveport, LA, USA
Varano, Susann	Clinical Research Consulting	Milford, CT, USA
Wadsworth, L. Tyler	Sundance Clinical Research	St Louis, MO, USA
Walsh, Edward	University of Rochester/Rochester General Hospital	Rochester, NY, USA
Walter, Emmanuel	Duke Human Vaccine Institute	Durham, NC, USA
Wappner, Diego	Fundacion INFANT	Buenos Aires, Argentina
Whiles, Rick	Holston Medical Group	Bristol, TN, USA
Williams, Hayes	Achieve Clinical Research	Birmingham, AL, USA
Wilson, Jonathan	Piedmont Medical Research of Winston-Salem	Winston-Salem, NC, USA
Winkle, Peter	Anaheim Clinical Trials	Anaheim, CA, USA
Winokur, Patricia	University of Iowa	Iowa City, IA, USA
Wolf, Thomas	Prairie Fields Family Medicine	Fremont, NE, USA
Yozviak, Joseph	Lehigh Valley Hospital Cedar Crest	Allentown, PA, USA
Zerbini, Cristiano	Centro Paulista de Investigação Clínica - CEPIC	São Paulo, Brazil

---

## **Ethical Conduct of the Study**

The trial was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the International Council for Harmonisation Good Clinical Practice Guidelines, the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, and applicable laws and regulations (including applicable privacy laws). An independent data monitoring committee reviewed efficacy and unblinded safety data.

## **Study Responsibilities**

Pfizer was responsible for the design, study conduct, data collection, data analysis, data interpretation, and writing of this manuscript. Both Pfizer and BioNTech manufactured clinical trial material. BioNTech was the sponsor of the study and contributed to data interpretation and writing of the manuscript. All study data were available to all authors who vouch for its accuracy and adherence of the study to the protocol.

## **Testing for SARS-CoV-2 Virus and Antibodies**

Testing for SARS-CoV-2 virus was conducted using the Cepheid Xpert Xpress SARS-CoV-2 RT-PCR test. Testing for SARS-CoV-2 antibodies was conducted using the Roche Elecsys® Anti-SARS-CoV-2 antibody test.

## **Determination of SARS-CoV-2 Lineage**

For determination of SARS-CoV-2 lineage, nucleic acid extraction of midturbinate swab specimens was performed using the MagMAX™ Viral/Pathogen Ultra Nucleic Acid Isolation Kit processed on a KingFisher™ Presto.

SARS-CoV-2 viral genome sequencing was performed using the Ion Torrent and Illumina NextSeq platforms. For the Ion Torrent sequencing platform, the Ion AmpliSeq™ SARS-CoV-2 Research Panel was used, which consists of 2 primer pools targeting a total of 237 PCR amplicons specific to SARS-CoV-2 and 5 human expression controls in each pool. Oligonucleotide primers based on available SARS-CoV-2 nucleotide sequences direct the amplification of the viral genome with amplicon lengths of 125–275 bp. The panel provides >99% coverage of the SARS-CoV-2 genome (~30 kb). To determine the optimal number of target amplification cycles, SARS-CoV-2 viral RNA content in the nucleic acid purified from the midturbinate specimens was quantified using the TaqMan™ 2019-nCoV Assay Kit v1, the TaqMan™ 2019-nCoV Control Kit v1, and TaqPath™ 1-Step RT-qPCR Master Mix, CG. cDNA was synthesized with the SuperScript VILO cDNA synthesis kit. Libraries were prepared using the Ion AmpliSeq™ Library Kit plus the Ion AmpliSeq™ SARS-CoV-2 Research Panel according to the manufacturer's instructions (ThermoFisher. Ion AmpliSeq™ Library Kit Plus USER GUIDE. Publication MAN0017003 version C.0.). Libraries underwent template preparation with Ion Chef according to the manufacturer's instructions. Prepared templates were loaded onto an Ion 530 chip for semiconductor sequencing on the Ion GeneStudio™ S5 plus sequencer according to the manufacturer's instructions. Raw sequencing reads generated by the Ion Torrent sequencer were quality and adaptor trimmed by Ion

Torrent Suite and the resulting reads were then mapped to the complete genome of the SARS-CoV-2 Wuhan-Hu-1 isolate (GenBank accession number MN908947.3) using TMAP 5.14.0. Variant calling was carried out with the Torrent Variant Caller using the BAM file from the mapping of the cleaned sequence reads onto the reference sequence of SARS-CoV-2.

SARS-CoV-2 viral genome sequencing performed using the Illumina NextSeq platform used the AmpliSeq for Illumina SARS-CoV-2 panel of PCR primers to enrich for SARS-CoV-2 in the biological specimen. This was a 2-pool design, containing a total of 237 SARS-CoV-2 specific amplicon/primer pairs plus 5 human expression controls in each pool. Oligonucleotide primers based on available SARS-CoV-2 nucleotide sequences directed the amplification of overlapping amplicons with lengths of 125–275 bp that cover >99% of the viral genome. Nucleic acid extracted from the midturbinate specimens was digested initially with DNase (Invitrogen TURBO DNA-free™ Kit, AM1907), and RNA was purified using MagMAX™ beads before cDNA synthesis. Synthesis of cDNA using random sequence primers and downstream steps were as described by the manufacturer. SARS-CoV-2 amplicons were generated from the cDNA, followed by ligation of Universal Next Generation Sequencing Adaptors to the ends of the amplicons. Amplicon libraries were purified with magnetic beads and loaded onto a flow cell for sequence determination using the Illumina NextSeq instrument, according to the manufacturer's instructions. Sequences with  $\geq 30$ -fold coverage across the entire spike gene were advanced for viral lineage assignment. Single nucleotide variants were called using the “Low Frequency Variant Detection” function with the cut-off for sequence heterogeneity set at >10%.

SARS-CoV-2 lineage assignment was based on Pangolin 2.0 software, which runs a multinomial logistic regression model trained against lineage assignments based on isolate data from the Global Initiative on Sharing All Influenza Data (GISAID), a global science initiative established in 2008 that provides open-access to genomics data of influenza virus and SARS-CoV-2.

### **Definitions of Confirmed and Severe COVID-19 Cases**

The definition of SARS-CoV-2-related cases was the presence of  $\geq 1$  of the following symptoms and SARS-CoV-2-NAAT positivity during or within 4 days before or after the symptomatic period: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, and/or vomiting. The onset date of the case was the date that symptoms were first experienced by the participant. If new symptoms were reported  $\leq 4$  days after resolution of all previous symptoms, they were considered part of a single illness.

Confirmed severe COVID-19 required confirmation of COVID-19 and the presence of  $\geq 1$  of the following: clinical signs at rest indicative of severe systemic illness (respiratory rate  $\geq 30$  breaths per minute, heart rate  $\geq 125$  beats per minute,  $SpO_2 \leq 93\%$  on room air at sea level, or  $PaO_2/FiO_2 < 300$  mmHg); respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation); evidence of shock (systolic blood pressure  $< 90$  mmHg, diastolic blood pressure  $< 60$  mmHg, or requiring vasopressors); significant acute renal, hepatic, or neurologic dysfunction; intensive care unit admission; and/or death (<https://www.fda.gov/media/137926/download>).



Figure/Table Number	Figure/Table Title	Population(s)/Sample Size	Explanation
Figure 1	Disposition of Participants	All enrolled safety population $\geq 16$ years of age N=44,165	Per protocol
Figure 2	Efficacy of BNT162b2 against COVID-19 Occurrence after Dose 1 During the Placebo-controlled Follow-up Period	N=46,077 (all available)	All randomized participants $\geq 12$ years of age
Table 1	Demographics	Participants $\geq 16$ years of age N=44,047	Includes HIV-infected individuals
Table 2	Vaccine Efficacy against COVID-19 from 7 Days after Dose 2 During the Blinded Placebo Controlled Follow-up Period (Evaluable Efficacy Population, $\geq 12$ Years Old)	a. Efficacy endpoint including individuals <b>without</b> evidence of prior infection (N=42,094)  b. Efficacy endpoint including individuals <b>with and those without</b> evidence of prior infection (N=44,486)	Evaluable population: <ul style="list-style-type: none"> <li>received 2 vaccinations as randomized</li> <li>no major protocol deviations</li> </ul> Excludes HIV+ participants
Table 3	Vaccine Efficacy Overall and by Subgroup in Participants Without Evidence of Infection Prior to 7 Days After Dose 2 During the Blinded Placebo Controlled Follow-up Period	N=42,094 (same as efficacy endpoint in Table 2, participants $\geq 12$ years of age)	
Table S2	Baseline Comorbidities in Participants $\geq 16$ Years of Age	N=44,047	Includes HIV-infected individuals
Table S3	Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 During the Blinded Follow-up Period	Participants $\geq 16$ years of age N=43,847	Vaccinated minus 200 HIV-infected participants
Table S4	Causes of Death from Dose 1 to Unblinding (Safety Population, $\geq 16$ Years Old)	Participants $\geq 16$ years of age N=43,847	Vaccinated minus 200 HIV-infected participants
Table S5	Vaccine Efficacy Overall and by Subgroup after Dose 1 During the Blinded Placebo Controlled Follow-up Period (All-Available Population)	N=46,077 (all available)	
Table S6	Vaccine Efficacy against Severe COVID-19 Occurrence after Dose 1 (All-Available Population)	N=46,077 (all available, participants $\geq 12$ years of age)	
Table S7	Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities (Risk Status) among Participants without Evidence of Infection Prior to 7 Days after Dose 2 (Evaluable Efficacy Population)	N=42,094 (same as efficacy endpoint in Table 2, participants $\geq 12$ years of age)	
Figure S1	Local Reactions and Systemic Events Reported within 7 Days after Receipt of BNT162b2 or Placebo by Baseline SARS-CoV-2 Status	Reactogenicity subset of participants $\geq 16$ years of age (ie, participants who used an electronic diary for reporting local reactions and systemic events) N=9839	Per protocol

**Table S1 | Explanation of the Changes in Denominator Numbers in Various Analyses.**

Charlson Comorbidity Index Category	BNT162b2 (N <sup>a</sup> =22,026)	Placebo (N <sup>a</sup> =22,021)	Total (N <sup>a</sup> =44,047)
	n <sup>b</sup> (%)	n <sup>b</sup> (%)	n <sup>b</sup> (%)
Participants with any Charlson comorbidity	4628 (21.0)	4511 (20.5)	9139 (20.7)
AIDS/HIV	100 (0.5)	100 (0.5)	200 (0.5)
Any malignancy	812 (3.7)	757 (3.4)	1569 (3.6)
Cerebrovascular disease	227 (1.0)	198 (0.9)	425 (1.0)
Chronic pulmonary disease	1783 (8.1)	1775 (8.1)	3558 (8.1)
Congestive heart failure	109 (0.5)	102 (0.5)	211 (0.5)
Dementia	7 (0.0)	11 (0.0)	18 (0.0)
Diabetes with chronic complication	116 (0.5)	130 (0.6)	246 (0.6)
Diabetes without chronic complication	1700 (7.7)	1699 (7.7)	3399 (7.7)
Hemiplegia or paraplegia	15 (0.1)	25 (0.1)	40 (0.1)
Leukemia	14 (0.1)	11 (0.0)	25 (0.1)
Lymphoma	26 (0.1)	36 (0.2)	62 (0.1)
Metastatic solid tumor	4 (0.0)	3 (0.0)	7 (0.0)
Mild liver disease	152 (0.7)	115 (0.5)	267 (0.6)
Moderate or severe liver disease	2 (0.0)	3 (0.0)	5 (0.0)
Myocardial infarction	225 (1.0)	218 (1.0)	443 (1.0)
Peptic ulcer disease	63 (0.3)	84 (0.4)	147 (0.3)
Peripheral vascular disease	144 (0.7)	139 (0.6)	283 (0.6)
Renal disease	140 (0.6)	153 (0.7)	293 (0.7)
Rheumatic disease	75 (0.3)	71 (0.3)	146 (0.3)

**Table S2 | Baseline Comorbidities in Participants  $\geq 16$  Years of Age.** Baseline comorbid conditions are classified according to the Charlson Comorbidity Index (Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245-51.). a. N=number of participants in the specified group. This value is the denominator for the percentage calculations. b. n=number of participants with the specified characteristic. Participants with multiple occurrences within each category are counted only once. For ‘Participants with any Charlson comorbidity’, n=number of participants reporting  $\geq 1$  occurrence of any Charlson comorbidity.

<b>Adverse Event</b>	<b>BNT162b2 (N<sup>a</sup>=21,926) n<sup>b</sup> (%)</b>	<b>Placebo (N<sup>a</sup>=21,921) n<sup>b</sup> (%)</b>
Any event	6617 (30.2)	3048 (13.9)
Related <sup>c</sup>	5241 (23.9)	1311 (6.0)
Severe	262 (1.2)	150 (0.7)
Life-threatening	21 (0.1)	26 (0.1)
Any serious adverse event	127 (0.6)	116 (0.5)
Related <sup>c,d</sup>	3 (0.0)	0
Severe	71 (0.3)	66 (0.3)
Life-threatening	21 (0.1)	26 (0.1)
Any adverse event leading to withdrawal	32 (0.1)	36 (0.2)
Related <sup>c</sup>	13 (0.1)	11 (0.1)
Severe	10 (0.0)	10 (0.0)
Life-threatening	3 (0.0)	7 (0.0)
Death	3 (0.0)	5 (0.0)

**Table S3 | Participants Reporting at Least 1 Adverse Event from Dose 1 to 1 Month After Dose 2 During the Blinded Follow-up Period.** The population included all  $\geq 16$ -year-old participants who received  $\geq 1$  dose of vaccine irrespective of follow-up time. a. N=number of participants in the specified group. This value is the denominator for the percentage calculations. b. n=Number of participants reporting  $\geq 1$  occurrence of the specified event category. For ‘any event’, n=number of participants reporting  $\geq 1$  occurrence of any event. c. Assessed by the investigator as related to investigational product. d. Shoulder injury related to vaccine administration, right axillary lymphadenopathy, and paroxysmal ventricular arrhythmia (as previously reported). Adverse events for 12–15-year-old participants were reported previously.<sup>11</sup>

Reported Cause of Death <sup>a</sup>	BNT162b2 (N=21,926)	Placebo (N=21,921)
	n	n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1
Cardiac failure congestive	1	0
Cardiorespiratory arrest	1	1
Chronic obstructive pulmonary disease	1	0
Death	0	1
Dementia	0	1
Emphysematous cholecystitis	1	0
Hemorrhagic stroke	0	1
Hypertensive heart disease	1	0
Lung cancer metastatic	1	0
Metastases to liver	0	1
Missing	0	1
Multiple organ dysfunction syndrome	0	2
Myocardial infarction	0	2
Overdose	0	1
Pneumonia	0	2
Sepsis	1	0
Septic shock	1	0
<i>Shigella</i> sepsis	1	0
Unevaluable event	1	0

**Table S4 | Causes of Death from Dose 1 to Unblinding (Safety Population, ≥16 Years Old). a.** Multiple causes of death could be reported for each participant. There were no deaths among 12–15-year-old participants.

First COVID-19 Occurrence after Dose 1	BNT162b2 (N <sup>a</sup> =23,040)		Placebo (N <sup>a</sup> =23,037)		VE (%)	(95% CI <sup>e</sup> )
	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )		
Overall (≥12 years old)	131	8.412 (22,505)	1034	8.124 (22,434)	87.8	(85.3, 89.9)
<b>Efficacy endpoint by subgroup</b>						
Select age groups (years)						
16 to 17	3	0.094 (373)	19	0.090 (370)	84.8	(48.4, 97.1)
16 to 55	95	4.845 (12,645)	693	4.669 (12,626)	86.8	(83.6, 89.5)
>55	33	3.310 (8740)	306	3.204 (8689)	89.6	(85.0, 92.9)
≥65	12	1.645 (4455)	138	1.596 (4437)	91.6	(84.8, 95.7)
≥75	2	0.326 (905)	26	0.310 (877)	92.7	(70.7, 99.2)
Sex						
Male	70	4.355 (11,560)	500	4.115 (11,312)	86.8	(83.0, 89.9)
Female	61	4.057 (10,945)	534	4.009 (11,122)	88.7	(85.3, 91.5)
Race						
White	115	6.957 (18,538)	916	6.719 (18,479)	87.9	(85.3, 90.1)
Black or African American	6	0.783 (2042)	53	0.770 (2063)	88.9	(74.1, 96.1)
American Indian or Alaska Native	1	0.061 (216)	7	0.055 (209)	86.9	(-1.6, 99.7)
Asian	4	0.348 (995)	26	0.337 (990)	85.1	(57.0, 96.2)
Native Hawaiian or other Pacific Islander	0	0.021 (58)	1	0.011 (32)	100.0	(-2000.0, 100.0)
Multiracial	5	0.208 (565)	25	0.190 (546)	81.8	(51.6, 94.6)
Not reported	0	0.035 (91)	6	0.042 (115)	100.0	(-0.7, 100.0)
Ethnicity						
Hispanic/Latinx	52	2.351 (5701)	302	2.282 (5673)	83.3	(77.5, 87.8)
Non-Hispanic/non-Latinx	78	6.018 (16,692)	730	5.799 (16,647)	89.7	(87.0, 92.0)
Not reported	1	0.043 (112)	2	0.043 (114)	49.4	(-872.9, 99.1)
Country						
Argentina	32	1.282 (2846)	146	1.269 (2840)	78.3	(68.0, 85.7)
Brazil	14	0.554 (1430)	95	0.520 (1420)	86.1	(75.6, 92.7)
Germany	2	0.067 (246)	1	0.069 (250)	-104.5	(-11,965.9, 89.4)
South Africa	0	0.128 (367)	11	0.125 (365)	100.0	(61.1, 100.0)
Turkey	3	0.048 (246)	12	0.045 (244)	76.4	(12.4, 95.7)
USA	80	6.333 (17,370)	769	6.095 (17,315)	90.0	(87.4, 92.1)
Baseline SARS-CoV-2 status						
Positive <sup>f</sup>	13	0.250 (692)	17	0.265 (736)	19.2	(-76.6, 63.9)
Positive N-binding only	2	0.192 (521)	7	0.198 (542)	70.5	(-54.7, 97.0)

Positive NAAT only	10	0.020 (66)	9	0.020 (69)	-10.5	(-207.3, 59.7)
Positive NAAT and N-binding	1	0.038 (105)	1	0.046 (124)	-20.5	(-9359.2, 98.5)
Negative <sup>g</sup>	116	8.101 (21,615)	1015	7.804 (21,521)	89.0	(86.6, 91.0)
Unknown	2	0.061 (198)	2	0.055 (177)	9.7	(-1145.4, 93.5)

**Table S5 | Vaccine Efficacy Overall and by Subgroup after Dose 1 During the Blinded Placebo Controlled Follow-up Period (All-Available Population).** Efficacy data are presented for participants  $\geq 12$  years old. a. N=number of participants in the specified group. b. n1=Number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from dose 1 to the end of the surveillance period. d. n2=number of participants at risk for the endpoint. e. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. f. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. g. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

Efficacy Endpoint Subgroup	BNT162b2 (N <sup>a</sup> =23,040)		Placebo (N <sup>a</sup> =23,037)		VE (%)	(95% CI <sup>e</sup> )
	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )		
First severe COVID-19 occurrence after dose 1	1	8.439 (22,505)	30	8.288 (22,435)	96.7	(80.3, 99.9)
After dose 1 to before dose 2	0	1.351 (22,505)	6	1.360 (22,435)	100.0	(14.5, 100.0)
Dose 2 to 7 days after dose 2	0	0.425 (22,170)	1	0.423 (22,070)	100.0	(-3783.5, 100.0)
≥7 Days after dose 2	1	6.663 (22,142)	23	6.505 (22,048)	95.7	(73.9, 99.9)

**Table S6 | Vaccine Efficacy against Severe COVID-19 Occurrence after Dose 1 (All-Available Population).** Efficacy data are presented for participants ≥12 years old. a. N=number of participants in the specified group. b. n1=number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for severe COVID-19 case accrual is from dose 1 to the end of the surveillance period for the overall row, and from the start to the end of the range stated for each time interval. d. n2=number of participants at risk for the endpoint. e. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. Severe COVID-19 as defined by the US FDA [<https://www.fda.gov/media/137926/download>].

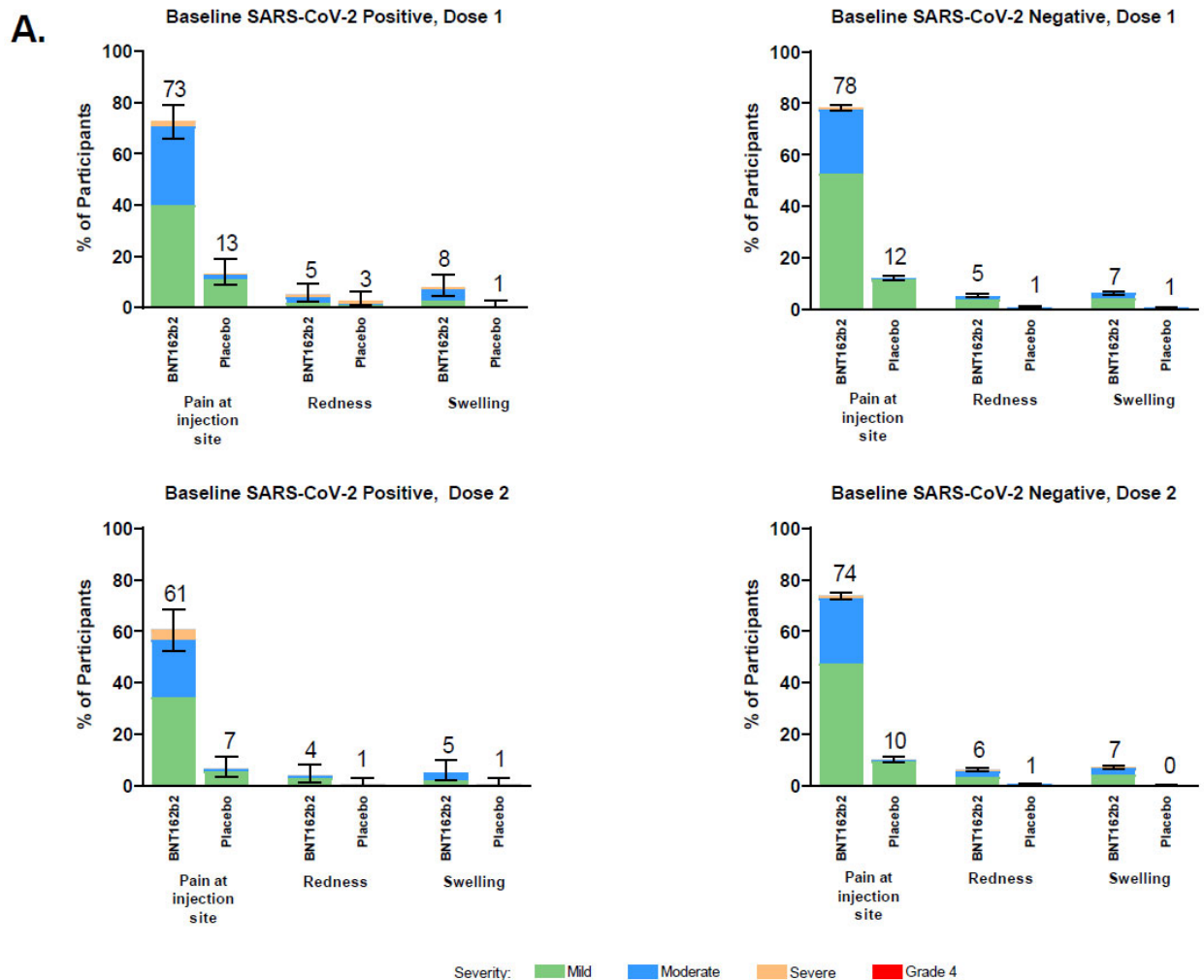
Efficacy Endpoint Subgroup	BNT162b2 (N <sup>a</sup> =20,998)		Placebo (N <sup>a</sup> =21,096)		VE (%)	(95% CI <sup>e</sup> )
	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )	n1 <sup>b</sup>	Surveillance Time <sup>c</sup> (n2 <sup>d</sup> )		
<b>First COVID-19 occurrence from 7 days after dose 2</b>						
Overall (≥12 years old)	77	6.247 (20,712)	850	6.003 (20,713)	91.3	(89.0, 93.2)
At risk <sup>f</sup>						
Yes	35	2.797 (9167)	401	2.681 (9136)	91.6	(88.2, 94.3)
No	42	3.450 (11,545)	449	3.322 (11,577)	91.0	(87.6, 93.6)
Age group (years) and at risk						
16–64 and at risk	29	2.083 (6632)	325	1.993 (6629)	91.5	(87.5, 94.4)
≥65 and at risk	6	0.680 (2322)	71	0.656 (2304)	91.8	(81.4, 97.1)
Obese <sup>g</sup>						
Yes	27	2.103 (6796)	314	2.050 (6875)	91.6	(87.6, 94.6)
No	50	4.143 (13,911)	536	3.952 (13,833)	91.1	(88.1, 93.5)
Age group (years) and obese						
16–64 and obese	24	1.680 (5303)	266	1.624 (5344)	91.3	(86.7, 94.5)
≥65 and obese	3	0.404 (1370)	45	0.410 (1426)	93.2	(78.9, 98.7)

**Table S7 | Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities (Risk Status)**

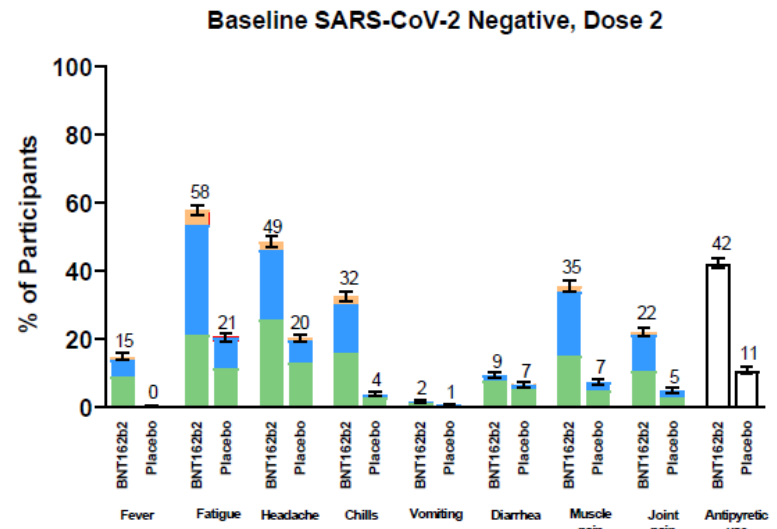
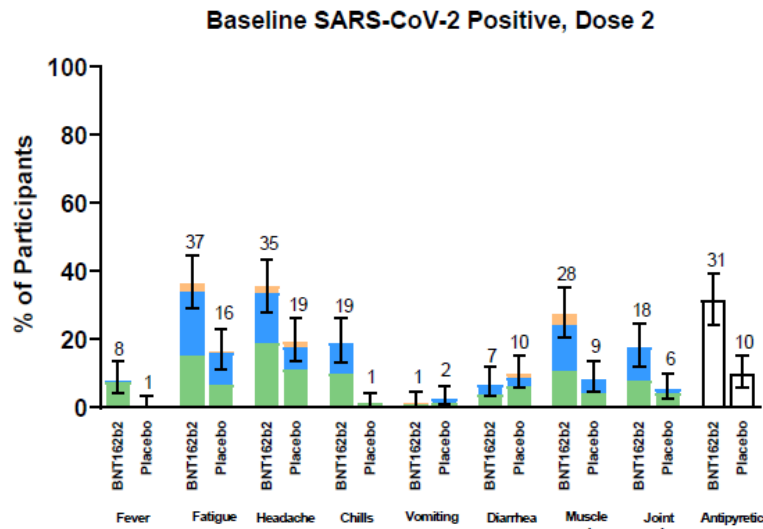
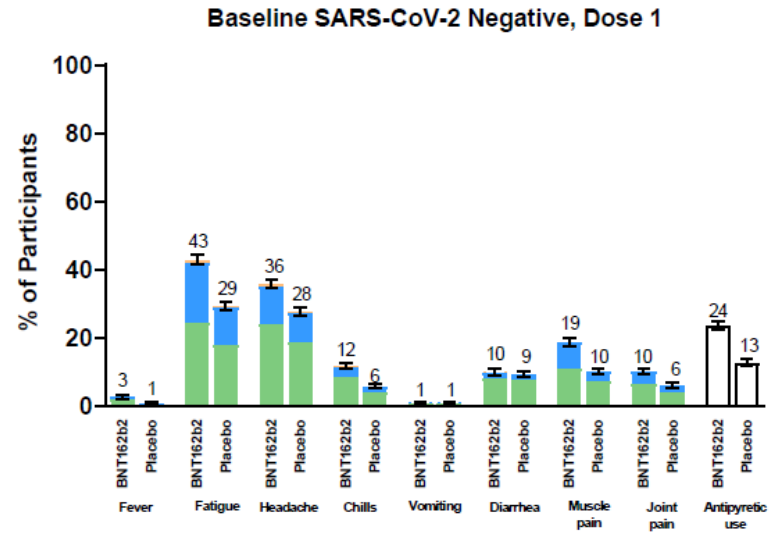
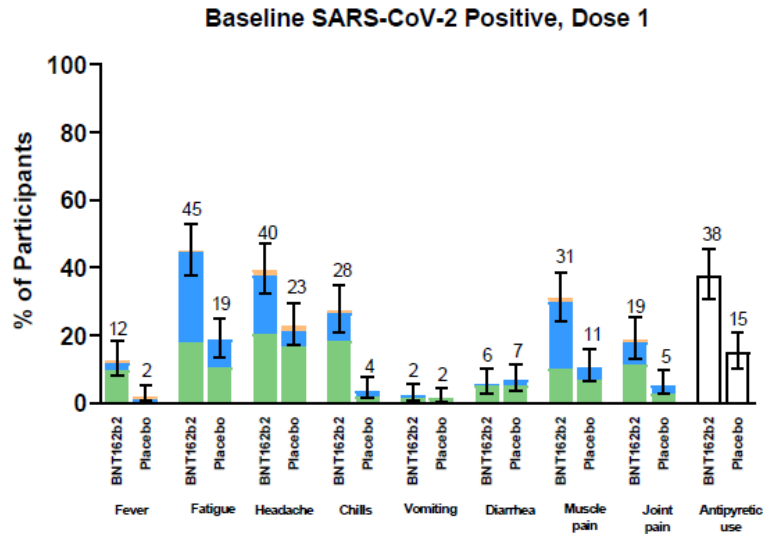
**among Participants Without Evidence of Infection Prior to 7 Days after Dose 2 (Evaluable Efficacy Population).** Efficacy data are presented for participants ≥12 years old. a. N=number of participants in the specified group. b. n1=number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after dose 2 to the end of the surveillance period. d. n2=number of participants at risk for the endpoint. e. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. f. Includes participants who had ≥1 Charlson Comorbidity Index (CMI) category or obesity (body mass index [BMI] ≥30 kg/m<sup>2</sup> [≥16 years old] or BMI ≥95th percentile [12–15 years old]). g. Participants who had BMI ≥30 kg/m<sup>2</sup> (≥16 years old) or BMI ≥95th percentile (12–15 years old; refer to the CDC growth charts at [https://www.cdc.gov/growthcharts/html\\_charts/bmiagerev.htm](https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm)).



**Figure S1 | Local Reactions and Systemic Events Reported within 7 Days after Receipt of BNT162b2 or Placebo by Baseline SARS-CoV-2 Status.** Local reactions and systemic events and medication use were collected with electronic diaries for 7 days after each vaccination from  $\geq 16$ -year-old participants in the reactogenicity subset ( $n=9839$ ; ie, participants who used an electronic diary for reporting local reactions and systemic events). **A.** Solicited injection-site (local) reactions. Pain at the injection site scale: mild, does not interfere with activity; moderate: interferes with activity; severe, prevents daily activity; Grade 4, emergency room visit or hospitalization). Redness and swelling scale: mild, 2.0 to 5.0 cm in diameter; moderate,  $>5.0$  to 10.0 cm in diameter; severe,  $>10.0$  cm in diameter; Grade 4, necrosis or exfoliative dermatitis for redness and necrosis for swelling. **B.** Systemic events and medication use. Fever scale as indicated in the key. Medication use is not graded. Fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain scale: mild, does not interfere with activity; moderate, some interference with activity; severe, prevents daily activity; Grade 4, emergency room visit or hospitalization. Vomiting scale: mild, 1 to 2 times in 24 hours; moderate,  $>2$  times in 24 hours; severe, requires intravenous hydration; Grade 4, emergency room visit or hospitalization. Diarrhea scale: mild, 2 to 3 loose stools in 24 hours; moderate, 4 to 5 loose stools in 24 hours; severe, 6 or more loose stools in 24 hours; Grade 4, emergency room visit or hospitalization. Whiskers represent 95% CIs. Numbers above the whiskers are the overall percentage of participants in each group reporting the specified local reaction or systemic event. One participant who received BNT162b2 reported a fever of  $>40.0^{\circ}\text{C}$ , but this is not visible on the graph. Local reactions and systemic events for 12-15-year-old participants have been reported previously (Frenck RW, et al. *N Engl J Med* 2021;385(3):239-250).



**B.**



Severity: Mild Moderate Severe Grade 4  
 Fever: 38.0°C-38.4°C >38.4°C-38.9°C >38.9°C-40.0°C >40.0°C