Supplementary Appendix

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

Supplement to: Walsh EE, Frenck RW Jr, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. N Engl J Med. DOI: 10.1056/NEJMoa2027906

SUPPLEMENTARY APPENDIX

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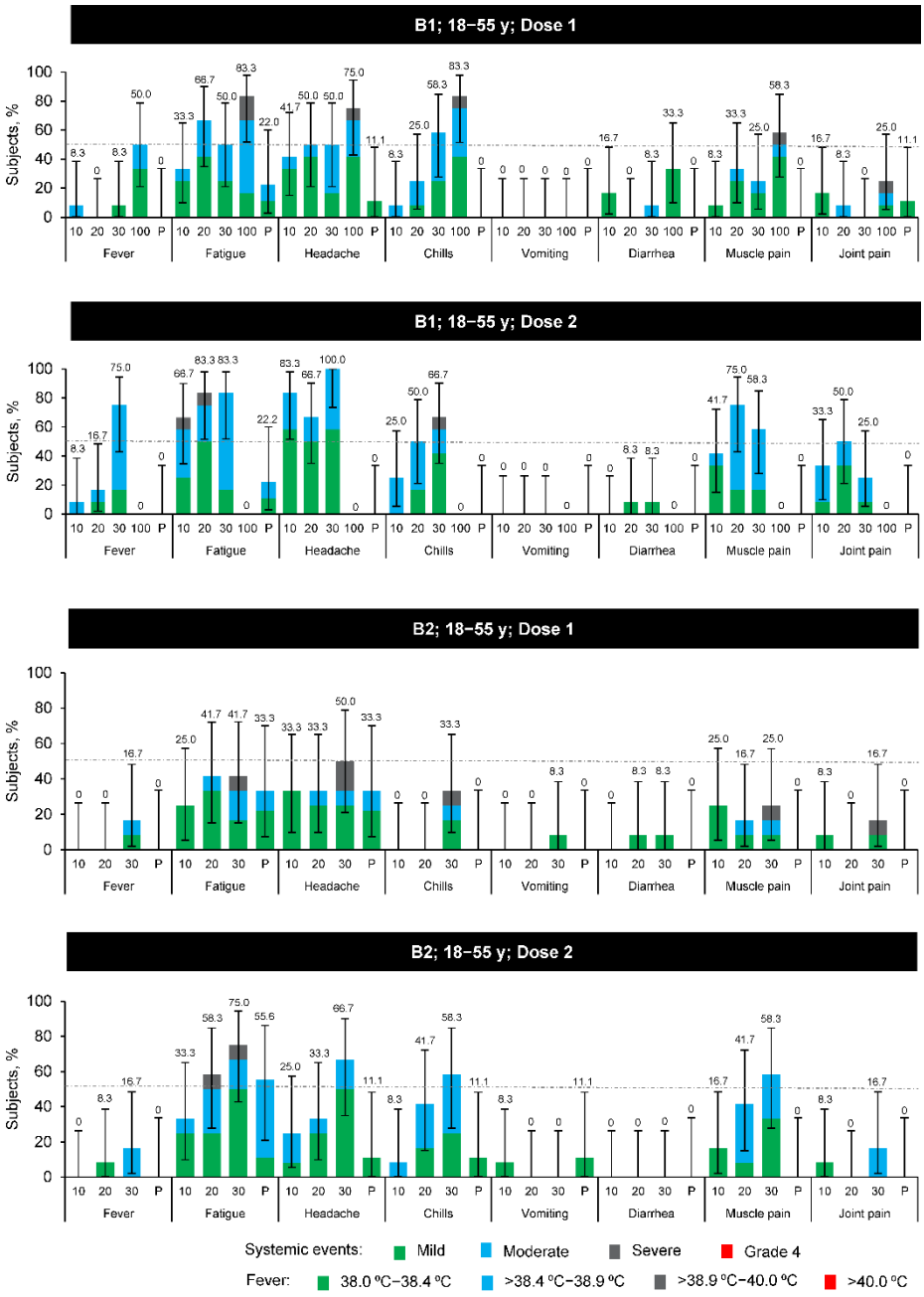


Figure S1 | Systemic events reported within 7 days after vaccination, 18–55 years of age. Systemic events were collected with electronic diaries for 7 days after each vaccination. Fever scale as indicated in the key. Fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain (mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity), vomiting (mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration) and diarrhea (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 for all events: emergency room visit or hospitalization; 10 = 10 µg; 20 = 20 µg; 30 = 30 µg; P = placebo; B1 – BNT162b1; B2 – BNT162b2. A second dose of BNT162b1 100 µg was not given to participants in the 18–55 year old group because of unsatisfactory tolerability after the first dose. Whiskers represent 95% confidence limits. Numbers above the whiskers are the overall percentage of subjects in each group reporting the specified systemic event.

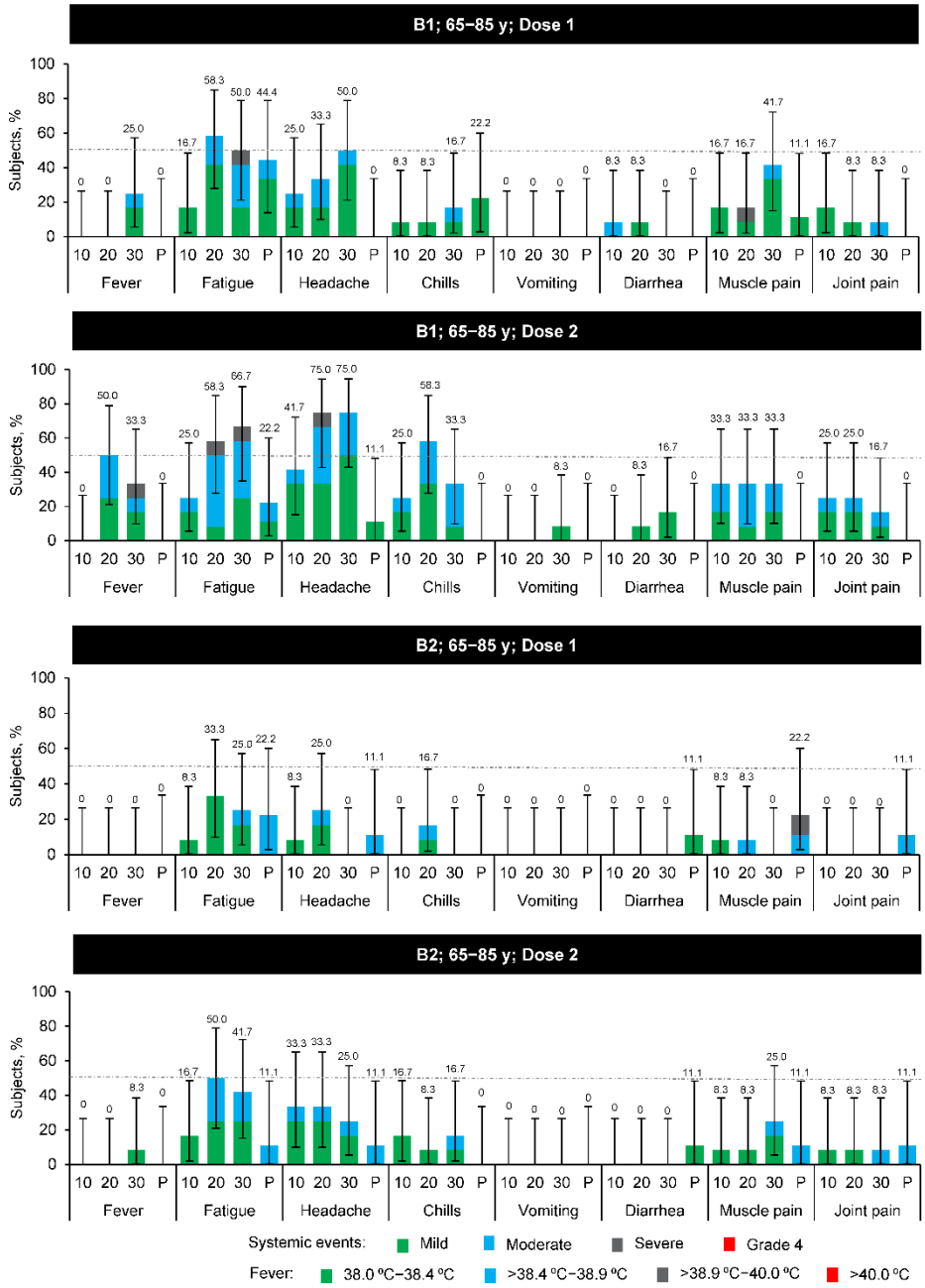
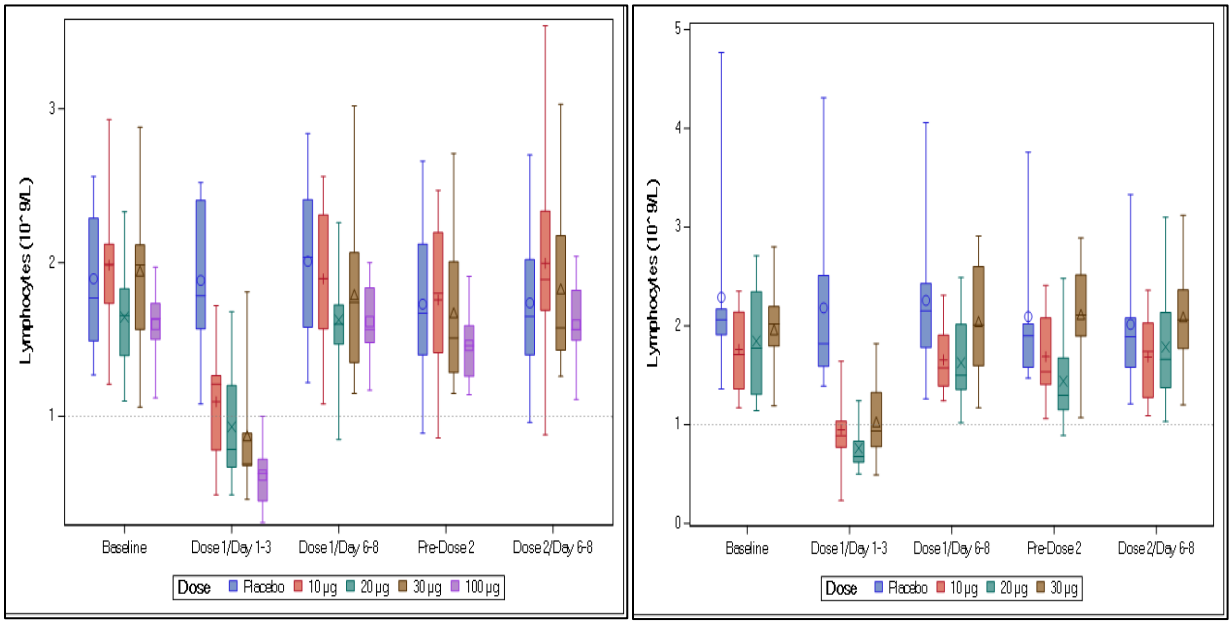


Figure S2 | Systemic events reported within 7 days after vaccination, 65–85 years of age. Systemic events were collected with electronic diaries for 7 days after each vaccination. Fever scale as indicated in the key. Fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain (mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity), vomiting (mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration) and diarrhea (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 for all events: emergency room visit or hospitalization; 10 = 10 µg; 20 = 20 µg; 30 = 30 µg; P = placebo; B1 – BNT162b1; B2 – BNT162b2. A second dose of BNT162b1 100 µg was not given to participants in the 18–55 year old group because of unsatisfactory tolerability after the first dose. Whiskers represent 95% confidence limits. Numbers above the whiskers are the overall percentage of subjects in each group reporting the specified systemic event.

a. **b.**



c. **d.**

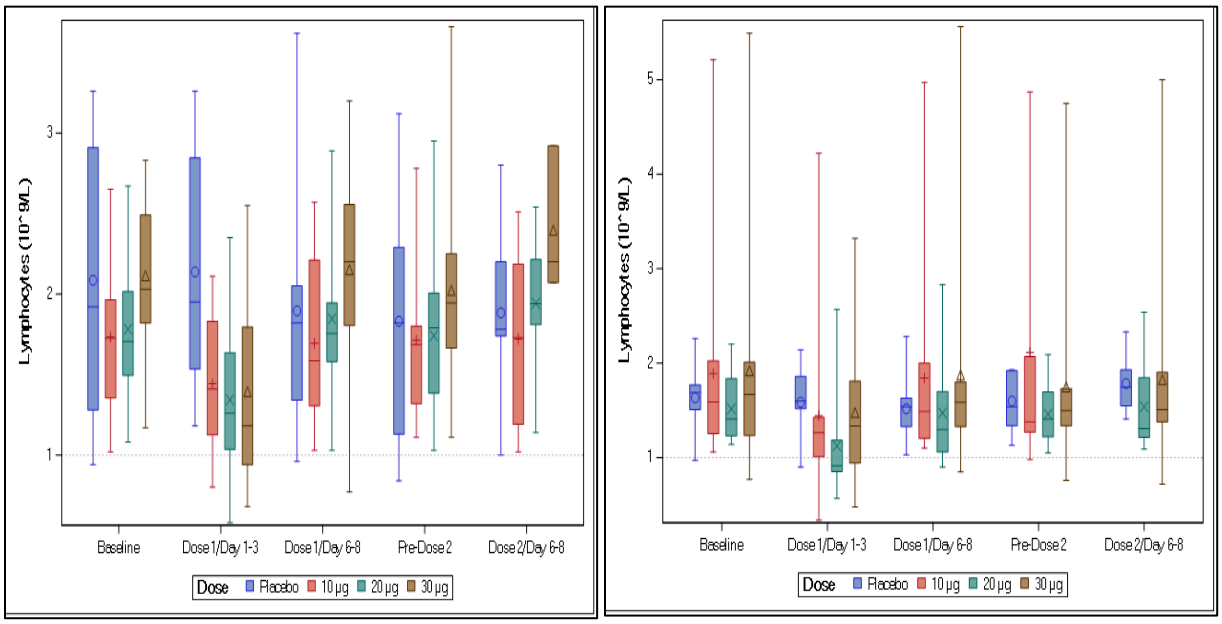


Figure S3 | Postvaccination changes in lymphocyte count over time. Figure represents box-and-whisker plots for observed values at the following time points: Dose 1/Day 1-3: ~1 day after Dose 1; Dose 2/Day 6-8: ~7 days after Dose 1; Pre-Dose 2: before Dose 2; Dose 2/Day 6-8: ~ 7 days after Dose 2. Symbols denote group means – O: placebo; **+:** 10 µg; X: 20 µg; △: 30 µg; □: 100 µg. Center line of box denotes median; lower and upper edges denote first and third quartiles; lower and upper whiskers denote minimum and maximum. **a.** BNT162b1 18–55 years of age; **b.** BNT162b1 65–85 years of age; **c.** BNT162b2 18–55 years of age; **d.** BNT162b2 65–85 years of age.

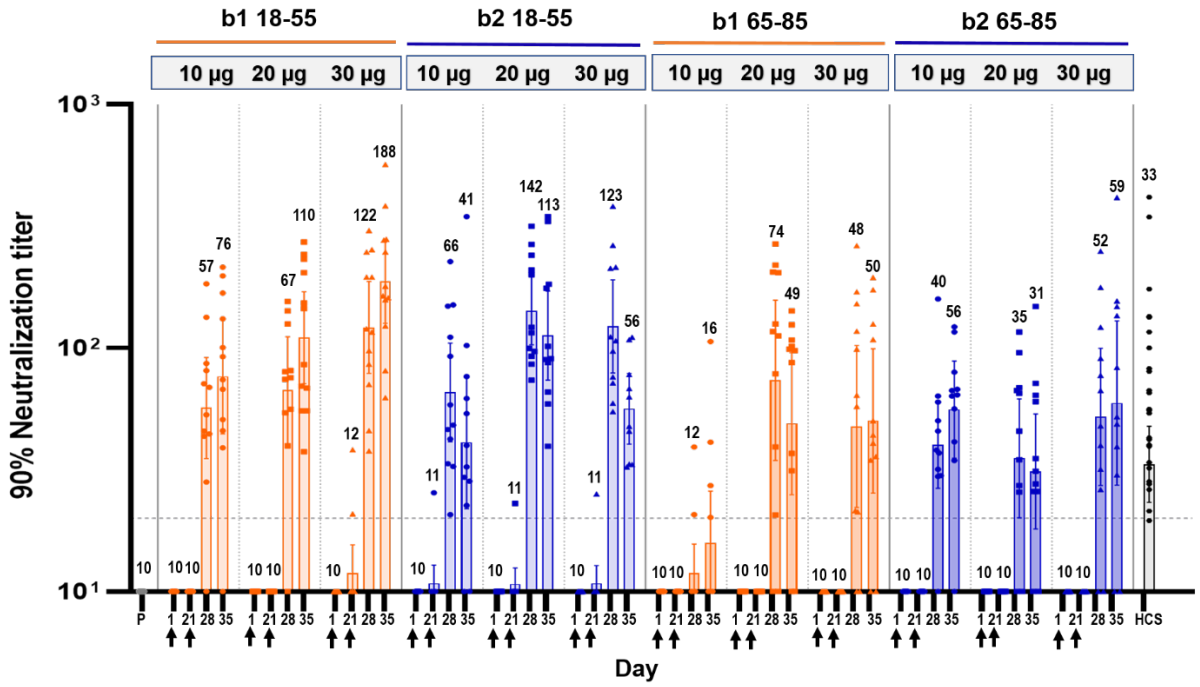


Figure S4 | 90% neutralization titers elicited by BNT162b1 and BNT162b2. Participants in groups of 15 were vaccinated with the indicated dose levels of either BNT162b vaccine candidate (n=12) or with placebo (n=3) on Days 1 and 21. Reponses in placebo recipients for each of the dosing groups are combined (P). Sera were obtained before vaccination (Day 1) and 21, 28 and 35 days after Dose 1. The 28-day blood collection is 7 days after Dose 2 and Day 35 14 days after Dose 2. Human COVID-19 convalescent sera (HCS, n=38) were obtained at least 14 days after polymerase chain reaction-confirmed diagnosis and at a time when the donors were asymptomatic. 90% SARS-CoV-2–neutralizing geometric mean titers (GMTs). LLOQ is 20. All groups had 12 valid results from evaluable samples at each time point except for: 20 µg BNT162b1, age 18-55, Day 28, n=11; 30 µg BNT162b2, age 18-55, Day 28 n=11; 30 µg BNT162b2, age 18-55, Day 35, n=10; 30 µg BNT162b1, age 65-85, Day 35, n=11; 10 µg BNT162b2, age 65-85, Day 35, n=11; and 30 µg BNT162b2, age 65-85, Day 35, n=11**.** Each data point represents a serum sample, and each vertical bar represents a geometric mean with 95% CI. The numbers above the bars are the GMTs for the group. Arrows indicate timing of vaccination (blood draws were conducted prior to vaccination on vaccination days).

BNT162b1	18–55 Years of Age					65–85 Years of Age			
	10 µg (n=12)	20 µg (n=12)	30 µg (n=12)	100 µg (n=12)	Placebo (n=12)	10 µg (n=12)	20 µg (n=12)	30 µg (n=12)	Placebo (n=9)
Any event, n (%)	6 (50.0)	5 (41.7)	6 (50.0)	7 (58.3)	2 (16.7)	7 (58.3)	7 (58.3)	3 (25.0)	4 (44.4)
Related	3 (25.0)	4 (33.3)	6 (50.0)	6 (50.0)	1 (8.3)	3 (25.0)	4 (33.3)	2 (16.7)	1 (11.1)
Severe	0	0	1 (8.3)	1 (8.3)	0	0	1 (8.3)	1 (8.3)	0
Life-threatening	0	0	0	0	0	0	0	0	0
Any SAE, n (%)	0	0	0	0	0	0	0	0	0
Any AE leading to withdrawal, n (%)	0	0	0	0	0	0	0	0	0
Death, n (%)	0	0	0	0	0	0	0	0	0
BNT162b2	**18–55 Years of Age**					**65–85 Years of Age**			
	10 µg (n=12)	**20 µg (n=12)**	**30 µg (n=12)**	**100 µg (n=0)**	**Placebo (n=9)**	**10 µg (n=12)**	**20 µg (n=12)**	**30 µg (n=12)**	**Placebo (n=9)**
Any event, n (%)	4 (33.3)	5 (41.7)	5 (41.7)	–	2 (22.2)	1 (8.3)	2 (16.7)	3 (25.0)	2 (22.2)
Related	2 (16.7)	4 (33.3)	3 (25.0)	–	1 (11.1)	0	1 (8.3)	0	0
Severe	0	0	1 (8.3)	–	0	0	0	1 (8.3)	1 (11.1)
Life-threatening	0	0	0	–	0	0	0	0	0
Any SAE, n (%)	0	0	0	–	0	0	0	0	0
Any AE leading to withdrawal, n (%)	0	0	0	–	0	0	0	0	0
Death, n (%)	0	0	0	–	0	0	0	0	0

Table S1 | Adverse events by age group and vaccine candidate. AE=adverse event. Related AE=adverse event that in the opinion of the investigator was possibly related to study vaccine. SAE=serious adverse event.