

## Supplemental Online Content

Spitzer A, Angel Y, Marudi O, et al. Association of a third dose of BNT162b2 vaccine with incidence of SARS-CoV-2 infection among health care workers. *JAMA*. Published online January 10, 2021. doi:10.1001/jama.2021.23641

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

## **eMethods**

### **Laboratory methods**

SARS-Cov-2 was detected in nasopharyngeal specimens using reverse-transcriptase polymerase chain reaction (RT-PCR). The following assays were used at the hospital's clinical virology laboratory: 1) the Seegene Allplex™ 2019-nCoV assay, targeting the E, N and RdRP genes; 2) the cobas® SARS-CoV-2 assay, targeting the E and the ORF genes; 3) the Xpert® Xpress SARS-CoV-2, targeting the E and the N genes; 4) the Simplexa™ COVID-19 Direct assay, targeting the S and the ORF genes.

Cycle threshold values of each gene were documented and values of <30 were considered a positive result.

Serologic testing for anti-spike protein receptor binding domain (anti-S1 RBD) IgG were performed using indirect chemiluminescent microparticle immunoassay on the ADVIA Centaur XP system (Siemens, Tarrytown, NY). Antibody levels are presented as an index value. A conversion factor between Index Values and the WHO binding antibody units (BAU/mL) has been established: 1.00 Index on the sCOVG Assay would have a WHO BAU/mL value of 21.8<sup>1</sup>.

### **External R packages**

Cox regression and Kaplan-Meier analysis were implemented with R's survival and survminer packages.

**eTable 1.**

Candidate covariates for inclusion in the Cox regression analysis. Only the covariates with a statistically significant contribution were included in the final regression model. For categorical variables, the first value represents the baseline level.

<b>Covariate name</b>	<b>Variable type</b>	<b>Chisq</b>	<b>Df</b>	<b>P(&gt; Chi )</b>	<b>Significant</b>
Baseline serology titer	Categorical (Low, High)	5.5	1	0.01	*
Age	Continuous	0.17	1	0.7	
Age group	Categorical (<30, 30-39, 40-49, 50-59, 60+)	6.3	4	0.2	
Sex	Categorical (Female, Male)	0.48	1	0.5	
Marital status	Categorical (Single, Married, Divorced, Widow)	1.4	3	0.7	
Number of children	Continuous	6.8	1	0.009	*
Employment sector	Categorical (Administration, Medicine, Nursing, Other health profession, Research)	5.6	4	0.2	
Employment risk level	Categorical (Low, Medium, High)	0.02	2	0.99	
Number of influenza vaccinations in past 3 years	Categorical (0, 1, 2, 3)	3.4	3	0.3	
Month of 2nd dose receipt	Categorical (January, February-May)	10.8	1	0.001	*
Number of PCR tests in each exposure state	Continuous	8.1	1	0.004	*
BMI	Continuous	2.8	1	0.09	
Smoking	Categorical (Never, Past, Current)	1.2	2	0.55	
Day of enrollment to the study	Continuous	1.1	1	0.3	

**eTable 2.** Characteristics of SARS-CoV-2 positive participants (n=44).

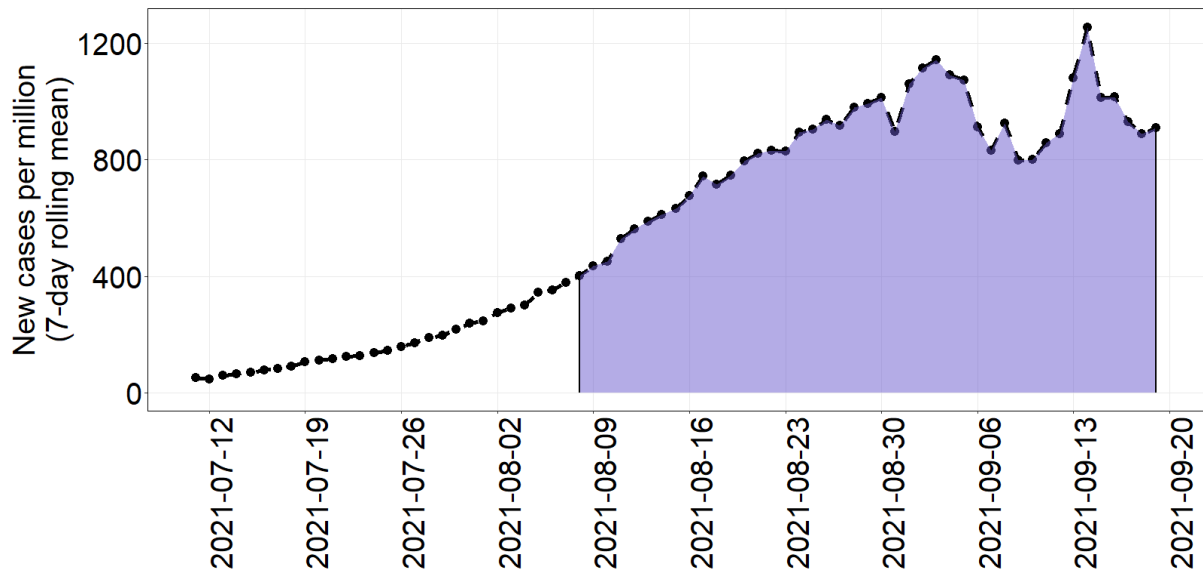
No. of participants	44
Symptomatic (%)	31 (70.4)
Female sex (%)	31 (70.4)
Male sex (%)	13 (29.5)
Age (median [IQR])	43.00 [34.00, 47.50]
Age group (%)	
<30	5 (11.4)
30-39	10 (22.7)
40-49	20 (45.5)
50-59	8 (18.2)
60+	1 (2.3)
Marital status (%)	
Married	28 (63.6)
Single	12 (27.3)
Divorced	4 (9.1)
Widow	0 (0.0)
No. of children (mean (SD))	2.09 (1.74)
Employment sector (%)	
Administration	22 (50.0)
Nursing	8 (18.2)
Medicine	7 (15.9)
Health Professions	5 (11.4)
Research	2 (4.5)
Estimated risk of exposure to SARS-CoV-2 (%)	
Low	38 (86.4)
Medium	1 (2.3)
High	5 (11.4)
Height, cm (mean (SD))	167.18 (9.91)
Weight, KG (mean (SD))	74.09 (16.28)
BMI, KG/m <sup>2</sup> (mean (SD))	26.40 (4.98)
Smoking history (%)	
Current smoker	5 (11.4)
Never smoked	29 (65.9)
Past smoking	10 (22.7)
Number of influenza vaccinations in past 3 years (%)	
0	9 (20.5)
1	9 (20.5)
2	13 (29.5)

No. of participants	44
3	13 (29.5)
Hypertension (%)	5 ( 11.4)
Diabetes mellitus (%)	3 ( 6.8)
Hypercholesterolemia (%)	9 ( 20.5)
Ischemic heart disease (%)	1 ( 2.3)
Solid malignancy in past 5 years (%)	0
Hematological malignancy in past 5 years (%)	0
Pulmonary disease (%)	0
Renal disease (%)	1 ( 2.3)
Liver disease (%)	1 ( 2.3)
Hospitalizations in past 3 years (%)	2 ( 4.5)
Baseline serology, Index Value (median [IQR])	5.1 [3.8, 8.5]
Time from 2nd dose to enrollment, days (median [IQR])	210 [207.7, 212.2]
2nd dose administration month (%)	
January 2021	43 (97.7)
February 2021	1 (2.3)
March 2021	0
April 2021	0
May 2021	0
Surveillance time, days (median [IQR])	12.50 [7.00, 19.50]
Number of RT-PCR tests per participant (median [IQR])	2.00 [1.00, 3.00]
Number of tests performed during the study period (%)	
At least one test	39 (88.6)
At least two tests	24 (54.5)
Three or more tests	16 (36.6)

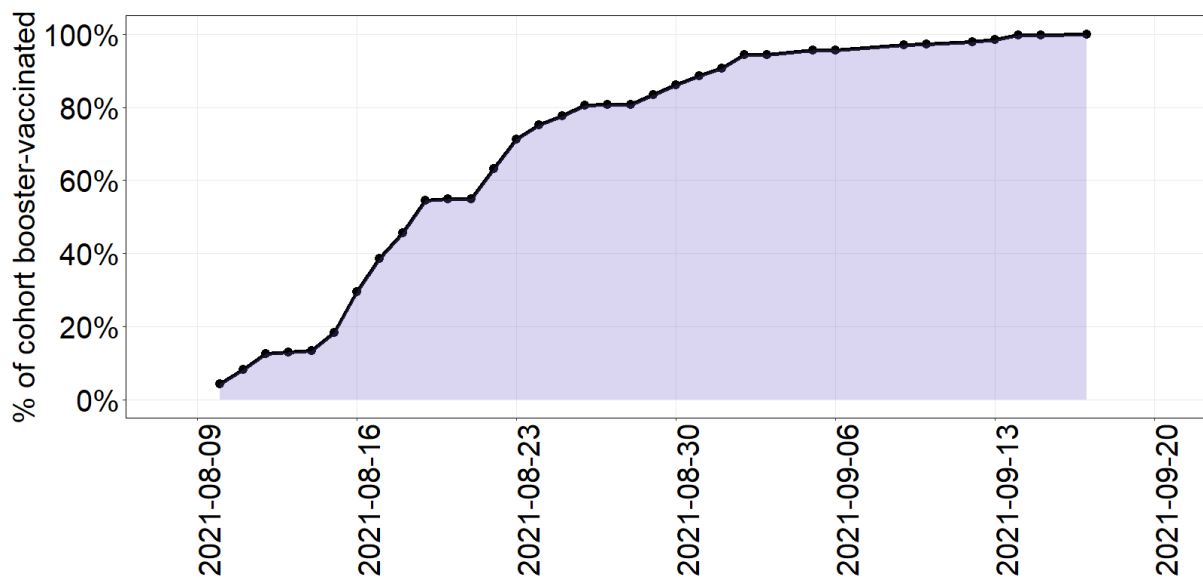
**eTable 3.** Baseline characteristics stratified by booster dose receipt status.

	Booster non-recipients	Booster recipients	SMD
No. of participants	278	1650	
Baseline serology, Index Value (median [IQR])	9.25 [5.41, 18.97]	5.42 [3.02, 9.60]	0.527
Baseline serology > 5.5 index values (%)	205 (73.7)	814 (49.3)	0.518
Age (median [IQR])	42.00 [34.00, 51.00]	45.00 [36.00, 52.00]	0.168
Age group (%)			0.223
<30	38 (13.7)	128 ( 7.8)	
30-39	79 (28.4)	454 (27.5)	
40-49	81 (29.1)	507 (30.7)	
50-59	63 (22.7)	474 (28.7)	
60+	17 ( 6.1)	87 ( 5.3)	
Sex			0.298
Male sex (%)	49 (17.6)	498 (30.2)	
Female sex (%)	229 (82.4)	1152 (69.8)	
2nd dose administration month (%)			0.758
January 2021	173 (62.2)	1518 (92%)	
February-May 2021 (%)	105 (37.8)	132 ( 8.0)	

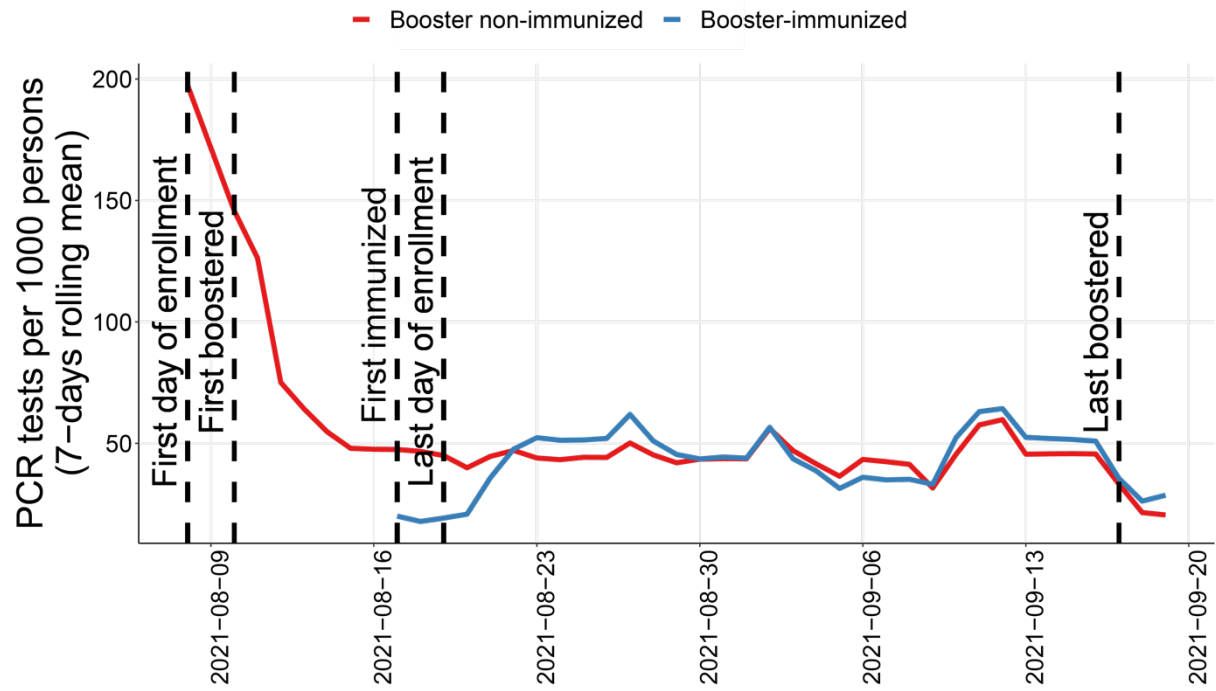
**eFigure 1.** SARS-CoV-2 spread in Israel throughout the study period (marked in the shaded area). Data taken from Our World In Data.



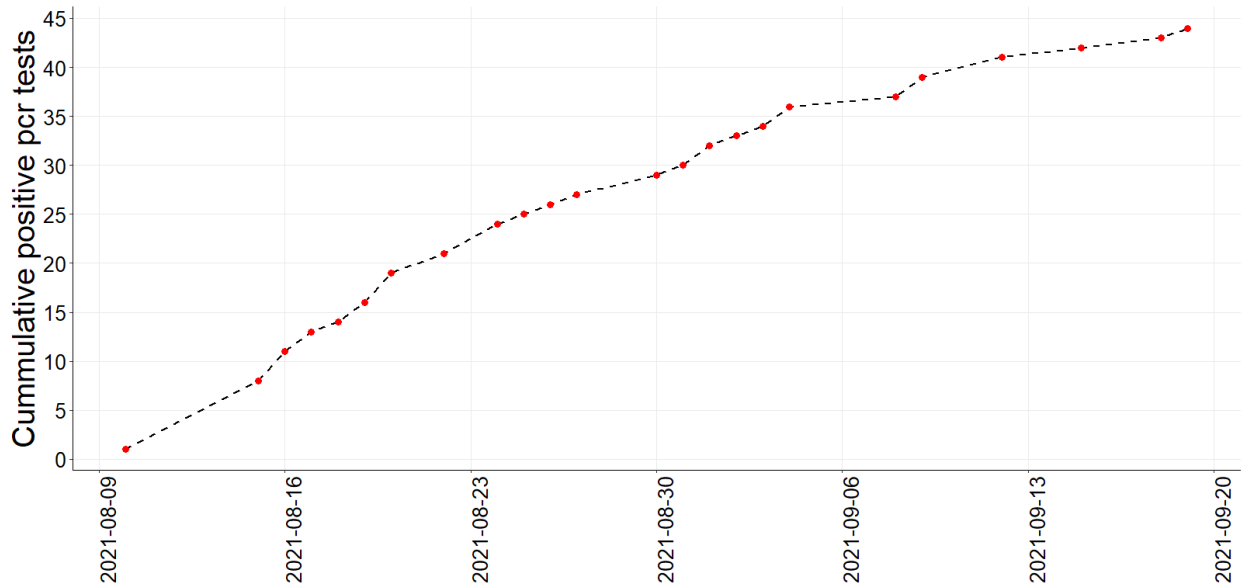
**eFigure 2.** Vaccine uptake over time in booster cohort.



**eFigure 3.** Daily PCR test density (7-day rolling mean) in booster-immunized and non-immunized participants.

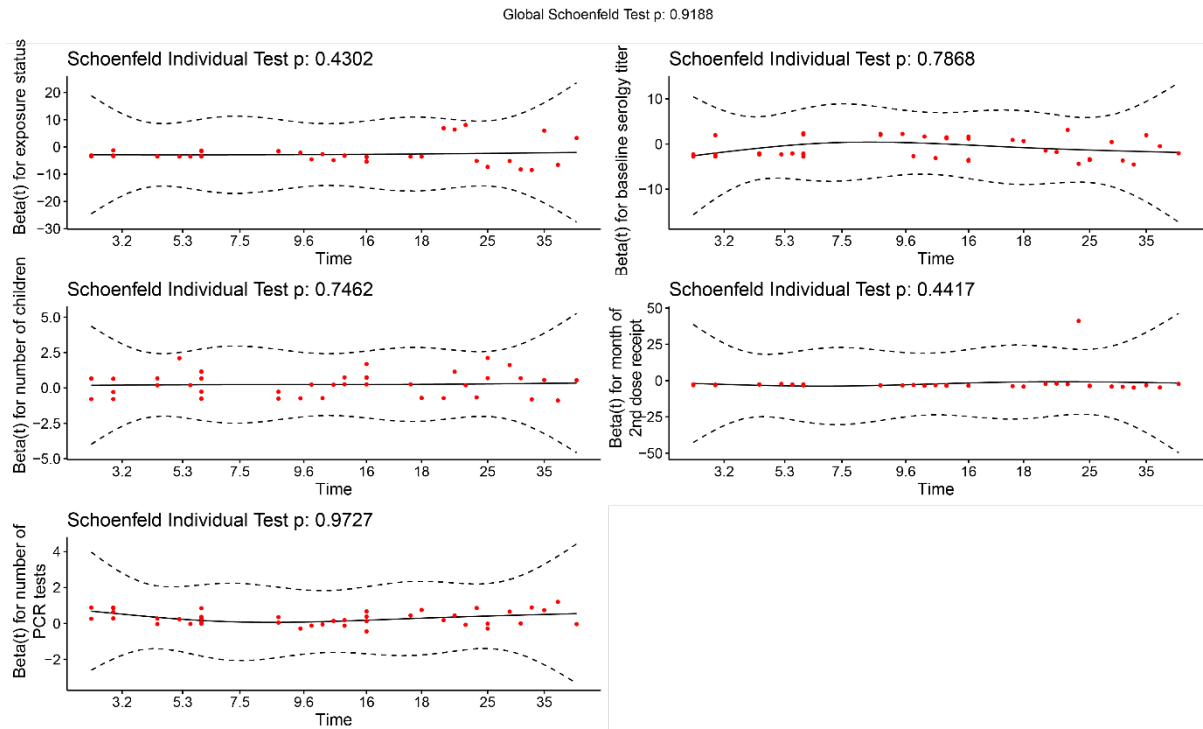


**eFigure 4.** Cumulative number of positive PCR tests over time from study initiation.

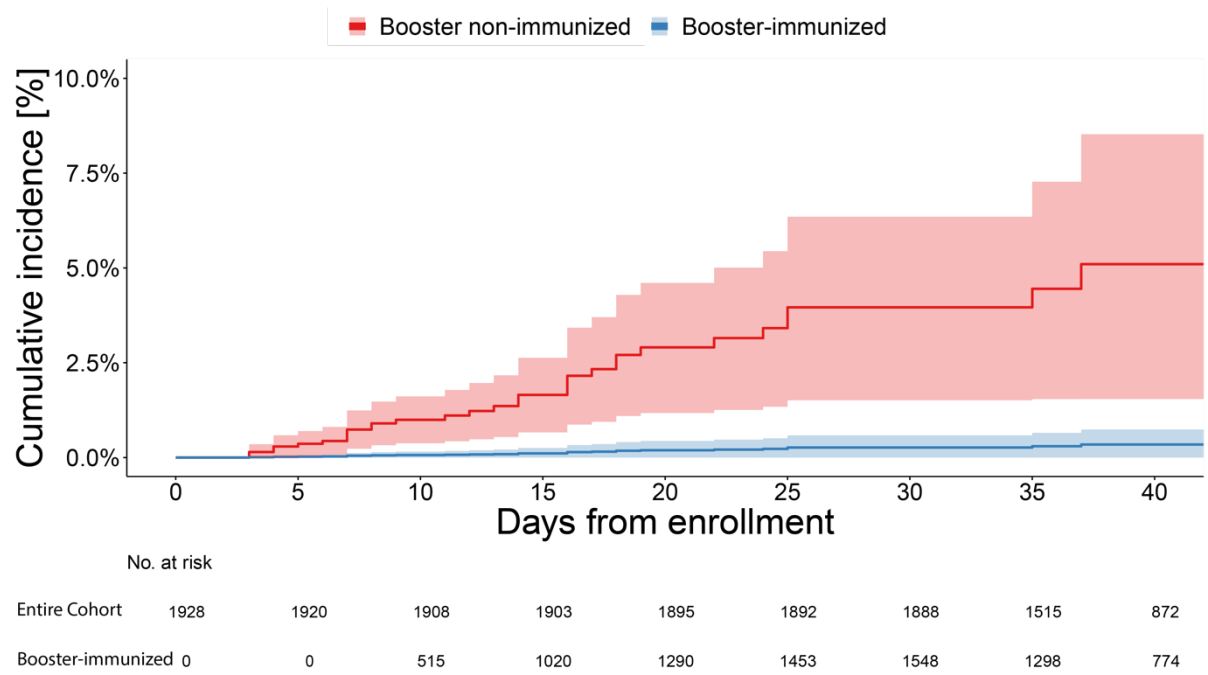




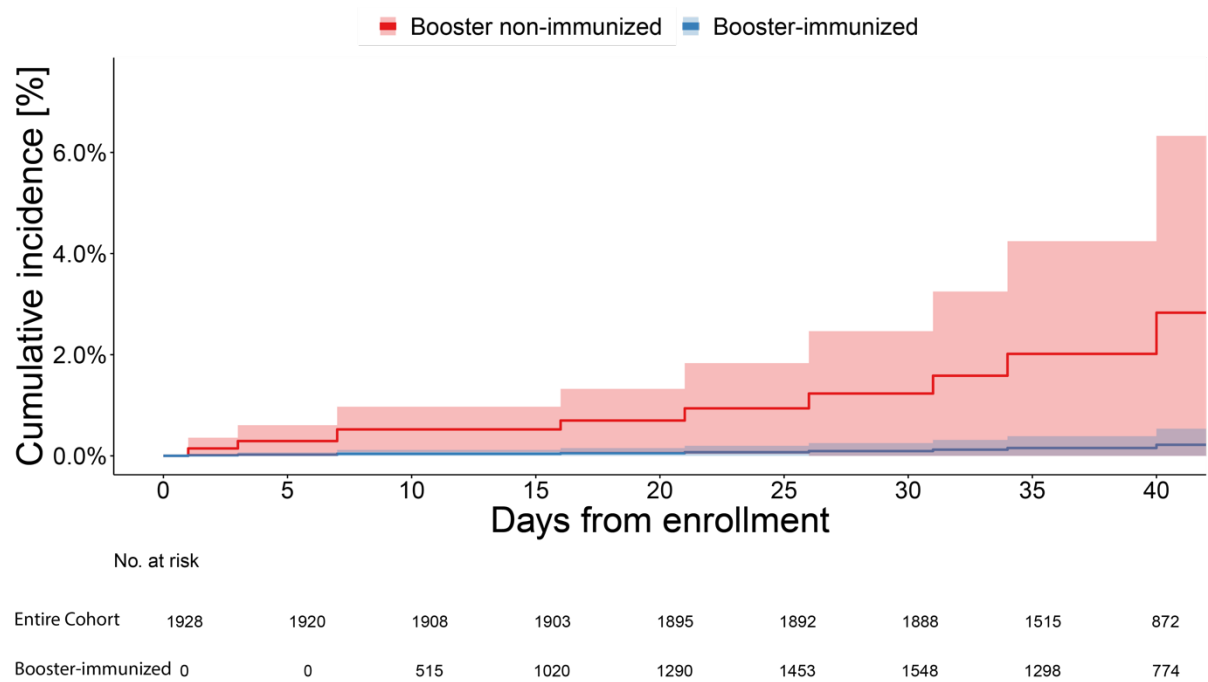
**eFigure 5.** Cox model diagnostics (shown only for covariates with statistically significant contribution). P value  $> 0.05$  indicates that the hazard in question is proportional.



**eFigure 6.** Cumulative incidence of symptomatic SARS-CoV-2 infections.



**eFigure 7.** Cumulative incidence of SARS-CoV-2 asymptomatic infection.



**DATA SHARING STATEMENT:**

The data that support the findings of this study, including study protocol and deidentified participant data might be made available following publication to researchers who provide a methodologically sound proposal, subject to applicable rules and regulations and following signing of a data access agreement. Requests should be addressed to the corresponding author.

**eReference**

1 Siemens Healthcare Diagnostics Inc. Understanding SARS-CoV-2 IgG Immunity Thresholds and the Process of Standardization. 2021.  
<https://cdn0.scrvt.com/39b415fb07de4d9656c7b516d8e2d907/b2406e708bf287e5/506564e9207f/Understanding-SARS-CoV-2-IgG-Immunity-Thresholds-and-the-Process-of-Standardization.pdf>.