Supplementary Appendix

Supplement to: Arbel R, Hammerman A, Sergienko R, et al. BNT162b2 vaccine booster and mortality due to Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2115624

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

Supplementary Material

Contents

Data Sources

Data in this study comes from the electronic medical records of Clalit Health Services (CHS). CHS is the largest of four integrated payer-provider health care organizations that provide mandatory health care coverage in Israel. CHS covers approximately 52% of the population of Israel (4.7 million persons). The dropout rate from CHS is 1- 2% yearly (1).

CHS pools the data from its many operational systems into a unified central data warehouse used for policy and research. This data repository includes detailed primary and secondary care information on hospitalizations, medications, laboratory results, and imaging tests. Due to the early adoption of electronic medical records and the low yearly dropout rate, CHS has good long-term follow-up of patients, ranging from the year 2000 (2).

Since the COVID-19 pandemic, the Israeli Ministry of Health (MOH) has centrally collected all COVID-19 related data. These include complete data on PCR testing, vaccination status, hospitalizations, and COVID-19 related deaths, as reported daily to the MOH by all Israeli hospitals. The MOH transfers this data day-to-day to the Israeli health funds (3). This allows integration of background medical information with vaccination status and COVID-19 related outcomes for the entire CHS patient population. The integrated data was used to generate the dataset for this study.

Study Oversight

All the authors participated in the study design. Dr. Yaron oversaw the data gathering; Ruslan Sergeinko analyzed the data with the guidance of Prof. Friger. All authors vouch for the data and analysis. Dr. Arbel wrote the initial manuscript. All authors contributed to the writing and critical review of the manuscript and decided to submit it for publication. The study was approved by the CHS Community Helsinki committee and the CHS data utilization committee.

Figure S1: Study timeline

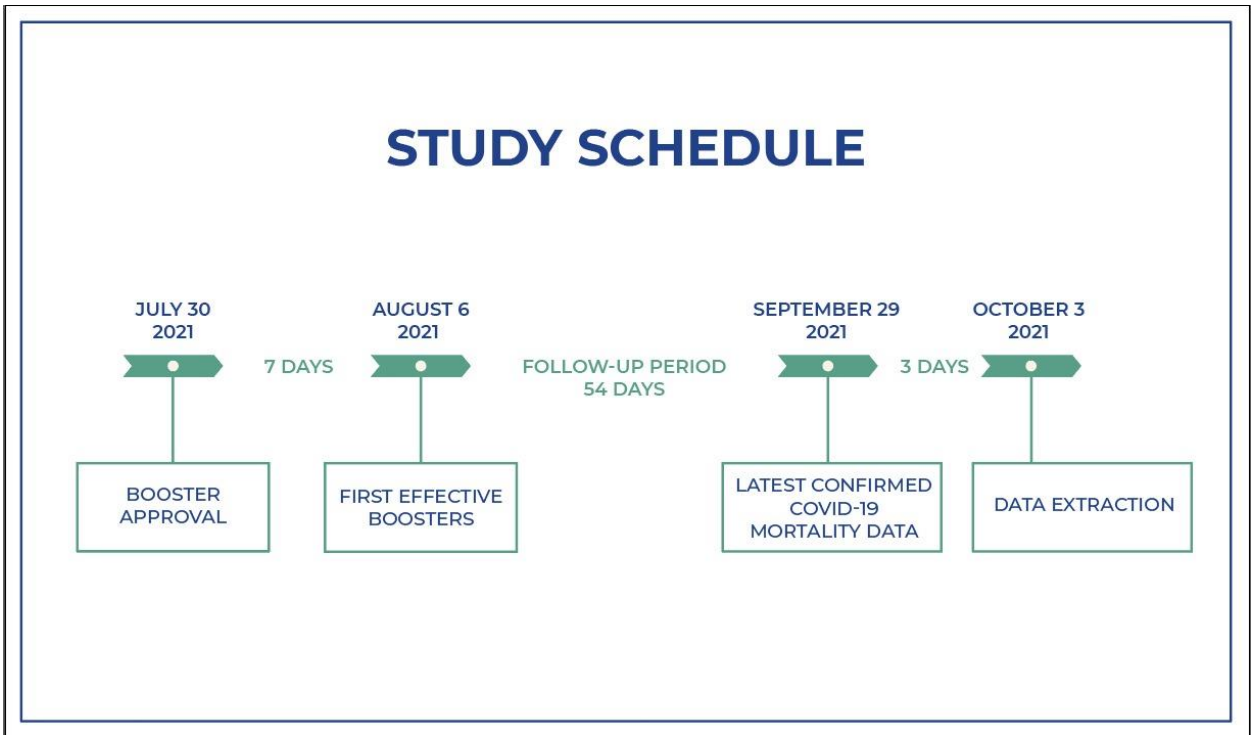
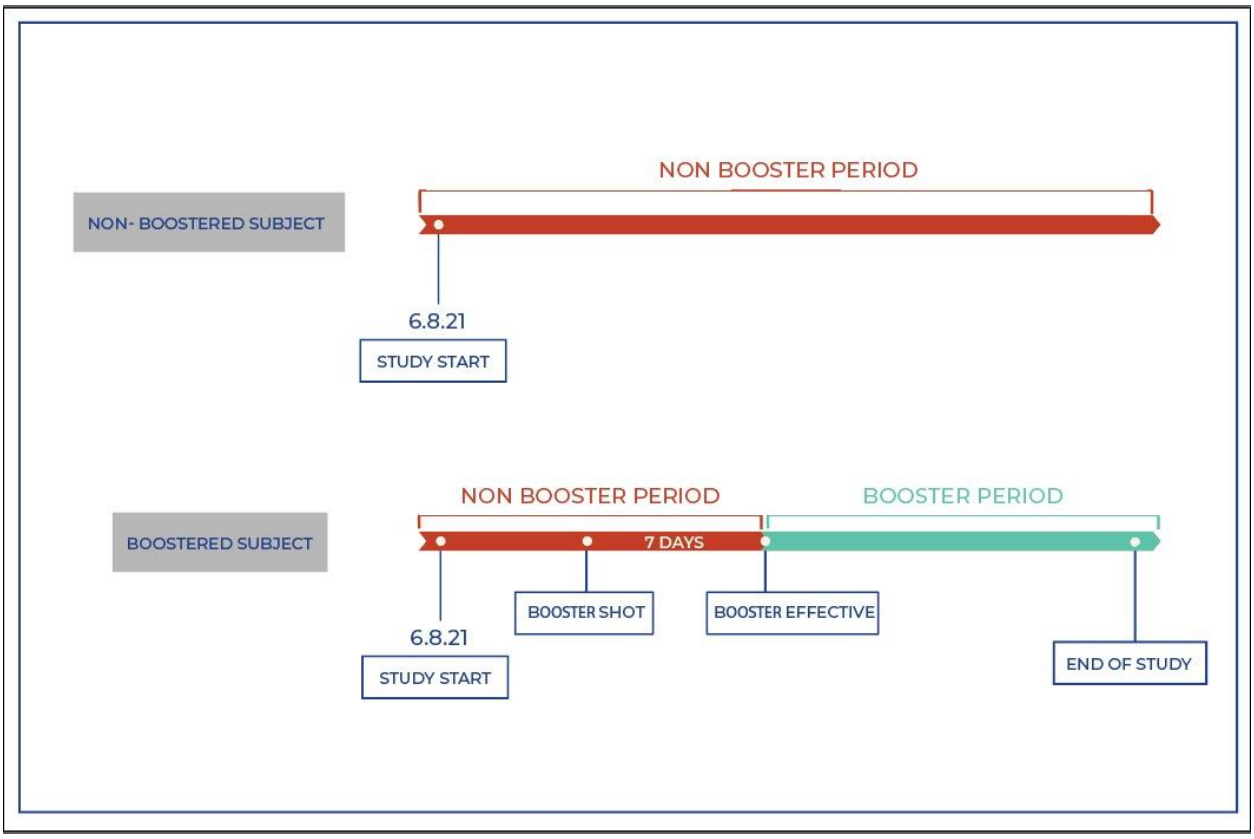


Figure S2: Transition from non-booster to booster status



Explanation on the Socio-Economic Status (SES) Measure

SES was based on the small statistical areas (SSA) used in the 2008 Israeli census. SSAs contain 3000–4000 people and are created to maintain homogeneity in terms of the sociodemographic composition of the population (4). The Israeli Central Bureau of Statistics (CBS) utilized demography, education, employment, housing conditions, and income to define the SSAs, and these were grouped into 20 categories. This data was updated by the POINTS Location Intelligence Company (5) to improve the accuracy of the SES measure, using up-to-date sociodemographic, commercial, and housing data (6). The entire CHS population was grouped into ten categories, ranging from 1 (lowest) to 10 (highest).

Table S1: Results of Schoenfeld's Global test for the proportional hazards assumption.

	chisq	df	p
Effective Vaccination Group	2.12678	1	0.145
Sex (male)	1.43970	1	0.230
age	0.51585	1	0.473
Socio-economic status	1.54119	1	0.214
DM	2.77995	1	0.095
COPD	0.00908	1	0.924
CVA	0.15241	1	0.696
CRF	0.00904	1	0.924
IHD	1.24592	1	0.264
CHF	2.25373	1	0.133
obesity	0.31515	1	0.575
Smoking history	0.03695	1	0.848
Lung cancer	1.60740	1	0.205
TIA	0.00113	1	0.973
GLOBAL	14.83077	14	0.390

Table S2: Validation testing of the 7 day effectiveness period by Cox regression

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.318**	**0.949**	**0.856**	**1.052**
Sex (male)	0.000	2.605	1.901	3.569
age	0.000	1.103	1.089	1.118
Socio-economic status	0.779	1.009	0.945	1.078
DM	0.080	1.297	0.969	1.735
COPD	0.270	1.268	0.832	1.933
CVA	0.028	1.474	1.042	2.086
CRF	0.000	2.241	1.612	3.116
IHD	0.901	0.980	0.709	1.353
CHF	0.113	1.372	0.928	2.027
obesity	0.266	1.182	0.880	1.587
Smoking history	0.476	1.117	0.825	1.512
Lung cancer	0.003	3.215	1.497	6.906
TIA	0.637	0.876	0.506	1.516

Table S3: Validation testing of the 14 day effectiveness period by Cox regression

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.000**	**0.665**	**0.600**	**0.736**
Sex (male)	0.000	2.610	1.904	3.576
age	0.000	1.103	1.089	1.118
Socio-economic status	0.692	1.013	0.949	1.082
DM	0.078	1.299	0.971	1.737
COPD	0.276	1.264	0.829	1.926
CVA	0.030	1.467	1.037	2.076
CRF	0.000	2.237	1.608	3.110
IHD	0.903	0.980	0.710	1.354
CHF	0.113	1.371	0.928	2.026
obesity	0.267	1.182	0.880	1.587
Smoking history	0.466	1.119	0.827	1.516
Lung cancer	0.003	3.238	1.508	6.955
TIA	0.639	0.877	0.507	1.518

Table S4: Results of the Cox regression analysis for subjects 65 and older

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.000**	**0.09**	**0.07**	**0.13**
Sex (male)	0.000	2.61	1.87	3.64
age	0.000	1.10	1.08	1.11
Socio-economic status	0.771	0.99	0.92	1.06
DM	0.419	1.13	0.84	1.54
COPD	0.124	1.40	0.91	2.14
CVA	0.021	1.52	1.06	2.17
CRF	0.000	2.14	1.52	3.00
IHD	0.596	0.91	0.65	1.28
CHF	0.112	1.39	0.93	2.08
obesity	0.435	1.13	0.83	1.54
Smoking history	0.471	1.12	0.82	1.55
Lung cancer	0.003	3.23	1.50	6.96
TIA	0.431	0.79	0.44	1.42

Table S5: Results of the Cox regression analysis for subjects younger than 65

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.000**	**0.13**	**0.04**	**0.40**
Sex (male)	0.417	1.53	0.55	4.22
age	0.011	1.19	1.04	1.37
Socio-economic status	0.292	0.90	0.73	1.10
DM	0.025	3.31	1.16	9.45
COPD	0.978	0.00	-	
CVA	0.570	1.51	0.36	6.34
CRF	0.001	6.74	2.09	21.77
IHD	0.526	1.48	0.44	4.99
CHF	0.285	2.25	0.51	10.00
obesity	0.618	1.28	0.49	3.35
Smoking history	0.613	0.78	0.29	2.06
Lung cancer	0.993	0.00	-	
TIA	0.245	2.67	0.51	13.92

Table S6: Results of the Cox regression analysis for females

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.000**	**0.06**	**0.03**	**0.11**
age	0.000	1.11	1.08	1.13
Socio-economic status	0.791	0.98	0.88	1.10
DM	0.051	1.65	1.00	2.73
COPD	0.745	1.16	0.48	2.78
CVA	0.241	1.46	0.77	2.77
CRF	0.954	1.02	0.49	2.15
IHD	0.791	1.08	0.60	1.96
CHF	0.057	1.94	0.98	3.82
obesity	0.540	1.17	0.71	1.94
Smoking history	0.777	1.09	0.61	1.93
Lung cancer	0.531	1.89	0.26	13.71
TIA	0.361	0.57	0.18	1.88

Table S7: Results of the Cox regression analysis for males

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	**0.000**	**0.12**	**0.08**	**0.18**
age	0.000	1.10	1.08	1.12
Socio-economic status	0.486	0.97	0.90	1.05
DM	0.475	1.14	0.80	1.62
COPD	0.227	1.35	0.83	2.18
CVA	0.033	1.57	1.04	2.38
CRF	0.000	2.94	2.01	4.30
IHD	0.607	0.90	0.62	1.33
CHF	0.350	1.25	0.78	2.02
obesity	0.413	1.16	0.81	1.68
Smoking history	0.534	1.12	0.78	1.61
Lung cancer	0.002	3.64	1.58	8.38
TIA	0.999	1.00	0.54	1.86

Table S8: Results of the Cox regression analysis for infection- all subjects

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Booster group	0.000	**0.17**	**0.16**	**0.18**
Sex (male)	0.000	1.16	1.12	1.20
age	0.000	0.99	0.98	0.99
Socio-economic status	0.000	0.98	0.97	0.98
DM	0.000	1.08	1.04	1.12
COPD	0.000	1.18	1.09	1.28
CVA	0.001	1.12	1.05	1.20
CRF	0.006	1.11	1.03	1.20
IHD	0.985	1.00	0.95	1.05
CHF	0.001	1.16	1.06	1.26
obesity	0.000	1.09	1.06	1.14
Smoking history	0.000	0.78	0.75	0.81
Lung cancer	0.453	0.92	0.73	1.15
TIA	0.032	1.11	1.01	1.22

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