Supplementary Appendix

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

SUPPLEMENTARY APPENDIX

This appendix has been provided by the authors to give readers additional information about their work. Supplement to: Olson S.M., Newhams M.M., Halasa N.B. et al. Effectiveness of BNT162b2 Covid-19 Vaccine against Critical COVID-19 in Adolescents

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Supplementary Methods

Multisystem inflammatory syndrome in children (MIS-C)

Cases of MIS-C were excluded from this analysis. Vaccine effectiveness against MIS-C was not evaluated in this for 3 reasons: 1) the limited sample size in the registry during the enrollment period due to the lower incidence in this age group; 2) the time window of risk for MIS is longer after infection (occurring 3-5 weeks after infection) which complicates a retrospective analysis of vaccine effectiveness and requires more time for cases to accumulate; 3) case-definition of MIS-C is broad, and thus cases require adjudication to avoid misclassification. For these reasons, enrollment is still not complete. Characteristics of MIS-C cases enrolled through October 25, 2021 are presented in **Table S1**.

Sample size for vaccine effectiveness

We estimated that 81 case-patients were needed for computing vaccine effectiveness of 90% with confidence limit width of 30%, with a control to case ratio of 1 to 1 and vaccine coverage of 30%. Enrollment through October 25th with full vaccination coverage of 38% in controls in this report provided sufficient sample size to achieve assessment of vaccine effectiveness against each of the primary outcomes COVID-19 illness requiring hospitalization, ICU admission, or life-threatening interventions (ie, life-support).

TABLE S1. Characteristics of suspected hospitalized Multisystem Inflammatory Syndrome in Children (MIS-C) cases aged 12–18 years excluded from the COVID-19 vaccine effectiveness analysis

Characteristic	MIS-C cases (N=23)
Age in Years, Median (IQR)	14 (13-16)
Age Category, No. (%)	
12-15 years	19 (82.6)
16-18 years	4 (17.4)
Female, No. (%)	16 (69.6)
Race/Ethnicity, No. (%)	
White, non-Hispanic	5 (21.7)
Black, non-Hispanic	8 (34.8)
Hispanic, any race	8 (34.8)
Other, non-Hispanic	1 (4.3)
Unknown	1 (4.3)
U.S. Census Region, No. (%)	
Northeast	2 (8.7)
Midwest	2 (8.7)
South	15 (65.2)
West	4 (17.4)
Month of admission, No. (%)	
July	0
August	3 (13.0)
September	13 (56.5)
October	7 (30.4)
Underlying Health Conditions, No. (%)	
At least one underlying condition	14 (60.9)
Vaccination status 4 weeks prior to hospitalization, No. (%)	
Unvaccinated	19 (82.6)
Vaccinated 0-13 Days Prior	2 (8.7)
Partially Vaccinated	1 (4.3)
Fully Vaccinated	1 (4.3)

TABLE S2. Primary admission diagnosis among 37 hospitalized patients* with SARS-CoV-2 positive test who were hospitalized for a non-COVID-19 reason

Primary reason for admission	N (%)	
Psychiatric admission	15	(41%)
Trauma	9	(24%)
Shunt malfunction	3	(8%)
Abscess	1	(3%)
Cellulitis	1	(3%)
Cholelithiasis	1	(3%)
Feeding tube malfunction	1	(3%)
Gynecologic	1	(3%)
Medication infusion	1	(3%)
New cancer diagnosis	1	(3%)
Post-operative complication	1	(3%)
Suicidal ideation	1	(3%)
Trauma	1	(3%)

*One patient is partially vaccinated and is not represented in vaccine effectiveness against non-COVID-19 hospitalizations (Table S4).

TABLE S3. Underlying conditions and vaccination status among COVID-19 case-patients with ECMO or death

Number	Vaccination status	Underlying conditions
1	Unvaccinated	Respiratory system disorder, asthma, other chronic condition*
2	Unvaccinated	Respiratory system disorder, asthma, endocrine disorder, Type I diabetes, other chronic condition*
3	Unvaccinated	Respiratory system disorder, asthma, other chronic condition*
4	Unvaccinated	Endocrine disorder, Type II diabetes, other chronic condition*
5	Unvaccinated	Respiratory system disorder and asthma
6	Unvaccinated	Respiratory system disorder and other chronic condition*
7	Unvaccinated	Disorder of cardiovascular system and other chronic condition*
8	Unvaccinated	Respiratory system disorder and asthma
9	Unvaccinated	Disorder of cardiovascular system, endocrine disorder, other chronic condition*
10	Unvaccinated	Other chronic condition*
11	Unvaccinated	Other chronic condition*
12	Unvaccinated	Respiratory system disorder, asthma, endocrine disorder
13	Unvaccinated	Respiratory system disorder, Endocrine disorder, Type II Diabetes, other chronic condition*
14	Unvaccinated	Endocrine disorder, Type I Diabetes
15	Unvaccinated	Disorder of cardiovascular system, neurologic or neuromuscular disorder, non-oncologic immunosuppressive disorder, endocrine disorder, other chronic condition*
16	Unvaccinated	Endocrine disorder, Type II diabetes

*Other chronic conditions included, but not limited to, obesity, rheumatologic/autoimmune disorder, hematologic disorder, renal or urologic dysfunction, gastrointestinal/hepatic disorder, metabolic or confirmed or suspected genetic disorder, or atopic or allergic condition.

TABLE S4. Supplemental analysis of vaccine effectiveness*[†] (with 95% confidence intervals) against SARS-CoV-2 positive[§] hospitalized patients admitted for non-COVID-19 reasons[§] aged 12–18 years, July–October 25, 2021

	No. of vaccinated/Total (%)		
	Case-patients	**Controls**	**Vaccine effectiveness (95% CI)**
All	5/36 (13.9)	282/723 (39.0)	78 (48–91)

Abbreviation: CI = confidence interval.

* Vaccine effectiveness estimates were adjusted for U.S. Census region, calendar biweek of admission, continuous age in years, sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic other, Hispanic of any race, or unknown). Firth penalized regression was used for models with less than 5 vaccinated cases. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer vaccine effectiveness against secondary outcomes.

[†] COVID-19 vaccination status included the following two categories: 1) unvaccinated, defined as no receipt of any SARS CoV-2 vaccine before illness onset; 2) fully vaccinated, defined as receipt of both doses of a 2-dose Pfizer-BioNTech vaccination ≥14 days before illness onset.

§ Includes participants excluded from the primary analysis who had a SARS-CoV-2 positive test but were hospitalized for non-COVID-19 reasons (n=37) which are outlined in Table S2. One patient is partially vaccinated in Table S3 and is not represented in VE against non-COVID-19 hospitalizations.