RESEARCH LETTER

Asymptomatic and Symptomatic SARS-CoV-2 Infections After BNT162b2 Vaccination in a Routinely Screened Workforce

A 2-dose regimen of the BNT162b2 vaccine (Pfizer-BioNTech) against SARS-CoV-2 was authorized in December 2020 based on reported 94.8% efficacy.[1] Although an association between vaccination and a reduction in symptomatic disease has been well described, an association with asymptomatic infection remains unclear.[2,3]

Methods | In March 2020, St Jude Children's Research Hospital initiated routine, test-based screening of asymptomatic workers and targeted testing for symptomatic individuals and those with known exposure. Polymerase chain reaction–based testing of midturbinate samples from asymptomatic employees was performed at least weekly. On December 17, 2020, vaccination with BNT162b2 was initiated. "Vaccine-eligible" workers were individuals meeting state vaccination guidelines.[4] Vaccinated employees receiving BNT162b2 were followed up from their first dose date. Unvaccinated employees were followed up from December 17, 2020, or their first asymptomatic screen result, whichever was later. The end of surveillance was March 20, 2021, employment termination, a positive test result, or receipt of other vaccines, whichever was earlier. No person contributed to both groups. Individuals with prior COVID-19 exposure were excluded. When asymptomatic infections were analyzed, symptomatic and known exposure cases were treated as competing risks; when symptomatic infections were analyzed, positive results from asymptomatic screening were treated as competing risks.

Related article page 2457

The incidence rate ratio (IRR), the ratio of confirmed COVID-19 cases per person-days of follow-up in vaccinated compared with unvaccinated groups, with 95% CIs,[5] was used as a measure of association between vaccination and infection. An analysis by time after doses 1 and 2 was also performed. Cumulative incidence curves were estimated with the Kaplan-Meier estimator. Analyses were performed in R version 4.0.3.

The study was determined by the St Jude institutional review board to be exempt (secondary use of data), for which participant informed consent is not required.

Results | Between December 17, 2020, and March 20, 2021, 5217 workers met vaccination criteria, 3052 (58.5%) received at least 1 BNT162b2 dose, and 2776 (53.2%) received 2 doses; 2165 (41.5%) were unvaccinated. Median follow-up was 81 days in the unvaccinated group and 72 days among vaccinated employees. In the vaccinated group, 66.0% were women, 60.3% White individuals, 19.4% Black individuals, 88.7% younger than 65 years, and 47.2% health care personnel[6]; in the unvaccinated group, 58.3% were women, 40.3% White individuals, 24.6% Black individuals, 84.8% younger than 65 years, and 25.7% health care personnel.

Among vaccinated employees, 51 tested positive for SARS-CoV-2 during follow-up (41 before and 10 after the second dose); 29 (56.9%) were diagnosed through asymptomatic screening. Among unvaccinated employees, 185 tested positive and 79 (42.7%) were asymptomatic. The IRR was 0.21 (95% CI, 0.15-0.28) for any SARS-CoV-2 infection, 0.28 (95% CI, 0.18-0.42) for asymptomatic screen results, and 0.16 (95% CI, 0.10-0.25) for symptomatic or known exposure cases (**Table**).

Table. Estimated Incidence Rate Ratio Against Any SARS-CoV-2 Infection and Asymptomatic or Symptomatic/Contact SARS-CoV-2 Infection[a]

Vaccination status	Follow-up time, person-days (No. at risk)	Any positive test result		Asymptomatic screening positive test result		Screening positive test result based on the presence of symptoms or known COVID-19 exposure	
		No.	IRR (95% CI)[b]	No.	IRR (95% CI)	No.	IRR (95% CI)
Unvaccinated total follow-up[c]	149 718 (2165)	185		79		106	
Vaccinated total follow-up	198 480 (3052)	51	0.21 (0.15-0.28)	29	0.28 (0.18-0.42)	22	0.16 (0.10-0.25)
Vaccinated periods							
0-11 d after dose 1	32 807 (3052)	24	0.59 (0.39-0.91)	10	0.58 (0.30-1.12)	14	0.60 (0.35-1.05)
≥12 d after dose 1 and before dose 2	32 481 (2942)	17	0.42 (0.26-0.70)	10	0.58 (0.30-1.13)	7	0.30 (0.14-0.65)
0-6 d after dose 2	16 492 (2776)	4	0.20 (0.07-0.53)	3	0.35 (0.11-1.09)	1	0.09 (0.01-0.61)
≥7 d after dose 2	116 700 (2724)	6	0.04 (0.02-0.09)	6	0.10 (0.04-0.22)	0	0[d]

Abbreviation: IRR, incidence rate ratio.

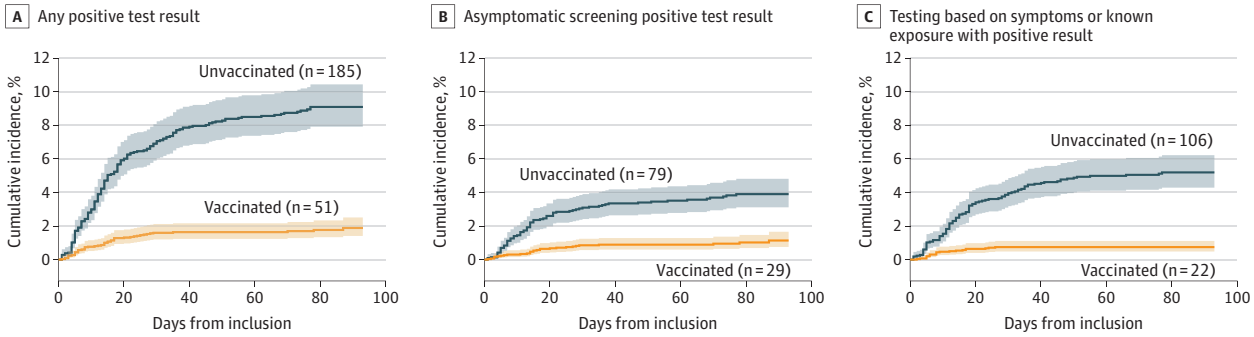
[a] Follow-up periods for unvaccinated employees began on December 17, 2020, or on their first asymptomatic screening date, whichever was later. Individuals who received vaccines other than BNT162b2 were censored on vaccination. Follow-up periods for vaccinated workers began when they received their first dose. Workers who remained SARS-CoV-2 negative during follow-up were censored on March 20, 2021, or on the employment termination date, whichever was earlier. No person contributed to both groups. Individuals with prior COVID-19 exposure were excluded.

[b] Incidence rate ratio is the ratio of confirmed COVID-19 cases per person-days of follow-up in vaccinated compared with unvaccinated groups.

[c] The unvaccinated group was treated as the reference group for all calculations.

[d] 95% CI does not apply.

Figure. Cumulative Incidence of COVID-19 Against SARS-CoV-2 Infections After the First Dose



A total of 2165 unvaccinated employees and 3052 vaccinated employees were included. A, Any SARS-CoV-2 infection among St Jude employees during follow-up. B, Asymptomatic infections identified through routine asymptomatic screening; SARS-CoV-2 cases through testing based on the presence of symptoms or known COVID-19 exposure were treated as competing risks. C, Positive results via testing based on the presence of symptoms or known COVID-19 exposure; positive results from asymptomatic screening were treated as competing risks. Shaded areas are 95% CIs.

The IRR within the first 11 days after the first dose was 0.58 to 0.60 for all 3 outcomes. The IRR for positive results via asymptomatic screening from 12 days after the first vaccine dose until the second dose (median interval between doses, 21 days [range, 11-49 days]) was 0.58 (95% CI, 0.30-1.13), within 7 days after the second dose, 0.35 (95% CI, 0.11-1.09), and 7 days or more after the second dose, 0.10 (95% CI, 0.04-0.22). There were no positive symptomatic or known exposure cases more than 7 days after the second dose. Unvaccinated employees had higher cumulative incidence of a positive test result than vaccinated employees and higher incidences of positive test results via asymptomatic screening, for symptoms, or for known exposure (**Figure**).

Discussion | This study found an association between vaccination with BNT162b2 in hospital employees and a decreased risk of symptomatic and asymptomatic infections with SARS-CoV-2. Limitations include the observational design; short follow-up time; small cohort size, which led to an inability to match the 2 groups and unequal follow-up; differential temporal risk during the surveillance; and that the group choosing not to be vaccinated may have been more prone to higher-risk behavior. The unequal follow-up time and the latter 2 limitations may have biased the results in favor of vaccination. Further research is needed to determine whether a reduction in risk of asymptomatic infection leads to reduced transmission.

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Association of Initial Treatment With Antibiotics vs Surgery With Treatment Success and Disability in Subgroups of Children With Uncomplicated Appendicitis

Initial treatment with antibiotics alone is a reasonable option for children presenting with uncomplicated appendicitis, as demonstrated in a patient choice study that found nonoperative management was successful in 67% at 1 year and led to fewer disability days compared with laparoscopic appendectomy.[1] Because differences in outcomes by age, race and ethnicity, family income, and transfer status have been described in patients undergoing appendectomy, we evaluated whether the primary outcomes of that study varied in subgroups based on clinical and socioeconomic factors.[2,3]

Supplemental content

Methods | This was a planned secondary analysis of a multiinstitutional, nonrandomized, controlled interventional study investigating nonoperative management and surgery for children with uncomplicated appendicitis. Caregivers of children aged 7 to 17 years treated at 10 US children's hospitals from May 2015 to October 2018 chose treatment with either antibiotics alone or urgent appendectomy. Follow-up was through October 2019. The primary results have been previously published, and the study protocol is available in Supplement 1.[1] Comparisons between groups used propensity score methods to account for confounding by baseline characteristics by balancing covariates between treatment groups in the final analysis.[4-6] Multiple imputation was used to account for missing data in estimating the propensity score. Analyses used inverse probability of treatment weighting, as estimated with the propensity score, to calculate adjusted treatment estimates for 2 primary outcomes, number of disability days experienced by children and success rate of nonoperative management at 1 year. Three factors were specified a priori for subgroup analyses: age (≤10 years or >10 years), annual household income (<$50 000 or

Table 1. Stratified IPTW-Adjusted Treatment Estimates for the Primary Outcome of 1-Year Success Rate of Nonoperative Management of Appendicitis

Factors	No. of patients with medical record review	Success rate of nonoperative management at 1 y, No. (%) [95% CI]	*P* value[a]
Patient age, y			
≤10	93	59 (63.8) [52.7-73.5]	.47
>10	277	189 (68.1) [62.0-73.7]	
Annual household income, $			
<50 000	109	72 (65.9) [55.7-74.9]	.70
≥50 000	217	148 (68.3) [61.3-74.5]	
Transfer status			
Not transferred	211	144 (68.3) [61.3-74.6]	.60
Transferred	159	104 (65.6) [57.1-73.1]	
Sex[b]			
Male	229	155 (67.8) [60.9-74.0]	.72
Female	141	93 (65.9) [57.3-73.6]	
Race and ethnicity[b,c]			
Non-Hispanic White	199	140 (70.4) [63.2-76.8]	.14
Other race/ethnicity	171	107 (62.7) [54.6-70.1]	
Insurance status[b]			
Private insurance	251	176 (70.0) [63.6-75.7]	.20
Medicaid	109	68 (62.5) [52.2-71.7]	
Primary caregiver education[b]			
Some college or less	149	105 (70.2) [61.8-77.5]	.42
At least college degree	190	125 (65.8) [58.3-72.6]	
Primary language spoken at home[b]			
English	284	191 (67.1) [61.0-72.6]	.82
Other	69	47 (68.6) [56.1-78.9]	

[a] Main effects for 1-year success rate of nonoperative management were tested through inverse probability of treatment weight (IPTW) logistic regression models. In all models, inference relied on robust sandwich-type standard errors to account for the estimated IPTWs.

[b] Factor was added to the analysis post hoc.

[c] Race and ethnicity were assessed because of evidence from the available literature suggesting an association with outcomes in pediatric patients treated for appendicitis. Related data were reported by caregivers using surveys with predefined categories listed in the table. Other includes Black, Hispanic, Asian, American Indian, Alaska Native, and biracial patients. For patients managed nonoperatively, this included 23 non-Hispanic Black patients, 37 Hispanic patients, 106 patients who reported another race or ethnicity, and 5 patients who did not report race or ethnicity.