Letters

SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adults

Confirmed cases of coronavirus disease 2019 (COVID-19) and case-fatality rates vary among countries. One reason could be national policies regarding childhood BCG vaccination, with fewer confirmed cases and a lower death toll reported in countries with vs without universal BCG vaccine coverage.[1,2] Comparing outbreak characteristics between countries is influenced by potential confounders such as different phases of outbreak, mean age of affected population, management of the pandemic, amount of tests being administered, definitions of COVID-19–related deaths, or underreporting.

The BCG vaccine was routinely administered to all newborns in Israel as part of the national immunization program between 1955 and 1982. Overall, the vaccine acceptance rate in Israel is high, with greater than 90% coverage. Since 1982, the vaccine has been administered only to immigrants from countries with high prevalence of tuberculosis. This change allowed comparison of infection rates and proportions with severe COVID-19 disease in 2 similar populations with differing BCG status: individuals born during the 3 years before and 3 years after cessation of the universal BCG vaccine program.

Methods | The current policy of the Israeli Ministry of Health is to test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in every patient with symptoms that could be compatible with COVID-19 (cough, dyspnea, fever). Nasopharyngeal swabs were tested by real-time reverse transcriptase–polymerase chain reaction in approved laboratories between March 1 and April 5, 2020. Only 1 test per patient was included. Results were stratified by birth year. Population data for specific birth years were obtained from the national Central Bureau of Statistics. χ^2 Tests were used to compare proportions and rates per 100 000 population of positive test results among persons with symptoms compatible with COVID-19 born from 1979 to 1981 (aged 39-41 years) with those born from 1983 to 1985 (aged 35-37 years). A 2-sided significance threshold was set at $P < .05$. The study was deemed exempt by the Shamir Medical Center institutional review board as all data were deidentified. Statistical analyses were performed using R software, version 3.5.3 (R Foundation).

Results | Of 72 060 test results reviewed, 3064 were from patients born between 1979 and 1981 (1.02% of birth cohort of that period; 49.2% male; mean age, 40 years) and 2869 were among likely unvaccinated people born between 1983 and 1985 (0.96% of total birth cohort; 50.8% male; mean age, 35 years). There was no statistically significant difference in the proportion of positive test results in the BCG-vaccinated group (361 [11.7%]) vs the unvaccinated group (299 [10.4%]; difference, 1.3%; 95% CI, −0.3% to 2.9%; $P = .09$) or in positivity rates per 100 000 (121 in vaccinated group vs 100 in unvaccinated group; difference, 21 per 100 000; 95% CI, −10 to 50 per 100 000; $P = .15$). There was 1 case of severe disease (mechanical ventilation or intensive care unit admission) in each group, and no deaths were reported (**Table**).

Discussion | In this cohort of Israeli adults aged 35 to 41 years, BCG vaccination in childhood was associated with a similar rate of positive test results for SARS-CoV-2 compared with no vaccination. Because of the small number of severe cases, no conclusion about the association between BCG status and severity of disease can be reached. Although the BCG vaccine is given to protect against tuberculosis, it has also been found to exert nonspecific beneficial effects such as protection against other infectious diseases[3] and to enhance immunogenicity of

Table. Results of SARS-CoV-2 PCR Testing by Age Group

	Birth year		Difference (95% CI)	P value
	1979-1981 (BCG vaccinated)	1983-1985 (BCG unvaccinated)		
Total population	297 340	301 600		
Immigrants in total population, No. (%)[a]	14 569 (4.9)	13 873 (4.6)		
No. of tests	3064	2869		
Proportion of population tested, %	1.02	0.96		
Men tested, No. (%)	1509 (49.2)	1458 (50.8)		.29
Positive results				
No. (%)	361 (11.7)	299 (10.4)	1.3 (−0.3 to 2.9)	.09
No. per 100 000 population in age group[b]	121	100	21 (−10 to 50)	.15
Men with positive result, No. (%)	181 (50)	152 (51)		.87
No. with severe disease	1	1		

Abbreviations: PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Number of immigrants from countries that have a BCG vaccination policy and are included in the total population for the different birth-year groups.[6]

[b] Rates per 100 000 population do not represent the positivity rate in the population because the persons tested were preselected based on symptoms.

certain vaccines, such as the influenza vaccine.[4] These effects are thought to be mediated partly by heterologous effects on adaptive immunity such as T cell–mediated cross-reactivity but also by the potentiation of innate immune response.[5]

The strengths of this study are the large population-based cohort and the comparison of 2 similar age groups, thus limiting confounders to a minimum. The main limitation is the inclusion of populations who were not born in Israel, with unknown vaccination status. However, immigrants from countries that vaccinate with BCG, within these age groups, are a minority (4.9% and 4.6% of the older and younger population groups, respectively) and should not be overrepresented in one group.[6] In addition, the rates per 100 000 do not represent the positivity rate in the population, as persons tested were preselected based on reported symptoms.

In conclusion, this study does not support the idea that BCG vaccination in childhood has a protective effect against COVID-19 in adulthood.

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