UC SANTA BARBARA

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Vaccination Insights

While scientists race to develop and test a vaccine effective against SARS-CoV-2, the virus that causes COVID-19, recent studies have indicated that countries with widespread BCG vaccination appear to be weathering the pandemic better than their counterparts. This has led many researchers to suspect that BCG vaccine, which immunizes against tuberculosis, might offer protection against COVID-19.

Controlled trials with the vaccine are in progress, but in the meantime Clément de Chaisemartin, an assistant professor of economics at UC Santa Barbara, and his coauthor — and cousin — Luc de Chaisemartin, an immunologist at Paris-Saclay University, decided to see what they could learn from existing public health data.

Using information from the Swedish public health agency, the pair determined that BCG vaccination during infancy actually does not protect against the virus. Their results, which appear in the journal Clinical Infectious Diseases, suggest that other, related factors likely underlie the disparities between countries.

“Having a study like ours, which builds upon a natural experiment, is useful,” Clément de Chaisemartin explained, “because even though it does not look at exactly the same research question as the controlled trials — which will measure the effect of a recent BCG vaccination — our results are available much more quickly.”

The inspiration for the study was rather idiosyncratic. Clément de Chaisemartin is the oldest of five siblings. He received the BCG vaccine and its boosters as a child, but he recalled that his 18-year-old youngest brother had not. His native France did

away with mandatory BCG vaccination in the early 2000s. In fact, many developed countries gradually went this way as tuberculosis became ever rarer.

The economist remembered this fact when studies began reporting that countries that had mandatory BCG vaccinations were faring better in the pandemic than those that didn't.

"So then I just went onto Wikipedia and tried to find a country were the BCG interruption was less recent, so that the people affected would be older and at higher risk of COVID-19," he recalled.

Sweden, he discovered, had discontinued the practice in April 1975. That fit his needs perfectly, so he reached out to the country's public health agency, which agreed to share data with him.

Usually, non-randomized studies can provide evidence only of correlations, not actual causation. But the type of analysis that the Chaisemartins applied is different. "The regression discontinuity method we used is considered almost as reliable as a randomized controlled trial in terms of teasing out correlation from causation," said Clément de Chaisemartin.

The researchers took advantage of the fact that the Swedish policy essentially created a randomized controlled trial. People born in March and April 1975 are extremely similar in terms of their susceptibility to COVID-19. Meanwhile, those born in March got the BCG vaccine, while those born in April did not. It's almost as if the individuals were randomly placed in the two different groups.

The researchers compared the COVID-19 outcomes between the two groups and found that cases per capita, hospitalizations per capita, and deaths per capita were very similar for people born just before and just after the April 1st cutoff.

The results were enlightening. The correlation between mandatory BCG vaccination and COVID-19 outcomes is very strong, and shows up even when controlling for a number of relevant factors, such as per-capita income. But the similar COVID-19 outcomes between those who received the vaccine in childhood and those who didn't indicate that immunization can't be the cause.

"Our study shows that this correlation is probably not due to the BCG vaccination, but rather to some omitted variable," explained Clément de Chaisemartin. "This

raises the question as to what this omitted variable is, because if it is something that policymakers can act upon, then maybe we would have something actionable against COVID-19."

He hypothesized that mandatory child BCG vaccination may reflect the overall strength of a country's public health agency. "Countries that have many mandatory vaccinations may be countries where public health agencies are more powerful," he said. "So maybe those public health agencies are also able to implement effective policies against COVID-19."

Another hypothesis is that the mandatory vaccination relates to risk aversion. "Maybe countries where many mandatory vaccinations are in place are countries where people tend to be more risk averse," he continued. In that case, the public may adhere to more cautious guidelines during the pandemic.

Clément de Chaisemartin is quick to point out that these conjectures are preliminary, and would require more research to corroborate. Also, despite having found no connection between vaccination in infancy and protection from COVID-19, current experiments may still find that a recent BCG vaccination can provide some benefit.

One thing is abundantly clear, though, said Luc de Chaisemartin, "Without sound evidence that BCG protects against COVID-19, it is important to wait for the results of the ongoing trials, rather than deplete stocks of a vaccine already difficult to get for those who really need it, namely children in countries with a high prevalence of tuberculosis."

About UC Santa Barbara

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