

## Streszczenie w języku angielskim

Vaccination against *Mycobacterium tuberculosis* infection (Bacillus Calmette-Guérin, BCG) was introduced in 1921 and is still recommended by the World Health Organisation (WHO) in countries with a high incidence of tuberculosis, where it should be administered to newborns as early as possible after birth. The BCG vaccine uses a live attenuated strain of *Mycobacterium bovis*. This vaccination provides sustained protection against disseminated forms of tuberculosis in childhood, such as meningeal tuberculosis and miliary tuberculosis, but its protective efficacy against pulmonary tuberculosis in adults is not entirely sufficient. BCG prevention is carried out in many countries. Still, in some of them, these vaccinations have been discontinued due to an improved epidemiological situation (Spain 1981, Denmark 1986), and some countries have never carried out this prophylaxis (Canada, USA, Italy, Belgium, The Netherlands).

It has been observed in studies and observations of different populations and infectious diseases that vaccinated populations have reduced early-life mortality and lower disease incidence. During the COVID-19 pandemic, it was hypothesised that countries without universal tuberculosis prophylaxis had higher rates of severe disease (Italy, France, Spain, and The Netherlands) than countries with long-standing universal prevention (Japan, Denmark, South Korea). Medical personnel are crucial in managing the impact of any epidemic or pandemic. And given that in Poland, BCG vaccination has been widely and mandatorily administered since the 1950s, the vast majority of healthcare workers have been covered by TB prophylaxis. In this light, and consideration of the still not fully understood knowledge of the tuberculosis vaccine, it seemed appropriate to undertake a study on the impact of this prophylaxis on the frequency and course of SARS-CoV-2 infections in the population of healthcare workers in Poland, as well as to attempt to define the specific characteristics influencing the results.

The doctoral dissertation aimed to verify the hypothesis of whether vaccination against tuberculosis with the BCG vaccine has an impact on the frequency of SARS-CoV-2 infection and the course of COVID-19 disease. The data used for the doctoral dissertation are based on the obtained results of a clinical, controlled, multicentre, randomised, double-blind trial conducted in six centres: Rzeszów, Kraków, Katowice, Warsaw (2 centres) and Trzebnica on a group of volunteers, health care workers, both men and women aged  $\geq 25$  years employed in health care institutions. All included study participants had a tuberculin test. On the day of the

reading, 72 hours after the test was set up, those with a negative result were randomised (in a 1:1 ratio) and received a BCG vaccine or placebo. From then on, the participants were followed up for three months with weekly telephone contact to determine their health status. At the onset of symptoms that might indicate SARS-CoV-2 virus infection, nasopharyngeal swabs and blood were collected. In the next phase of the study, after the introduction of widespread vaccination against COVID-19, volunteers participating in phase I of the study had their blood collected at 1-2 and 7-8 months after the second dose of Comirnaty® vaccine (Pfizer/BioNTech, USA/Germany).

Out of approximately 2,000 healthcare workers potentially meeting the inclusion criteria, 717 individuals who provided informed consent were finally included in the study. The RT23 tuberculin test was positive in 363 participants (50.6%) and negative in 354 (49.4%). From this group, 177 participants received the BCG vaccine after randomisation, and another 177 received a placebo. By the end of phase I of the study, 22 participants had dropped out of further follow-up, and the final analysis was performed on a group of 695 participants.

The results of the study showed no correlation between BCG vaccine revaccination and COVID-19 incidence, nor was there statistical significance between tuberculin test results and COVID-19 incidence. At the same time, a significantly higher number of COVID-19 infections were found among nurses compared with other medical professions. Anti-SARS-CoV-2 antibodies in the IgG class were detected in 150 study participants, but antibody concentrations did not differ substantially between the three study groups, and statistical significance was not demonstrated. Additional analysis showed no correlation between antibody concentrations and positive tuberculin test results.

In phase II of the study, 352 participants were included for the final assessment of antibody levels at a visit 1-2 months after receiving the second dose of Comirnaty® vaccine and 200 at a visit 6 months after the previous one (7-8 months after the second dose of Comirnaty®). The antibody concentrations in the three study groups did not differ significantly. There was also no correlation between antibody concentrations and the age, gender or BMI of the study participants.