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| 1 | RAPID POLICY BRIEF NUMBER: 006-04 |
| 2 | RESEARCH DOMAIN: COVID-19 AND PREVENTION |
| 3 | TITLE: Effects of BCG vaccination on COVID-19 |
| 4 | DATE OF PUBLICATION: 02/16/2021 |
| 5 | <p>BACKGROUND</p> <p>Coronavirus disease 2019 (COVID-19) was first identified in Wuhan, China, in December 2019. By 25 December 2020, over 77.5 million people had been infected with SARS-Cov2, the virus that causes COVID-19, and over 1.7 million people had died[1]. In 2019, over 10 million people worldwide fell ill with tuberculosis (TB) and more than 1.4 million people died of TB[2]. Bacille Calmette-Guerin (BCG) vaccine has been used for close to a century to prevent TB. Several countries around the world have a mandated BCG vaccination program at birth while others only give BCG for high-risk individuals. BCG is known to have non-specific effects on other diseases and has also been used as treatment for bladder cancer [3]. Several studies have suggested that BCG could be protective against SARS-CoV-2 infection and COVID-19 and thus the evidence presented here originates from a systematic review of literature on the association of BCG vaccination and COVID-19 cases or deaths.</p> |
| 6 | <p>SEARCH STRATEGY / RESEARCH METHODS</p> <p>PubMed and WHO COVID-19 databases were systematically searched between 10 December and 23 December 2020 using a combination of the following search terms: COVID, COVID-19, SARS-CoV-2, Bacille Calmette-Guerin, Bacillus Calmette-Guerin, and BCG. In addition, we searched reference lists of potentially eligible studies and related reviews obtained from the two databases. We included studies of any design published in English between 01 December 2019 and 23 December 2020, which reported data on COVID-19 in people vaccinated or injected with BCG for any condition.</p> <p>The search yielded 167 studies in PubMed, 145 in the WHO COVID-19 database, and 15 from reference lists. After screening and removal of duplicates, 41 studies met the inclusion criteria. Of the 42 included studies, 1 was specifically conducted in Africa (Nigeria) and 1 was published as pre-prints with no peer-review yet. We provide a descriptive analysis of the findings.</p> |
| 7 | <p>SUMMARY OF GLOBALLY PUBLISHED LITERATURE RELATED TO THE SUBJECT</p> <p>Twenty-one studies identified as epidemiological studies, 1 case report, and the rest as either observational, cohort studies or ecological studies.</p> <p>Two studies were identified that use intravesical BCG for the treatment of bladder cancer[3, 4]. A few patients receiving BCG developed COVID-19 with favourable outcomes and it was concluded</p> |

that even though the patients are high risk for developing COVID-19, BCG did not have any effect on COVID-19 outcomes.

There were several epidemiological or ecological studies that analysed data from several countries around the world with or without mandated BCG vaccination programs [5-26]. Data on COVID-19 and BCG vaccination programs were collected from several sources including online case reporting and government databases. Results from these studies showed that, generally, countries with current or most recent BCG vaccination programs reported fewer COVID-19 case and death rates compared to countries with no BCG vaccinations or countries that ceased BCG vaccination several decades ago.

There were also several retrospective observational, cohort studies or case reports describing the effects of BCG vaccination on COVID-19 outcomes [27-43]. In summary, data from these studies indicated that BCG was associated with either fewer cases of COVID-19, less severity of COVID-19, fewer COVID-19-compatible symptoms, or lower death rates. Analyses by a few studies reported no association between BCG vaccination and case numbers, deaths or disease severity [10, 29, 32, 37].

Overall, several of the studies have shown that BCG may be protective against COVID-19 severity and mortality. This may be attributed to the “trained immunity” associated with the wider immune response associated with BCG [8].

8 SUMMARY OF AFRICA-SPECIFIC LITERATURE ON THE SUBJECT

Of the studies identified, only one was specifically conducted in Africa (Nigeria) [9], and the rest of the studies presented global data with some African countries included. Data from the study on Africa suggest that lower BCG vaccination coverage was associated with higher COVID-19 cases and deaths. In a meta-analysis study of 160 countries, it was reported that North African countries (and some Middle East countries) with >70% coverage in BCG vaccination still showed high rates of SARS-CoV-2 infections [13].

9 POLICY FINDINGS

- ✚ The studies show that BCG vaccination may be protective against severe COVID-19.
- ✚ BCG vaccination may also reduce mortality from COVID-19
- ✚ Intravesical BCG for bladder cancer treatment did not have any effect on COVID-19
- ✚ Countries with mandated BCG vaccination programs have lower infection and fatality rates compared to countries with no mandated BCG vaccination programs

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| | <p>In conclusion, people with history of BCG vaccination seems to have less severe COVID-19 and less likely to die. Epidemiological studies suggest that countries with mandated BCG vaccination programs have lower rates of infections and mortality associated with COVID-19</p> |
| <p>10</p> | <p>ONGOING RESEARCH IN THE AFRICAN REGION</p> <p>Several studies including clinical trials are ongoing around the world including several African countries to properly address the effects of BCG vaccination on SARS-CoV-2 infection and COVID-19 outcomes [11, 44]</p> |
| <p>11</p> | <p>AFRO RECOMMENDATIONS FOR FURTHER RESEARCH</p> <p>BCG vaccination at birth or other high-risk groups for tuberculosis and further preventive and management of COVID-19 need to continue while data on whether BCG vaccination is protective against COVID-19, especially in Africa, become available.</p> |

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