Stop playing with data: there is no sound evidence that Bacille Calmette-Guérin may avoid SARS-CoV-2 infection (for now)

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Summary. Since the beginning of the COVID-19 epidemic, a possible explanation for the high heterogeneity of infection/mortality rates across involved countries was hinted in the prevalence of tuberculosis vaccination with Bacille Calmette-Guérin (BCG). A systematic review was therefore performed on May 2, 2020. A total of 13 articles were ultimately retrieved, 12 of them as preprint papers. All articles were ecological studies of low quality. Most of them did not include main confounding factors (i.e. demographic of the assessed countries, share of people residing in urban settings, etc.), and simply assessed the differences among incidence/mortality of COVID-19 with vaccination rates or by having vs. having not any vaccination policy for BCG. Even though all studies shared the very same information sources (i.e. international registries for BCG vaccination rates and open source data for COVID-19 epidemics), results were conflicting, with later studies apparently denying any true correlation between COVID-19 occurrence and BCG vaccination rates and/or policies. As a consequence, there is no sound evidence to recommend BCG vaccination for the prevention of COVID-19. (www.actabiomedica.it)

Key words: BCG Vaccine, COVID-19, Correlation of Data, Incidence, Mortality, Tuberculosis

Introduction

The Bacille Calmette-Guérin (BCG) is a live attenuated vaccine against tuberculosis (1,2). Following early reports demonstrating that BCG may reduce infant mortality independent of its effects on tuberculosis (3), some studies have shown that BCG can enhance the reactivity of the innate immune system. Through an increased secretion of pro-inflammatory cytokines (i.e. "*trained immunity*"), BCG would improve reactivity against tumor cells (e.g. urothelial cancer), but also against some pathogens (e.g. staphylococci, candidiasis, yellow fever) (4), including respiratory viruses such as respiratory syncytial virus and influenza virus (5,6). More precisely, a study by Leentjens et al has shown that sequential BCG – influenza vaccination may elicit a more pronounced antibody

response against influenza A(H1N1) (7).

Because of the ongoing unavailability of specific preventive and/or therapeutic measures against SARS-CoV-2 infection, several stakeholders have suggested that the BCG vaccine may be repurposed as a preventive and/or therapeutic option against COVID-19. As some conflicting results have been reported, an updated synthesis of the literature is required in order to better inform health policies and guidelines.

Methods

A systematic review and meta-analysis was undertaken following the "*Preferred Reporting Items for Systematic Reviews and Meta-Analysis*" (PRISMA) guidelines

(8). We searched different scholarly databases (namely, PubMed/MEDLINE and EMBASE) as well as the pre-print server medrxiv.org for relevant studies from inception up to 02/05/2020, without applying any backwards chronological restrictions. The search strategy was a combination of the following keywords (free text and Medical Subject Heading [MeSH] terms, where appropriate): (COVID-19 OR SARS-CoV-2 OR Coronarivus) AND (Bacille Calmette Guérin OR Bacillus Calmette Guérin). Records were handled using a references management software (Mendeley Desktop Version 1.19.5, Mendeley Ltd 2019), and duplicates were removed. Articles eligible for review were original research publications available online or through inter-library loan. A language filter was applied, by retaining articles written in Italian, English, German, French or Spanish, the languages spoken by the investigators. Two independent reviewers reviewed titles, abstracts, and the full-text of articles. Titles were screened for relevance with respect to the subject under study. Any articles reporting original results, which met one or more of the inclusion criteria, were retained for the full-text review. The investigators independently read full-text versions of eligible articles. Disagreements were resolved by consensus between the two reviewers; when it was not possible to reach consensus, input from the main investigator was searched and obtained. Further studies were retrieved from reference lists of relevant articles and consultation with experts in the field.

Results and Discussion

Briefly, a total of 161 entries were ultimately retrieved (more precisely: 4 in PubMed/Medline, 138 in Scopus, 19 in medrxiv.org). After removal of duplicates, and screening of titles and abstracts, a total of 13 full-text articles were retained, 12 of them not peer-reviewed preprint. As shown in Table 1, all the available studies were ecological ones, with raw data (i.e. COVID-19 epidemics, BCG vaccination coverage) derived from the same institutional sources.

In summary, three different blueprints were identified: a) studies comparing COVID-19 rates (i.e. incidence, mortality and case fatality rates, in absolute terms or focusing on their doubling time) in countries having a BCG vaccination policy vs. countries having not and/

or having discontinued (No. = 5) (4,9–12); b) studies assessing through regression models how a BCG vaccination policy may have affected the ongoing epidemic in terms of incidence and/or mortality (No. = 4) (13–16); c) assessing how BCG vaccination rates may have affected incidence and mortality for COVID-19 (No. = 4) (17–20). All studies were based on the same institutional databases, and differed on the modelling of the statistical analyses. Even among studies reporting an analogous study design, models were quite heterogeneous, particularly when focusing on control variables. For instance, only 4 studies (11,14,15,17) included in their modeling the demographic of the study population, with a further study that rather controlled the analyses for life expectancy (13). Moreover, only 6 studies included in the statistical models socio-economic factors, either as a raw data (e.g. Gross Domestic Income) or a synthetic index (e.g. Human development index; Healthcare Access and Quality Index, etc.) (12,14–17,19). Eventually, only two studies controlled the analyses for a critical factor such as the risk of social interaction, either through a proxy (i.e. percentage of total population residing in urban areas) (17), or by means of synthetic indices (16).

Not coincidentally, the results are conflicting. Despite the substantial sharing of the information sources, while certain studies hinted towards higher incidence and/or mortality rates in countries having and/or having implemented BCG vaccination policies, studies performed with different design and modeling substantially denied such a correlation (17, 20). As the latter studies were performed more recently, it is reasonable that the timeframe and the dynamics of the COVID-19 epidemic may a common distorting bias from the original reports. However, available estimates should be cautiously retained, as all studies were affected by similar shortcomings.

Firstly, most of reports assessed the effector variable BCG vaccination as the presence/absence of BCG policies. Even though some countries are deprived of national policies for BCG vaccine, certain population groups such as healthcare workers (HCWs) may be selectively vaccinated following specific recommendation (21). Despite nearly all Italian HCWs who began their formal education before 2000 were actively vaccinated against BCG, Italian National Institute for Occupational Injuries (IN-AIL) recently reported that around 10% of all COVID-19 positive cases had occurred among HCWs, with

Table 1. Characteristics of the studies included in the analyses.

Study	Study type	Outcome variable (COVID-19)	BCG estimate	Methodology	Control variables	Main findings
Akiyama et al. (9)	Ecological study	Doubling time for mortality	BCG vaccination policies (any vs. none)	Comparison of doubling time for countries with BCG vaccination policies for people aged 0-39 vs. those without	BCG strain	Doubling time of 5.4 days for countries with BCG vaccination policies vs. 4.2 days (p 0.007; Wilcoxon rank-sum test) in countries without BCG vaccination policies
Green C et al. (11)	Ecological study	Mortality	BCG vaccination policies (any vs. none)	Calculation of doubling time for death rate, comparison between countries with BCG vaccination policies vs. those without	Time Age gratification demographics Reporting times Timeframe for BCG vaccinations	Doubling time ≥ 5 days for countries with BCG vaccination policies vs. 4 to 1 days in countries without BCG vaccination policies.
Dayal et al. (12)	Ecological study	Case fatality rates	BCG vaccination policies (any vs. none)	Difference between case fatality rates in countries having or not a BCG policy	None	Case fatality rate of 5.2% in countries not having a BCG policy vs. 0.6% in those having a BCG policy
Dolgikh S (10)	Ecological study	Mortality	BCG vaccination policy (4 levels: countries administering BCG; countries never administering BCG; countries that had administer BCG to selected population groups; countries that had administered BCG in the past, but discontinued)	Descriptive analysis	None	All countries with very low levels of mortality have a BCG policy or had it recently
Hegarty et al (4)	Ecological study	Incidence Mortality	BCG policy (any vs. none)	Descriptive analysis	Single day of assessment (March 22, 2020)	Daily incidence of COVID-19 was 0.8/1,000,000 in countries with BCG vaccination vs. 34.8/1,000,000 in countries without such a program. Mortality 0.08/1,000,000 in countries with a BCG vaccination program vs. 34.8/1,000,000 in countries without a program. The crude case fatality rate was 4.1% in countries with BCG vaccination program vs. 5.1% in countries without BCG vaccination program.

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Shet et al. (14)	Ecological study	Mortality	BCG policy (any vs. none)	Log-linear regression model using crude COVID-19 mortality as outcome	Gross Domestic Product Days from 100th COVID-19 Percentage of population ≥ 65 years	Mortality of 0.4/1,000,000 inhabitants (IQR 0.06-0.4), 0.65 (IRQ 0.2-2.2), and 5.5 (IQR 1.6-13.9) for low-middle, upper-middle and high income countries. In log-linear regression, COVID-19-attributable mortality was 5.8 times lower in countries with BCG vaccination policies than in countries without.
Sala et al (13)	Ecological study	Incidence Mortality Case fatality rate	BCG vaccination policy (three levels: countries administering BCG, countries never administering BCG, countries that had administered BCG in the past, but discontinued)	Regression model including	Country life expectancy Mean temperature in February/March 2020	Never having had or having discontinued BCG vaccination was effector of incidence (b = 0.6483, p = 0.002, and b = 0.8666, p = 0.0025; R^2 = 0.6409) and mortality (b = 0.7262, p = 0.007; b = 1.495, p < 0.0001; R^2 = 0.5473). For case fatality rate only never having had a BCG policy was a significant effector (b = 1.1140, p = 0.0267; R^2 = 0.1019).
Klinger et al. (15)	Ecological study	Incidence Mortality	BCG policy (having or having had a national policy vs. never)	Correlation between years of BCG policy and incidence/ mortality rates. Multivariate model including BCG policy and characteristics of the country in three time lag models (15/20/25 days).	Population >65 years Economic development indicators Prevalence of chronic diseases Death rate from cardiovascular disorders	Negative correlation between years of BCG vaccination policy and incidence and mortality for COVID-19. In multivariate analysis, beta = -0.67 (p 0.0355) at 15 days; beta = -0.75 (p 0.0123) at 20 days; beta = -1.18 (p = 0.0235) at 25 days.
Berg et al. (16)	Ecological study	Incidence Mortality Growth Curves	BCG policy (any vs. none)	Regression analysis Multivariate model including BCG policy and characteristics of the country	Variation of BCG policy during the 20th century Cultural dimension (individualism vs. collectivism; tightness vs. looseness of social norms)	Growth rate for COVID-19 cases (b = -0.027, p < 0.001) and deaths (b = -0.038, p < 0.001) higher in countries without mandatory BCG vaccination.

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Singh S (19)	Ecological study	Incidence Mortality Case fatality rate	BCG vaccination rates Prevalence of Latent Tuberculosis infection (LTBI)	Correlation between death rate and LTBI	Healthcare Access and Quality index Incidence of Neglected tropical diseases Incidence of tuberculosis	Decline of SARS-CoV-2 infections by increasing LTBI ($r^2 = 0.6243$) Countries with higher LTBI rates show lower COVID-19 case fatality rates, and vice versa, with large heterogeneity and without any correlation
Goswami et al., 2020 (20)	Ecological study	Incidence	BCG vaccination rates	Comparison of COVID-19 data incidence in countries with higher vaccination rates (>95% coverage) vs. countries ≤95% coverage.	Incidence / mortality for Malaria	Higher incidence of COVID-19 (0.002%) for countries with higher vaccination rates compared to lower vaccination sates (0.0003%). In Europe and America, the relationship was inverted (i.e. 0.0002% vs. 0.0029%).
Shivendu et al., 2020 (17)	Ecological study	Incidence Mortality	BCG vaccination rates	Multiple regression models adjusted for economic and demographic factors	Number of COVID-19 tests actually performed Population density % population > 65 years of age % population living in urban areas Government transparency (Corruption Perception Index) Human development index	No significant differences between countries including BCG in National Immunization Programs (NIP) vs. countries without BCG in NIP
Miller et al. 2020 (18)	Ecological study	Incidence Mortality	BCG vaccination rates	Regression analysis modeled for economic and demographic factors	Dates of initiation of BCG vaccination Gross National Income	No occurrence of COVID-19 deaths in countries of lower income reporting BCG vaccination policies. Mortality for COVID-19 was higher in middle-high income countries that never had BCG vaccination policies compared to lower income countries (i.e. 16.4 ± 7.3/1,000,000 vs. 0.8 ± 4/1,000,000), linearly decreasing with older enforcing of BCG in NIP.

150 deaths among medical professionals, most of them aged 65 years or more (22-24).

Second, it should be stressed that all estimates depended on the quality of raw data on COVID-19 (22). On the one hand, some countries may have unreliably reported the number of cases for a variety of reasons, including the availability and the reliability of diagnostic tests, and the locally implemented policies (25-27). On the other hand, the incidence rate is rather a notification rate, whose significance is better understood when compared with the total number of processed samples – a figure that only few international authorities properly record (22, 25-28).

Eventually, the COVID-19 pandemic had a distinctive progression, with an initial outbreak in mainland China. Even though China had a universal BCG policy since 1950s (29), extensive BCG vaccination did not impaired Wuhan to becoming the initial epicenter of COVID-19 pandemic. Moreover, after a significant but limited involvement of nearby countries such as South Korea and Vietnam, COVID-19 pandemic had a sudden spread to Western Europe (22, 28). As Western Europe has progressively become a low-notification area for tuberculosis, also national vaccination policies have progressively restrained the official recommendations for BCG (2). In other words, as the global diffusion of SARS-CoV-2 has clearly followed economic highways connecting mainland China with high-developed areas in Europe and North America, we are dealing with higher occurrence of COVID-19 in highly-developed, highly interconnected areas rather than in countries deprived of vaccination policies for BCG. Similarly, as estimates from countries implementing a national policy for BCG vaccine (e.g. Russian Federation, African countries) have only recently showed the exponential increase that has previously affected Europe and North America, available figures are presumptively underestimating the actual morbidity of COVID-19 in countries with a national BCG policy (30).

In conclusion, there is no evidence that the BCG may protect people against infection with SARS-CoV-2. As a consequence, there is no evidence to recommend BCG vaccination for the prevention of COVID-19.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Hung WT, Lee SSJ, Sy CL, et al. Prevalence of latent tuberculosis infection in BCG-vaccinated healthcare workers by using an interferon-gamma release assay and the tuberculin skin test in an intermediate tuberculosis burden country. J Microbiol Immunol Infect 2015;48(2):147–52. https://doi.org/10.1016/j.jmii.2013.07.008

2. Odone A, Riccò M, Morandi M, Borrini BM, Pasquarella C, Signorelli C. Epidemiology of tuberculosis in a low-incidence Italian region with high immigration rates: Differences between not Italy-born and Italy-born TB cases. BMC Public Health 2011;11:376. https://doi.org/10.1186/1471-2458-11-376.

3. Moorlag SJCFM, Arts RJW, van Crevel R, Netea MG. Non-specific effects of BCG vaccine on viral infections. Clin Microbiol Infect. 2019;25(12):1473–8. https://doi.org/10.1016/j.cmi.2019.04.020

4. Hegarty PK, Sfakianos JP, Giannarini G, Dinardo AR. COVID-19 and Bacillus Calmette-Guérin. Eur Urol Oncol. 2020; S2588-9311(20)30049-3. https://doi.org/10.1016/j.euo.2020.04.001.

5. Wardhana, Datau EA, Sultana A, Mandang V V., Jim E. The efficacy of Bacillus Calmette-Guerin vaccinations for the prevention of acute upper respiratory tract infection in the elderly. Acta Med Indones. 2011;43(3):185–90.

6. Stensballe LG, Nante E, Jensen IP, Kofoed PE, Poulsen A, Jensen H, et al. Acute lower respiratory tract infections and respiratory syncytial virus in infants in Guinea-Bissau: A beneficial effect of BCG vaccination for girls: Community based case-control study. Vaccine. 2005;23(10):1251–7. https://doi.org/ 10.1016/j.vaccine.2004.09.006

7. Leentjens J, Kox M, Stokman R, Gerretsen J, Diavatopoulos DA, Van Crevel R, et al. BCG vaccination enhances the immunogenicity of subsequent influenza vaccination in healthy volunteers: A randomized, placebo-controlled pilot study. J Infect Dis. 2015;212(12):1930–8. https://doi.org/ doi: 10.1093/infdis/jiv332

8. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med. 2009;6(7):e1000097. https://doi.org/ doi: 10.1371/journal.pmed.1000097

9. Akiyama Y, Ishida T. Relationship between COVID-19 death toll doubling time and national BCG vaccination policy. medRxiv 2020;2020.04.06.20055251. Available from: https://www.medrxiv.org/content/10.1101/2020.04.06.20055251v1 https://doi.org/10.1101/2020.04.06.20055251v1

10. Dolgikh S. Further Evidence of a Possible Correlation Between the Severity of Covid-19 and BCG Immunization. medRxiv. 2020;2020.04.07.20056994. Available from: https://www.medrxiv.org/content/10.1101/2020.04.07.20056994v1 https://doi.org/10.1101/2020.04.07.20056994v1

11. Green CM, Dominguez-andres J, Fok ET, Moorlag SJCFM, Negishi Y, Joosten LAB, et al. COVID-19: A model correlating BCG vaccination to protection from mortality implicates trained immunity. medRxiv 2020;2020.04.10.20060905.

Available from: www.medrixiv.com/content/10.1101/2020.0
4.10.20060905v1 https://doi.org/10.1101/2020.04.10.2006
0905v1

12. Dayal D, Gupta S. Connecting BCG Vaccination and COV-
ID-19: Additional Data. medRxiv. 2020;2755657(M):2020.0
4.07.20053272. Available from: www.medrixiv.com/content/
10.1101/2020.04.07.20053272v1 https://doi.org/10.1101/20
20.04.07.20053272v1

13. Sala G, Miyakawa T. Association of BCG vaccination pol-
icy with prevalence and mortality of COVID-19. medRxiv
2020;2020.03.30.20048165. Available from: https://www.
medrxiv.org/content/10.1101/2020.03.30.20048165. https://
doi.org/10.1101/2020.03.30.20048165

14. Shet A, Ray D, Malavige N, Santosham M, Bar-Zeev N. Differ-
ential COVID-19-attributable mortality and BCG vaccine use
in countries. medRxiv 2020;2020.04.01.20049478. Available
from: https://www.medrxiv.org/content/10.1101/2020.04.01
.20049478v1 https://doi.org/10.1101/2020.04.01.20049478

15. Klinger D, Blass I, Rappoport N, Linial M. Significantly
Improved COVID-19 Outcomes in Countries with Higher
BCG Vaccination Coverage : A Multivariable Analysis. me-
dRxiv. 2020;2020.04.23.20077123. Available from: https://
www.medrxiv.org/content/10.1101/2020.04.23.20077123
https://doi.org/10.1101/2020.04.23.20077123

16. Berg MK, Yu Q, Salvador CE, Melani I, Kitayama S. Man-
dated Bacillus Calmette-Guérin (BCG) vaccination predicts
flattened curves for the spread of COVID-19. medRxiv.
2020;2020.04.05.20054163. Available from: https://www.
medrxiv.org/content/10.1101/2020.04.05.20054163 https://
doi.org/10.1101/2020.04.05.20054163

17. Shivendu S, Chakraborty S, Onuchowska A, Srivas-
tava A, Patidar A. Is there evidence that BCG vaccination
has non-specific protective effects for COVID 19 infec-
tions or is it an illusion created by lack of testing? medRxiv.
2020;2020.04.18.20071142. Available from: https://www.
medrxiv.org/content/10.1101/2020.04.18.20071142 https://
doi.org/10.1101/2020.04.18.20071142

18. Miller A, Raendelar MJ, Fasciglione K, Roumenova V,
Li Y, Otazu GH. Correlation between universal BCG
vaccination policy and reduced morbidity and mortal-
ity for COVID-19: an epidemiological study. medRxiv
2020;2020.03.24.20042937. Available from: https://www.
medrxiv.org/content/10.1101/2020.03.24.20042937v1 htt-
ps://doi.org/10.1101/2020.03.24.20042937

19. Singh S. Bcg Vaccines May Not Reduce Covid-19 Mortality Rates.
medRxiv 2020;2020.04.11.20062232. Available from: http://
medrxiv.org/content/early/2020/04/17/2020.04.11.20062232
https://doi.org/10.1101/2020.04.11.20062232

20. Goswami RP, Mittal D, Goswami RP. Interaction between
malarial transmission and BCG vaccination with COVID-19
incidence in the world map: A cross-sectional study. medRxiv
2020;2020.04.03.20052563 Available from: https://www.
medrxiv.org/content/10.1101/2020.04.03.20052563 https://
doi.org/2020;2020.04.03.20052563

21. Bonanni P, Ferrero A, Guerra R, Iannazzo S, Odone A, Pom-
pa M, et al. Vaccine coverage in Italy and assessment of the

2012-2014 National Immunization Prevention Plan. Epide-
miol Prev. 2015;39(4S1):146–158.

22. Signorelli C, Scognamiglio T, Odone A. COVID-19 in Italy:
impact of containment measures and prevalence estimates of
infection in the general population. Acta Biomed 2020;91(3-
S):175–9. doi: 10.23750/abm.v91i3-S.9511

23. Chirico F, Nucera G, Magnavita N. COVID-19: Protecting
Healthcare Workers Is a Priority. Infect Control Hosp Epide-
miol 2020;epub ahead of print doi: https://doi.org/10.1017/
ice.2020.148

24. Ferioli M, Cisternino C, Leo V, Pisani L, Palange P, Nava S.
Protecting Healthcare Workers From SARS-CoV-2 Infection:
Practical Indications. Eur Respir Rev 2020;29(155):200068.
https://doi.org/10.1183/16000617.0068-2020.

25. Riccò M, Ferraro P, Gualerzi G et al. Point-of-Care diag-
nostic of SARS-CoV-2: knowledge, attitudes, and percep-
tions (KAP) of medical workforce in Italy. Acta Biomed
2020;91:epub ahead of print https://doi.org/10.23750/abm.
v91i2.9573

26. Signorelli C, Odone A, Gianfredi V, et al. The spread of
COVID-19 in six western metropolitan regions: a false myth
on the excess of mortality in Lombardy and the defense of
the city of Milan. Acta Biomed 2020;91:epub ahead of print
https://doi.org/10.23750/abm.v91i2.9579

27. Baud D, Qi X, Nielsen-Saines K, et al. Real Estimates of
Mortality Following COVID-19 Infection. Lancet Infect Dis
2020;S1473-3099(20)30195-X.   https://doi.org/10.1016/
S1473-3099(20)30195-X.

28. Guzzetta G, Poletti P, Ajelli M, et al. Potential Short-
Term Outcome of an Uncontrolled COVID-19 Epidem-
ic in Lombardy, Italy, February to March Euro Surveill
2020;25(12):2000293.   https://doi.org/10.2807/1560-7917.
ES.2020.25.12.2000293.

29. Floyd K , Glaziou P, Zumla A et al. The Global Tuberculosis
Epidemic and Progress in Care, Prevention, and Research:
An Overview in Year 3 of the End TB Era. Lancet Respir
Med 2018;6(4):299-314. https://doi.org/10.1016/S2213-
2600(18)30057-2

30. Coronavirus (COVID-19) confirmed cases in Russia as of
May 3, 2020, by region https://www.statista.com/statis-
tics/1102935/coronavirus-cases-by-region-in-russia/   (ac-
cessed on May 4, 2020)

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