Efficacy of BCG vaccination in repeated exposure to TB

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Current statistics for TB and BCG vaccine

WHO (2018)

- One fourth of the world’s population is infected with TB.
- In 2017, 10.0 million people developed TB disease, and there were 1.3 million TB-related deaths worldwide and an addition 300,000 for HIV positive people.
- BCG vaccine is one of the most widely used vaccine, with high 90% vaccine rates in many countries.
# Current rates of BCG vaccination (by country)

<table>
<thead>
<tr>
<th>Country</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>87%</td>
</tr>
<tr>
<td>Albania</td>
<td>99%</td>
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<tr>
<td>Algeria</td>
<td>99%</td>
</tr>
<tr>
<td>Angola</td>
<td>58%</td>
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<tr>
<td>Argentina</td>
<td>92%</td>
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<tr>
<td>Armenia</td>
<td>99%</td>
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<tr>
<td>Azerbaijan</td>
<td>98%</td>
</tr>
<tr>
<td>Bahrain</td>
<td>93%</td>
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<tr>
<td>Bangladesh</td>
<td>99%</td>
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<tr>
<td>Barbados</td>
<td>46%</td>
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<tr>
<td>Belarus</td>
<td>98%</td>
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<tr>
<td>Belize</td>
<td>94%</td>
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<tr>
<td>Benin</td>
<td>97%</td>
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<tr>
<td>Bhutan</td>
<td>99%</td>
</tr>
<tr>
<td>Bolivia (Plurinational State of)</td>
<td>96%</td>
</tr>
</tbody>
</table>

*WHO (2016)*
Inspiration for project
Yaye et al. (2019)
Systematic reviews in the efficacy of BCG vaccination

- Several systematic reviews on the vaccine, with the most exhaustive being the *Abubakar et al. (2013)* study.
  - The vaccine is significantly efficacious in neonates and children
  - The vaccine however is insignificantly efficacious for all ages (including children)
Neonatal and children vaccination studies

Abubakar et al. (2013)
All ages vaccination studies

Abubakar et al. (2013)
All ages vaccination studies

Abubakar et al. (2013)
BCG RCT in Chingleput, South India
*Tuberculosis Prevention Trial (1968)*

- The largest BCG vaccination study done, with 281,161 people (1,128,696 PYs) either vaccinated with BCG (high or low dose) or given a placebo
- 15 year follow-up via:
  - Resurveys every 30 months
  - Selective follow-up every 10 months
  - Continuous passive case finding
High-dose (0.1mg) vaccine
Low-dose (0.01mg) vaccine
Our systematic review (in progress)

- Using the same search and elimination strategy as Abubakar et al. we will search from 2009-current
- Combining the data from Abubakar et al. (1920-2009), we will create a more consolidated systematic review
- Data will be reviewed again and stratified according to age
Hypothesis

- Age-related increased risk of developing TB could mean:
  - Immunological differences between adults and children and how BCG affects them differently
  - Repeated exposure to *myobacterium tuberculosis* (*mtb.*.) leads to higher risk of developing TB for those who have been vaccinated compared to those who aren’t
    - Areas with higher exposure to mtb. could mean that the vaccine is not that efficacious
Hypothesis

Nguipdop-Djomo et al. (2016)

Figure 2: BCG vaccine effectiveness against pulmonary tuberculosis by time since vaccination
Error bars are 95% CIs. Tuberculosis cases occurring in the first 2 years after screening are excluded.
What could this mean for future studies?

- Longer follow-up required for studies involving vaccinations for TB
- Many studies only focus on LTBI which is insufficient. Patients also need to be followed up for TB disease.
SUMMER project
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