

Prevention of Leprosy - Immunoprophylaxis: A systematic Review

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Research Question

The Global Leprosy Programme (GLP) has started the process to develop the first WHO guidelines for prevention, diagnosis and treatment of Leprosy based on GRADE and as part of that process has commissioned a literature review. The PICO question on vaccines for leprosy was as below:

Is there an effective and safe tool for prevention of leprosy in the form of immune-prophylaxis per se and/or in association with chemoprophylaxis for contacts of leprosy patients and also for the general population?

Systematic Review - methods

- Two electronic bibliographic databases: Medline and Embase were searched from 2010 to April 2017
- MeSH terms and key words for 'Leprosy', 'Immunoprophylaxis' 'chemoprevention', ICRC, IDRI, Mycobacterium w' were used
- Title and abstracts were scanned for inclusion and any queries with inclusion was checked by the GLP staff and with the review methodologist

Outcomes of interest

CRITICAL

Leprosy disease

Adverse effects (by
other reviewer)

IMPORTANT

Feasibility

Acceptability

Costs

Analysis plan

- **For observational Cohort and Cross-Sectional Studies, National Institute of Health USA risk assessment tool was used**
- **Cochrane risk of bias quality assessment for Randomized Controlled Trials (RCT)**
- **Utilized reviews for studies prior to 2010**
- **Evidence synthesis based on studies in prior reviews and new studies**
 - Evidence synthesized based on GRADE approach, based on:
 - Risk of bias: very low, low, moderate, high
 - Inconsistency: Unable to assess—single study
 - Indirectness: Not a factor
 - Imprecision: Very serious imprecision=total n <100, serious imprecision=total n<200=serious imprecision

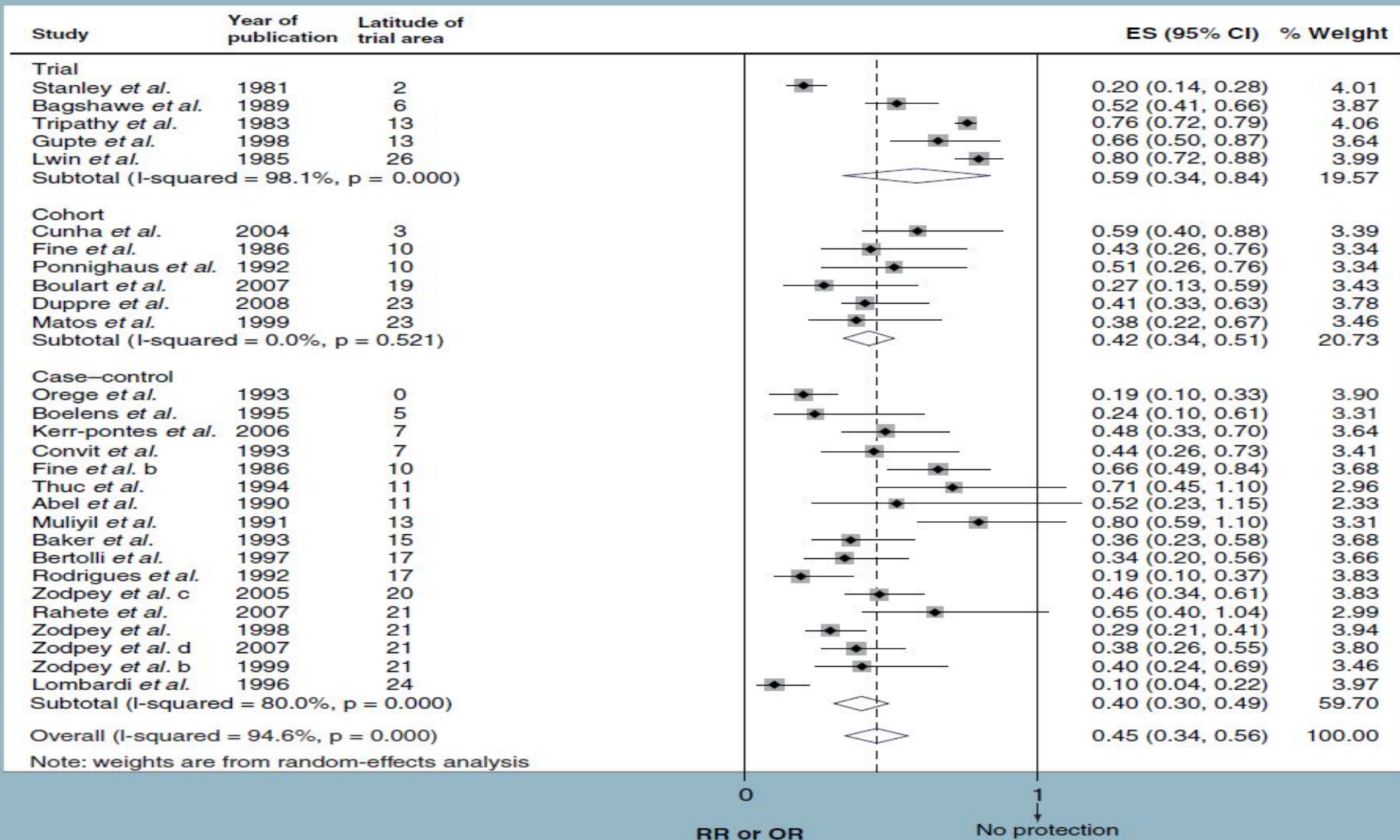
Results of search

- 87 citations scanned, 19 full-text articles reviewed
- For BCG: 2 Systematic Reviews, 1 Primary study and 1 study protocol was identified that met the inclusion criteria
- For other vaccines: 2 Systematic Reviews, 1 primary study
- No studies on costs/feasibility/acceptability

Overview of existing systematic reviews of BCG and leprosy included

Author	Publication year	Search period	No of studies	Outcomes
Smith et al [3]	2010	Up to 2009	6 Experimental/ 23 observational	Clinical leprosy (Multi and Pauci-bacillary)
Merle et al [4]	2010	Up to 2009	5 Experimental/ 23 Observational	Clinical leprosy (Multi and Pauci-bacillary)

“Pooled” results on BCG



Meta-Regression Analysis

Univariate: Proportion of variation in BCG protection

Latitude (1.2%)

Doses of BCG (6.8%)

General Population/Contacts (25.6%)

Year of publication (45.8%)

Study design (51.2%)

multivariable: Only study design significantly affected results



Meta-regression analysis of BCG vaccine efficacy and effectiveness against leprosy (n = 28)

<i>Dose of BCG</i>	<i>Relative Risk Reduction</i>	<i>p-value</i>
1 dose of BCG	55% (42–67)	0.43
2 doses or more	59% (50–68)	0.43
<i>Type of study</i>		
Experimental studies	41% (16–66)	0.09
Observational studies	60% (52–67)	0.09
<i>Target population studied</i>		
General population	53% (41–64)	0.03
Contacts	68% (56–80)	0.03

Details of additional study on BCG not in systematic reviews

Shuring et al 2009

- Sub-analysis from RCT of Single Dose Rifampicin, evaluated effects of having received BCG vs. no BCG (based on presence of BCG scar)
- N >20,000
- Single-Dose Rifampicin (SDR) and BCG: OR 0.20 (0.08-0.49)
- BCG alone: OR 0.43 (0.25-0.75)
- SDR alone: OR 0.42 (0.26-0.69)

BCG for prevention of leprosy

Outcome: Leprosy diagnosis	Number of studies and study design	Effect estimates	Quality
BCG at birth vs. placebo or no BCG	SR with 28 studies (5 trials) and 1 additional study (sub-study from a RCT)	<p>Overall: RR 0.45 (95% CI 0.34 to 0.56)</p> <p>Trials: RR 0.59 (95% CI 0.34 to 0.84)</p> <p>Cohort studies: RR 0.42 (95% CI 0.34 to 0.51)</p> <p>Case-control studies: OR 0.40 (95% CI 0.30 to 0.49)</p> <p>Additional analysis from RCT: OR 0.43 (95% CI 0.25 to 0.75)</p>	Moderate
BCG revaccination vs. no BCG revaccination	2 RCT	<p>RR 0.51 (0.26 to 0.99)</p> <p>RR 0.99 (0.69 to 1.43)</p>	Low

Other vaccines for prevention of leprosy

Outcome: Leprosy diagnosis	Number of studies and study design	Effect estimates	Quality
BCG plus killed M. Leprae vs. placebo	1 RCT	RR 0.36 (0.26-0.50)	Moderate
BCG plus killed M. Leprae vs. BCG alone	3 RCT	RR 1.06 (0.62-1.82) RR 0.89 (0.53-1.47) RR 0.50 (0.40-0.63)	Low
ICRC vaccine vs. placebo	1 RCT	RR 0.34 (0.23-0.52)	Moderate
Mycobacterium w vaccine vs. placebo	2 RCT	RR 0.61 (0.46-0.80) RR 0.74 (0.56-0.98)	Moderate

Summary of findings

- Evidence indicates BCG given to infants is effective for leprosy prevention
- Relative Risk Reduction (RRR) with BCG revaccination similar to vaccination at birth in systematic review; evidence mixed for the 2 largest RCT on protective effect of BCG re-vaccination
- SDR (chemoprophylaxis) may be more effective in persons who received BCG in childhood-current ongoing trial on revaccination of contacts of leprosy patients with/without SDR (Maltalep/Bangladesh)
- Evidence also suggests BCG + killed *M. Leprae*, ICRC vaccine and Mycobacterium w vaccine are also effective for leprosy prevention