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Does the efficacy of BCG decrease with time since vaccination? A meta analyis

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Estimates of the protective efficacy of BCG vaccination (BCG PE) against tuberculosis from different studies range from negative to over 90%. These estimates are heterogenous to a statistically significant degree. This study investigates the hypothesis that BCG PE decreases with time since vaccination, by performing a meta-analisys of the change in BCG-PE against tuberculosis over time observed in all nine randomised controlled trials which presented data separately for discrete time periods. For each trial, we derived log rate ratios for annual change in the rate of TB in controls and the annual change in BCG PE. We also compared BCG PE in the first two years, and the last 10 years, to that in the rest of the trial, There was statistically significant heterogeneity between trials in the annual change in BCG PE. In six trials BCG PE decreased over time (in one of the trials this decrease was statistically significant) while in three of the trials it increased. The annual change in PE was not related to overall PE. Because of the heterogeneity, it would not be appropriate to calculate an overall trend in BCG PE with time.

Trials reviewed

Location	Study — acumulation	Start date	Maximum Years of Follow-up	References
Canada				
Native Americans (USA)	3008 American Indians Individuals	1935	11	10-14
Chicago (USA)	3381 ?	1937	23	15
Georgia (USA)	4839 children	1949	20	16,17
Puerto Rico	77927 children	1949	20	18,19
Georgia (USA)	34567 individuals of 5+ years	1950	20	18, 20-23
England	26465 adolescents and early adults	1950	20	7, 24-27
Madanapalle (S. India)	10872 nigers	1950	21	28-30
Madras (S. India)	90000 gers	1968	15	31,32

Trials reviewed

Summary protection in trials:			Rate ratios (95% CI) for change in effect of BCG over time		
Trial	PE (95% CI)	RR (95% CI) for annual change in rate of TB in controls	Annual change in effect of vaccine	Effect after the first 2 years, compared to the first 2 years of the trial	Effect after the first 10 years, compared to the first 10 years of the trial
Saskatchewan (Canada)	78.5 (46.6, 92.8)	0.969 (0.866.1.086)	0.949 (0730, 1,232)	1.841 (0.268, 12.649)	-
Native Americans (USA)	80.8 (73.6, 86.2)	0.968 (0.919, 1.019)	1.182 (1.036, 1.348)	3.449 (1.807, 6.582)	-
Chicago (USA)	72.5 (51.6, 85.3)	0.780 (0.713, 0.855)	0.906 (0.761, 1.078)	0.336 (0.069, 1.641)	0.522 (0.044, 6.157)
Georgia School (USA)	-56.3 (-905.0,69.6)	1.026 (0.838, 1.257)	0.928 (0.717, 1.201)	- -	0.333(0.017, 6.648)
Puerto Rico (USA)	27.9 (9.6, 42.4)	0.940 (0.910, 0.970)	1,007 (0.965, 1.050)	0.859 (0.469, 1.572)	1.208 (0.768, 1.899)
Georgia Community (USA)	6.2 (-55.5, 43.6)	0.973 (0.915, 1.034)	0.952 (0.872, 1.038)	-	0.810 (0.310, 2.114)
MRC	76.7 (69.2, 82,6)	0.826 (0.801, 0.851)	0.919	0.783 (0.406, 1.510)	0,359 (0.169, 0.785)
(England) Madanapalle (India)	19-4 (-28, 4, 50.0)	1.106 (1.051, 1.165)	(0.868, 0.973) 0.933 (0.857, 1.016)	-	0.163 (0.034, 0.782)
Madras (India)	-2.9 (-24.0, 14.4)	1.133 (1.08,80)	1.044 (0.995, 1.095)	2.102 (0.846, 5.222)	1.031 (0.717, 1.482)
x^2 test for heterogeneity			22.85 (9 df) p = 0.004	16.82 (6 df) p = 0.005	13.05 (7 df) p = 0.042