

Background: Growing evidence supports the existence of a sex-difference in immunity to tuberculosis (TB). This is most often to the detriment of males. This study aimed to assess the association between scar size from Bacillus Calmette-Guérin (BCG) and mortality risk stratified by sex.

Methods: Kaplan-Meier survivor functions and Cox Proportional Hazard models were used to assess mortality risk by sex and scar size. Groups were further compared by clinical and epidemiological characteristics.

Results: Between 2003 and 2019, 2,944 eligible patients were identified of whom 1,003 were included in the final analysis. Males with BCG scars, particularly large scars, were less likely to die within a year of diagnosis than males with no scar (adjusted hazard ratio=0.36 (95% CI: 0.15–0.88)). On the contrary, females with small scars trended towards higher mortality than females with no scars or females with large scars.

Conclusion: BCG protects against death in male but not female patients with TB. More research is needed to determine the mechanisms underpinning these sex differences and whether they are generalizable beyond this setting.

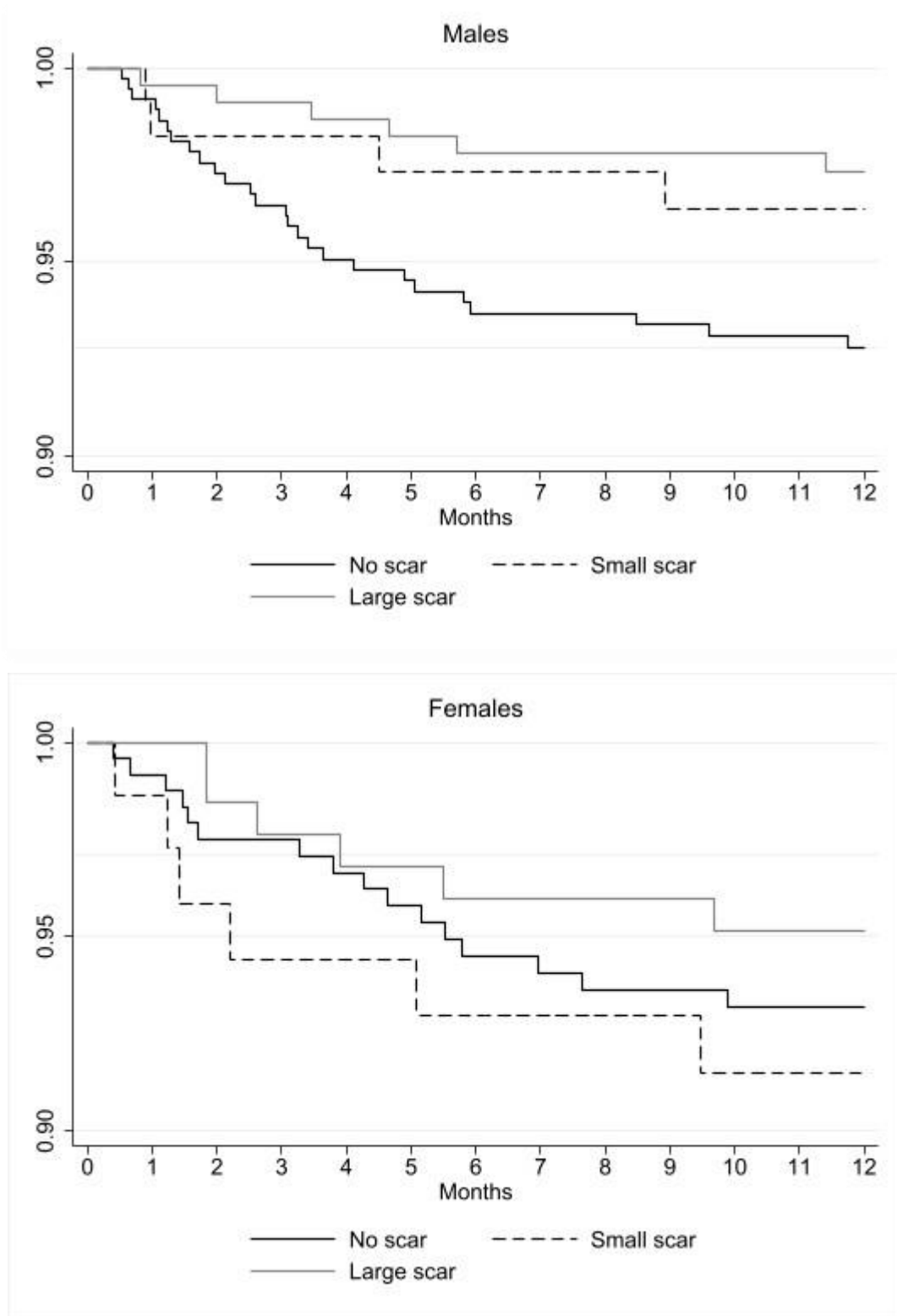


Figure 1. Kaplan-Meier survivor functions by reaction to vaccination and sex adjusted for age. Small scars were defined as the lower tertile in any given year (see Supplementary Table 1 for specific cut-offs).

Table 1

			Males		Females		Total	
			Crude (CI 95%)	Adjusted* (CI 95%)	Crude (CI 95%)	Adjusted* (CI 95%)	Crude (CI 95%)	Adjusted* (CI 95%)
Sex			1	1	1.38 (0.84 – 2.27)	0.61 (0.36 – 1.05)	-	-
Age (continuous)			1.09 (1.03 – 1.14)	1.07 (1.01 – 1.13)	1.11 (1.05 – 1.18)	1.07 (1.00 – 1.15)	1.09 (1.05 – 1.14)	1.07 (1.03 – 1.12)
Smear grade	+		1	1	1	1	1	1
	++		1.02 (0.29 – 3.61)	1.00 (0.28 – 3.64)	0.84 (0.19 – 3.74)	1.30 (0.28 – 6.04)	0.94 (0.36 – 2.48)	1.13 (0.42 – 3.02)
	+++		1.04 (0.33 – 3.22)	1.03 (0.33 – 3.25)	1.77 (0.51 – 6.22)	2.27 (0.63 – 8.12)	1.31 (0.57 – 3.02)	1.55 (0.66 – 3.62)
	Negative		2.72 (0.84 – 8.82)	1.56 (0.46 – 5.28)	1.47 (0.35 – 10.43)	1.31 (0.28 – 6.08)	2.13 (0.86 – 5.29)	1.54 (0.60 – 3.92)
	No data		2.86 (0.77 – 10.64)	1.67 (0.40 – 7.04)	2.10 (0.42 – 10.43)	1.58 (0.31 – 8.16)	2.53 (0.92 – 6.99)	1.71 (0.60 – 4.87)
BCG	No scar		1	1	1	1	1	1
	Scar		0.40 (0.19 – 0.83)	0.43 (0.19 – 0.96)	0.83 (0.39 – 1.75)	1.37 (0.61 – 3.06)	0.55 (0.33 – 0.93)	0.76 (0.44 – 1.30)
BCG scar size	All	No scar	1	1	1	1	1	1
		Small scar	0.47 (0.17 – 1.37)	0.95 (0.32 – 2.80)	1.18 (0.46 – 3.02)	1.99 (0.75 – 5.29)	0.74 (0.37 – 1.48)	1.29 (0.63 – 2.65)
		Large scar	0.36 (0.15 – 0.88)	0.36 (0.14 – 0.92)	0.64 (0.25 – 1.63)	0.87 (0.33 – 2.28)	0.46 (0.24 – 0.88)	0.56 (0.29 – 1.10)
	HIV-infected	No scar	1	1	1	1	1	1
		Small scar	1.39 (0.40 – 4.83)	3.06 (0.78 – 11.98)	1.29 (0.42 – 3.91)	1.58 (0.50 – 5.02)	1.29 (0.56 – 2.95)	1.77 (0.74 – 4.21)
		Large scar	0.80 (0.26 – 2.44)	0.58 (0.17 – 1.94)	0.99 (0.38 – 2.57)	1.05 (0.39 – 2.83)	0.89 (0.43 – 1.84)	0.86 (0.40 – 1.83)
	HIV-uninfected	No scar	1	1	1	1	1	1
		Small scar	0.23 (0.03 – 1.81)	0.37 (0.05 – 2.90)	2.71 (0.38 – 19.21)	3.46 (0.47 – 25.26)	0.60 (0.17 – 2.07)	0.89 (0.24 – 3.23)
		Large scar	0.24 (0.05 – 1.08)	0.27 (0.06 – 1.21)	-	-	0.21 (0.05 – 0.92)	0.26 (0.06 – 1.17)
PPD	All	>5 mm	1	1	1	1	1	1
		≤ 5 mm	11.42 (3.62 – 36.04)	4.19 (1.20 – 14.67)	5.05 (1.54 – 16.55)	3.13 (0.87 – 11.32)	7.84 (3.43 – 17.88)	3.88 (1.61 – 9.34)

* Adjusted for age (continuous), mid-upper-arm-circumference (continuous), smear grade, and HIV-status and -type.

BCG=Bacille Calmette-Guérin.

Small scars were defined as the lower tertile in any given year to account for variation in scar measurements over time (see Supplementary Table 1 for specific cut-offs).