# WEB MATERIAL

## Analyzing Vaccine Trials in Epidemics With Mild and Asymptomatic Infection

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**Web Table 1.** Model parameters

| Parameter | Meaning | Value/range |
|---|---|---|
| $R_0$ | Average number of secondary infections generated by an infected individual within the communities; function of force of infection (ß), infectious period, and network structure (7, 8) | Baseline: 1.0, 1.25, 1.5<br>Supplement: 2.5, 5.0 |
| Latent period | Latent period length (days) | Baseline: 6.0 (1)<br>Supplement (Ebola-like): 9.7 (2, 3) |
| Infectious period | Mean infectious period length (days); gamma-distributed with rate = 1.13 and shape = 0.188 | Baseline: 6.0 (4)<br>Supplement (Ebola-like): 5 (2, 3) |
| VE | Individual vaccine efficacy | Baseline: 0.6<br>Supplement: 0.4, 0.8 |
| $N_i$ | Size of community *i* | 20,000, 4,000, 3,500 |
| Number of communities | Number of communities in the network | 1, 5 |
| Symptomatic (vaccinated) | The proportion of infected individuals in the vaccinated group who become symptomatic | Baseline: 0.2<br>Supplement: 0.1, 0.3<br>Supplement (Ebola-like): 0.9 |
| Symptomatic (control) | The proportion of infected individuals in the control group who become symptomatic | Baseline: 0.2<br>Supplement (Ebola-like): 0.9 |
| *a* | Constant in calculation of importation rate into communities from main population<br>• $M_i = a \times \sqrt{N_i}$, where $M_i$ is importation rate and $N_i$ is the size of community *I* (5, 8) | 40 |
| Within degree | Average within-community degree (i.e. the average number of contacts each person has within their own community) | 30–52 |

| | | |
|---|---|---|
| Between degree | Average between-community degree (i.e., the average number of contacts each person has outside of their own community) | 0–5 |
| Trial size | Average number of individuals enrolled | 1,500 |
| Trial start day | First day of enrollment, vaccination and start of follow-up, relative to the first day of the epidemic in the main population | 100 |
| Trial length | Length of follow-up after trial start (days) | Baseline: 150<br>Supplement: 200 |
| % enrolled | % of each community enrolled into the trial | 7.5%, 3% |

**Web Table 2.** Median number of events

| Group | $R_0$ = 1.00 | | $R_0$ = 1.25 | | $R_0$ = 1.50 | |
|---|---|---|---|---|---|---|
| | 1 Community | 5 Communities | 1 Community | 5 Communities | 1 Community | 5 Communities |
| Vaccinated | 34 | 33 | 173 | 171 | 309 | 306 |
| Control | 82 | 81 | 361 | 353 | 543 | 544 |

**Web Table 3.** Median variance

| Approach | | $R_0$ = 1.00 | | $R_0$ = 1.25 | | $R_0$ = 1.50 | |
|---|---|---|---|---|---|---|---|
| | | 1 Community | 5 Communities* | 1 Community | 5 Communities* | 1 Community | 5 Communities* |
| 1 | Cox "perfect knowledge" | 0.042 | 0.043, 0.040 | 0.009 | 0.009, 0.009 | 0.005 | 0.005, 0.005 |
| 2 | Cox—symptomatic only | 0.217 | 0.228, 0.210 | 0.044 | 0.044, 0.044 | 0.026 | 0.026, 0.026 |
| 3 | Relative risk estimate | 0.039 | 0.040, 0.039 | 0.006 | 0.006, 0.006 | 0.002 | 0.002, 0.002 |
| 4 | Corrected relative risk estimate (6) | 0.007 | 0.007, 0.006 | 0.001 | 0.001, 0.001 | 0.001 | 0.001, 0.001 |
| 5 | Interval-censored Cox model (3 intervals) | 0.042 | 0.044, 0.044 | 0.009 | 0.009, 0.009 | 0.005 | 0.005, 0.005 |
| 6 | Interval-censored Cox model (1 interval) | 0.043 | 0.278, 0.044 | 0.009 | 0.046, 0.009 | 0.005 | 0.028, 0.005 |
| 7 | Imputation | 0.059 | 0.046, 0.21 | 0.01 | 0.009, 0.01 | 0.006 | 0.006, 0.007 |

* First number is from the analysis of the five communities as one large community and the second is from the stratified and meta-analyzed analyses.

**Web Table 4.** Median $VE_P$ estimate in full trial and sample from approach 7 when $VE_P \neq 0$

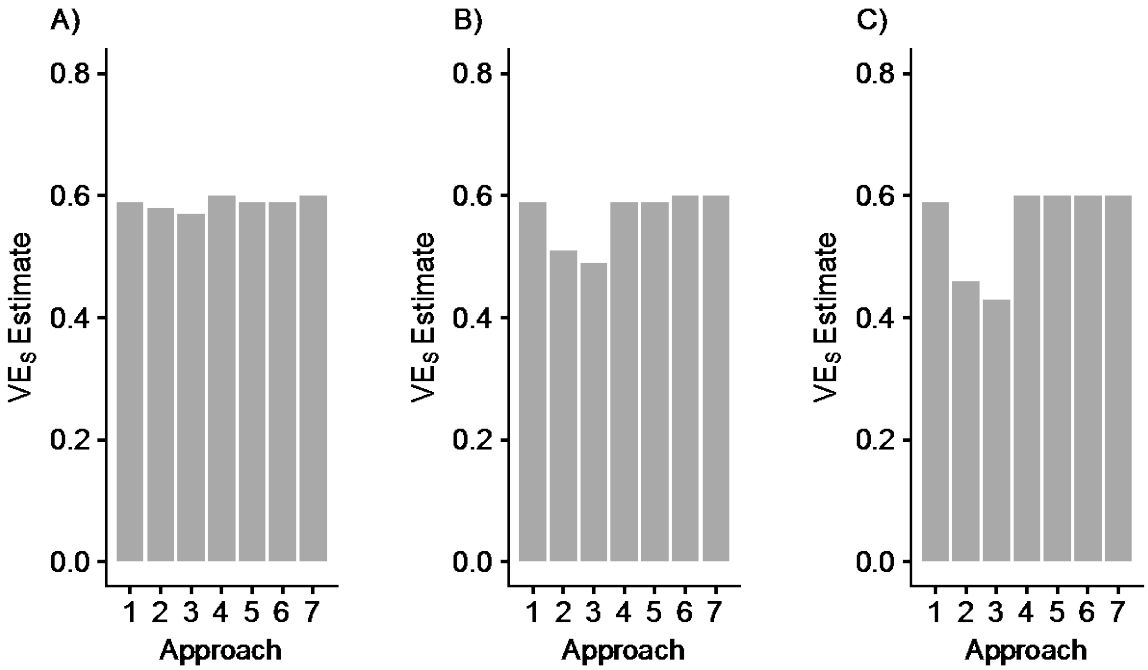
| True $VE_P$ | $R_0$ = 1.00 | | $R_0$ = 1.25 | | $R_0$ = 1.50 | |
|---|---|---|---|---|---|---|
| | **Full Trial** | **Sample** | **Full Trial** | **Sample** | **Full Trial** | **Sample** |
| 0.50 | 0.49 | 1 | 0.51 | 0.56 | 0.50 | 0.49 |
| -0.50 | -0.49 | -0.17 | -0.51 | -0.53 | -0.59 | -0.49 |

**Web Table 5.** $VE_S$ estimates (empirical coverage probabilities)[a]

| Approach | $R_0 = 1.00$ | | $R_0 = 1.25$ | | $R_0 = 1.50$ | |
|---|---|---|---|---|---|---|
| | **200-Day Trial** | | **200-Day Trial** | | **200-Day Trial** | |
| 1 | 0.59 (0.97) | | 0.59 (0.93) | | 0.59 (0.95) | |
| 2 | 0.58 (0.95) | | 0.51 (0.76) | | 0.46 (0.53) | |
| 3 | 0.57 (0.96) | | 0.49 (0.13) | | 0.43 (0) | |
| 4 | 0.6 (0.96) | | 0.59 (0.95) | | 0.6 (0.95) | |
| 5 | 0.59 (0.96) | | 0.59 (0.92) | | 0.6 (0.95) | |
| 6 | 0.59 (0.96) | | 0.60 (0.93) | | 0.6 (0.95) | |
| 7 | 0.60 (0.90) | | 0.60 (0.92) | | 0.60 (0.92) | |
| | **$VE_P = 0.50$** | **$VE_P = -0.50$** | **$VE_P = 0.50$** | **$VE_P = -0.50$** | **$VE_P = 0.50$** | **$VE_P = -0.50$** |
| 1 | 0.59 (0.94) | 0.59 (0.93) | 0.59 (0.96) | 0.59 (0.94) | 0.59 (0.93) | 0.59 (0.94) |
| 2 | 0.79 (0.87) | 0.37 (0.79) | 0.77 (0.46) | 0.27 (0.11) | 0.73 (0.49) | 0.17 (0) |
| 3 | 0.58 (0.95) | 0.58 (0.95) | 0.51 (0.48) | 0.51 (0.43) | 0.43 (0) | 0.43 (0) |
| 4 | 0.59 (0.96) | 0.59 (0.96) | 0.59 (0.97) | 0.59 (0.94) | 0.59 (0.93) | 0.59 (0.95) |
| 5 | 0.59 (0.94) | 0.59 (0.94) | 0.59 (0.95) | 0.59 (0.93) | 0.59 (0.92) | 0.59 (0.94) |
| 6 | 0.59 (0.94) | 0.59 (0.92) | 0.59 (0.94) | 0.59 (0.93) | 0.59 (0.93) | 0.59 (0.94) |
| 7 | 0.58 (0.88) | 0.57 (0.90) | 0.60 (0.90) | 0.60 (0.92) | 0.61 (0.92) | 0.59 (0.92) |
| | **$VE_S = 0.40$** | **$VE_S = 0.80$** | **$VE_S = 0.80$** | **$VE_S = 0.80$** | **$VE_S = 0.80$** | **$VE_S = 0.80$** |
| 1 | 0.4 (0.95) | 0.8 (0.94) | 0.39 (0.95) | 0.8 (0.94) | 0.39 (0.94) | 0.79 (0.92) |
| 2 | 0.42 (0.95) | 0.78 (0.9) | 0.33 (0.91) | 0.75 (0.84) | 0.26 (0.71) | 0.7 (0.46) |
| 3 | 0.38 (0.77) | 0.79 (1) | 0.32 (0.24) | 0.74 (0.99) | 0.24 (0) | 0.68 (0.25) |
| 4 | 0.4 (0.94) | 0.8 (0.95) | 0.4 (0.93) | 0.8 (0.95) | 0.39 (0.95) | 0.79 (0.93) |
| 5 | 0.4 (0.94) | 0.8 (0.95) | 0.4 (0.95) | 0.8 (0.94) | 0.39 (0.93) | 0.79 (0.91) |
| 6 | 0.4 (0.95) | 0.8 (0.95) | 0.4 (0.94) | 0.8 (0.94) | 0.39 (0.93) | 0.79 (0.92) |
| 7 | 0.37 (0.82) | 0.77 (0.96) | 0.40 (0.81) | 0.8 (0.98) | 0.40 (0.80) | 0.8 (1) |
| | **Ebola-Like Parameters** | | **$R_0 = 2.50$** | | **$R_0 = 5.00$** | |
| 1 | 0.59 (0.94) | | 0.59 (0.92) | | 0.58 (0.88) | |
| 2 | 0.57 (0.85) | | 0.3 (0.02) | | 0.13 (0.04) | |
| 3 | 0.45 (0) | | 0.27 (0) | | 0.09 (0.01) | |
| 4 | 0.59 (0.96) | | 0.59 (0.94) | | 0.59 (0.97) | |
| 5 | 0.59 (0.94) | | 0.59 (0.91) | | 0.59 (0.91) | |
| 6 | 0.59 (0.94) | | 0.59 (0.92) | | 0.58 (0.92) | |
| 7 | 0.59 (0.98) | | 0.64 (0.92) | | 0.73 (0.98) | |

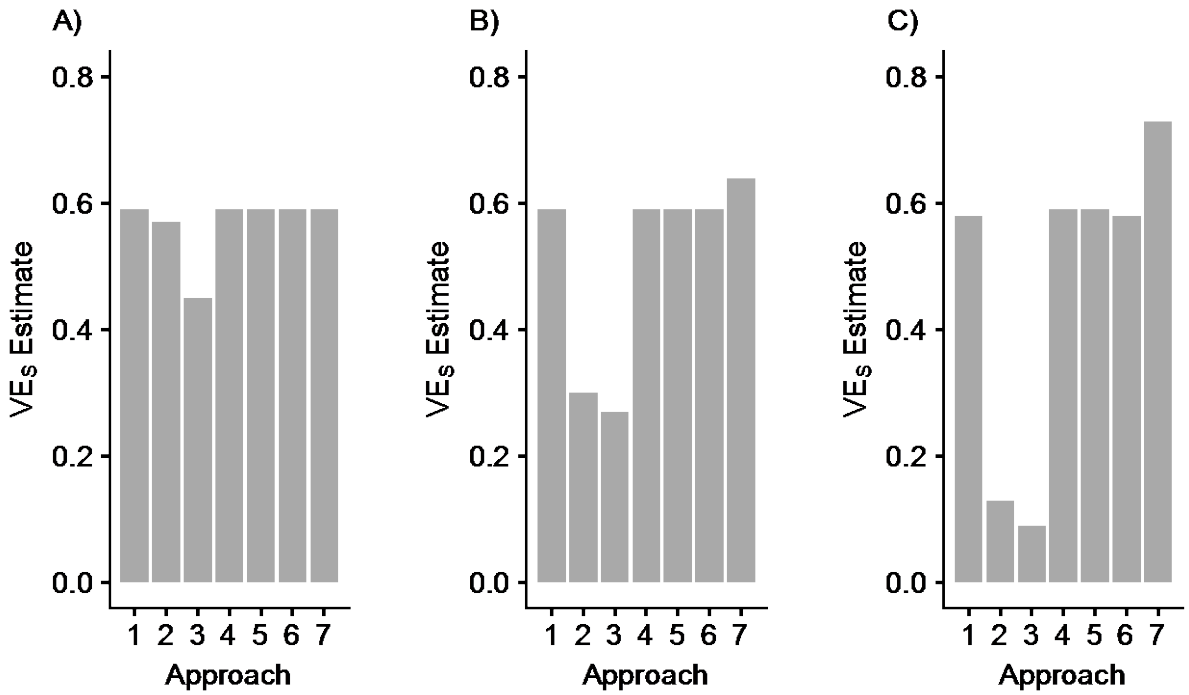
[a] Empirical coverage probabilities are calculated by the proportion of simulations with 95% confidence intervals that cover the true $VE_S$ parameter of the model.

**Web Figure 1.**



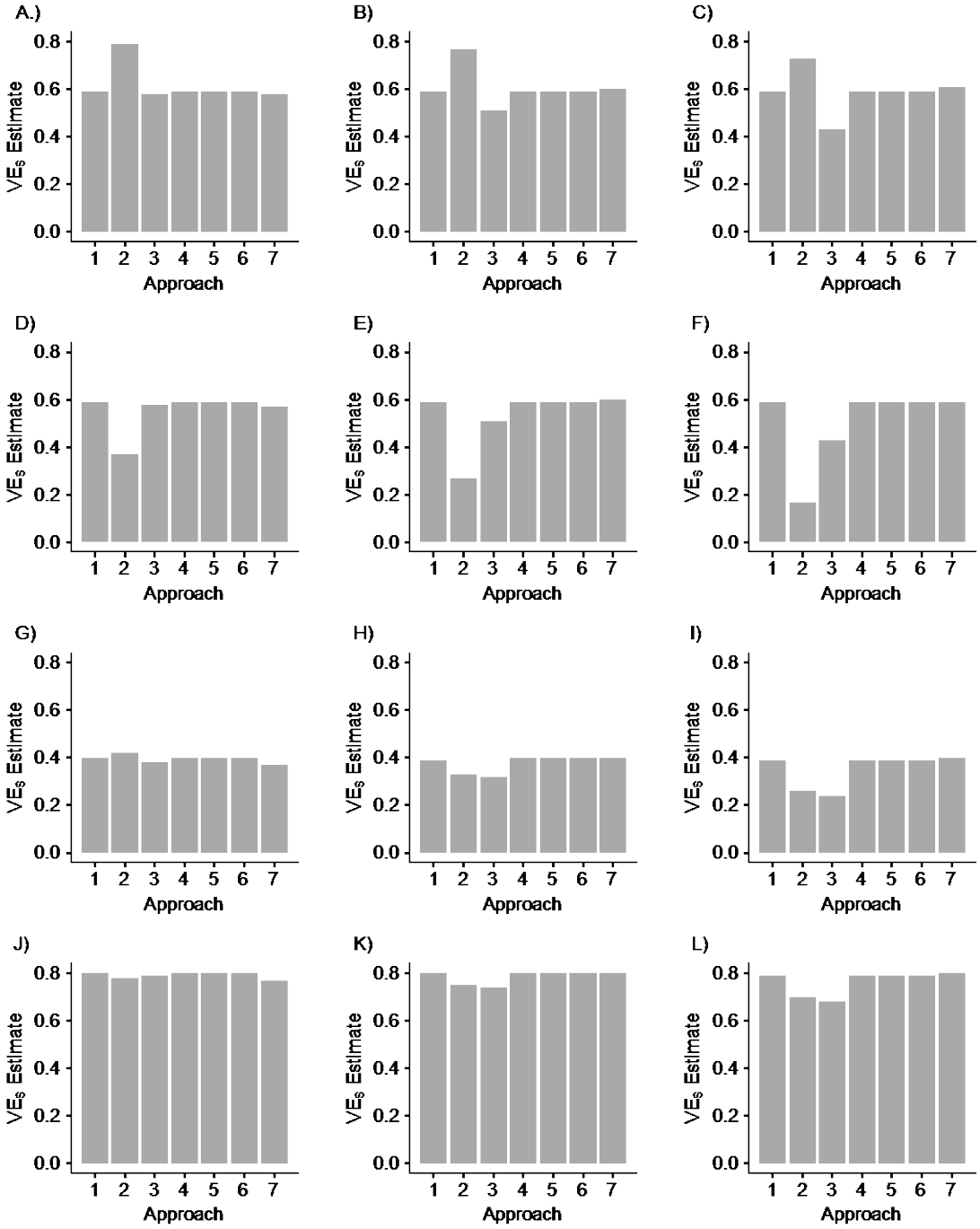

VE$_S$ estimates (200-day trial). The estimates for vaccine efficacy against susceptibility to infection (VE$_S$) using seven different approaches for A) $R_0 = 1$, B) $R_0 = 1.25$, and C) $R_0 = 1.5$ for a 200-day long trial. The seven approaches are: Cox "perfect knowledge" (1), Cox—symptomatic only (2), relative risk estimate (3), corrected relative risk estimate (4), interval-censored Cox model (3 intervals) (5), interval-censored Cox model (1 interval) (6), and imputation (7).

**Web Figure 2.**




VE$_S$ estimates (Ebola-like parameters and higher $R_0$). The estimates for vaccine efficacy against susceptibility to infection (VE$_S$) using seven different approaches, from simulations with A) Ebola-like parameters, B) the baseline parameters with $R_0 = 2.5$, and C) the baseline parameters with $R_0 = 5$. The seven approaches are: Cox "perfect knowledge" (1), Cox—symptomatic only (2), relative risk estimate (3), corrected relative risk estimate (4), interval-censored Cox model (3 intervals) (5), interval-censored Cox model (1 interval) (6), and imputation (7).

**Web Figure 3.**




Varying baseline parameters. The estimates for vaccine efficacy against susceptibility to infection ($VE_S$) using seven different methods when A) $R_0 = 1$, B) $R_0 = 1.25$, and C) $R_0 = 1.5$ and $VE_P = 0.50$, when D) $R_0 = 1$, E) $R_0 = 1.25$, and F) $R_0 = 1$ and $VE_P = -0.50$, when G) $R_0 = 1$, H) $R_0 = 1.25$, and I) $R_0 = 1.5$ and input $VE_S = 0.40$, and when J) $R_0 = 1$, K) $R_0 = 1.25$, and L) $R_0 = 1.5$ and input $VE_S = 0.80$.

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