Supplemental materials for "Estimating the Population Level Impact of a Gonococcal Vaccine Candidate: Predictions from a Simple Mathematical Model"

1 Mathematical model

Our model's state space is defined by infection status (S: susceptible, and I: infected), gender (F: female, M: male), the presence or absence of symptoms among the infected (A: asymptomatic, S: symptomatic), sexual activity level (H: high, L: low), and vaccination status (V: vaccinated, U: unvaccinated). All of these states are dynamic except for gender. These dynamics are discussed below with greater mechanistic details later.

1.1 Behavioral dynamics

We assume stable behavioral dynamics, where a specific proportion of people (ρ) are in the high activity class. People shift from high to low sexual activity at rate π_L and low to high at rate π_H. Assuming steady state dynamics, the rate shifting from low to high activity (π_H) can be written as a function of ρ and π_L as:

$$\pi_H = \frac{\rho}{1-\rho}\pi_L \tag{1}$$

1.2 Infection dynamics

Infection is modeled as an SIS process, where upon infection onset a percent (ϕ) of people are symptomatic and a complementary percent ($1-\phi$) are asymptomatic; these values are sex-specific (ϕ_F and ϕ_M); we also assume that women are less likely to be symptomatic than men such that $\phi_F = \epsilon_\phi\ \phi_M$.

1.2.1 Force of infection

The force of infection (λ) is both sex specific and sexual activity class specific. The sex specific aspects assume that women are less contagious to men per contact than vice versa, and thus the male per act transmission probability (β_M) is modified by a decreased contagiousness factor (ϵ_β) to give the female per act transmission probability (β_F). The force of infection felt by each sex-class category is defined as:

$$\begin{aligned}
\lambda_{MH} &= \kappa_1\beta_F\iota_{FH} + \kappa_2\beta_F\iota_{FL} \\
\lambda_{ML} &= \kappa_3\beta_F\iota_{FH} + \kappa_4\beta_F\iota_{FL} \\
\lambda_{FH} &= \kappa_1\beta_M\iota_{MH} + \kappa_3\beta_M\iota_{ML} \\
\lambda_{FL} &= \kappa_2\beta_M\iota_{MH} + \kappa_4\beta_M\iota_{ML}
\end{aligned} \tag{2}$$

where each ι represents the proportion of people with infection for each sex-class category and where κ_1, κ_2, κ_3, and κ_4 are the contact rates within and between activity classes and are defined based on the average contact rates in the high and low activity classes (κ_{high} and κ_{low}), the size of the high activity class (ρ), and

the proportion of contacts reserved for within class contact (ψ):

$$\begin{aligned}\kappa_1 =& \kappa_{high}\rho\psi \\ \kappa_2 =& \kappa_{high}\rho(1-\psi) \\ \kappa_3 =& \kappa_{low}(1-\rho)(1-\psi) \\ \kappa_4 =& \kappa_{low}(1-\rho)\psi\end{aligned} \tag{3}$$

The between-class contact must be balanced (i.e., κ_2 must equal κ_3). We achieve this by setting whichever contact rate is higher, equal to the smaller one, and then adjusting either κ_1 or κ_4 accordingly:

$$if \kappa_2 > \kappa_3, then \begin{cases} \kappa_2 = \kappa_3 \\ \kappa_1 = \kappa_{high}\rho - \kappa_2 \end{cases}$$

$$if \kappa_3 > \kappa_2, then \begin{cases} \kappa_3 = \kappa_2 \\ \kappa_4 = \kappa_{low}(1-\rho)\psi - \kappa_3 \end{cases}$$

1.2.2 Recovery

Recovery occurs based on three mechanisms: natural clearance (γ_i), background screening (γ_b), and symptomatic treatment seeking (γ_t); these recovery rates all have sex-specific variants, indicated by each subscript's final letter. Natural clearance and background screening occurs regardless of symptoms, while symptomatic treatment seeking only occurs among the symptomatic.

1.3 Population dynamics

We assume a constant population size, where people who exit the model are balanced by people entering the model. This is governed by the rate of exit (μ).

1.4 Vaccine modeling

We model a vaccine that provides only protection against infection acquisition. We define vaccine candidates based on their duration of protection ($\frac{1}{\delta}$) and vaccine efficacy (λ_v). We assume vaccination occurs just prior to sexual debut. The model is initiated with a given percent of people (σ) vaccinated; similarly, at entry into the model, we assume that σ% of newly sexually active people are vaccinated. Vaccine protection wanes at the rate δ. While σ might represent the initial coverage of the vaccine, the actual proportion with protection is lower, since the duration of protection is shorter than the expected sexual life-span ($\frac{1}{\mu}$).

1.5 Vaccine administration

We estimate vaccine impact at two levels of initial vaccine coverage (σ): 20% (low coverage) and 50% (high coverage).

1.5.1 Vaccine candidates

Our primary analysis assumes a vaccine candidate with vaccine efficacy λ_v=0.3 and duration of protection $\frac{1}{\delta}$=2 years. Specific sub-analyses compare vaccine candidates wither three levels of vaccine efficacy (0.3, 0.5, or 0.7) and three levels of duration of protection (2, 5, or 8 years)

1.6 Analytic procedures

For each vaccine candidate and each level of vaccine administration, we model the 10 year percent reduction in prevalence in 10,000 different model contexts. These model contexts all have the same baseline prevalence, but differ in terms of the model parameters that generated them (see supplemental table 1). Our primary analysis assumes a low baseline prevalence (1.125% in females and 0.75% in males) Sensitivity analyses

consider a different set of 10,000 model contexts that were fit assuming a higher baseline prevalence (2.25% in females and 1.5% in males). Both low and high contexts were fit assuming the same bounds presented in Supplemental Table 1.

1.7 Full model equations, with vaccination

$$
\begin{aligned}
dS_{MHV} =& -\mu S_{MHV} + (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSHV} + (\gamma_{bM} + \gamma_{iM}) I_{MAHV} - (1-\lambda_V)\lambda_{MH} S_{MHV} + \pi_H S_{MLV} \\
& - \pi_L S_{MHV} - \delta S_{MHV} + \rho\sigma\frac{\mu}{2} \\
dS_{MHU} =& -\mu S_{MHU} + (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSHU} + (\gamma_{bM} + \gamma_{iM}) I_{MAHU} - \lambda_{MH} S_{MHU} + \pi_H S_{MLU} \\
& - \pi_L S_{MHU} + \delta S_{MHV} + \rho(1-\sigma)\frac{\mu}{2} \\
dS_{MLV} =& -\mu S_{MLV} + (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSLV} + (\gamma_{bM} + \gamma_{iM}) I_{MALV} - (1-\lambda_V)\lambda_{ML} S_{MLV} - \pi_H S_{MLV} \\
& + \pi_L S_{MHV} - \delta S_{MLV} + (1-\rho)\sigma\frac{\mu}{2} \\
dS_{MLU} =& -\mu S_{MLU} + (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSLU} + (\gamma_{bM} + \gamma_{iM}) I_{MALU} - \lambda_{ML} S_{MLU} - \pi_H S_{MLU} \\
& + \pi_L S_{MHU} + \delta S_{MLV} + (1-\rho)(1-\sigma)\frac{\mu}{2} \\
dI_{MAHV} =& -\mu I_{MAHV} - (\gamma_{bM} + \gamma_{iM}) I_{MAHV} + (1-\lambda_V)\lambda_{MH} S_{MHV}(1-\phi_M) + \pi_H I_{MALV} - \pi_L I_{MAHV} - \delta I_{MAHV} \\
dI_{MAHU} =& -\mu I_{MAHU} - (\gamma_{bM} + \gamma_{iM}) I_{MAHU} + \lambda_{MH} S_{MHU}(1-\phi_M) + \pi_H I_{MALU} - \pi_L I_{MAHU} + \delta I_{MAHV} \\
dI_{MALV} =& -\mu I_{MALV} - (\gamma_{bM} + \gamma_{iM}) I_{MALV} + (1-\lambda_V)\lambda_{ML} S_{MLV}(1-\phi_M) - \pi_H I_{MALV} + \pi_L I_{MAHV} - \delta I_{MALV} \\
dI_{MALU} =& -\mu I_{MALU} - (\gamma_{bM} + \gamma_{iM}) I_{MALU} + \lambda_{ML} S_{MLU}(1-\phi_M) - \pi_H I_{MALU} + \pi_L I_{MAHU} + \delta I_{MALV} \\
dI_{MSHV} =& -\mu I_{MSHV} - (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSHV} + (1-\lambda_V)\lambda_{MH} S_{MHV}\phi_M + \pi_H I_{MSLV} - \pi_L I_{MSHV} - \delta I_{MSHV} \\
dI_{MSHU} =& -\mu I_{MSHU} - (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSHU} + \lambda_{MH} S_{MHU}\phi_M + \pi_H I_{MSLU} - \pi_L I_{MSHU} + \delta I_{MSHV} \\
dI_{MSLV} =& -\mu I_{MSLV} - (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSLV} + (1-\lambda_V)\lambda_{ML} S_{MLV}\phi_M - \pi_H I_{MSLV} + \pi_L I_{MSHV} - \delta I_{MSLV} \\
dI_{MSLU} =& -\mu I_{MSLU} - (\gamma_t + \gamma_{bM} + \gamma_{iM}) I_{MSLU} + \lambda_{ML} S_{MLU}\phi_M - \pi_H I_{MSLU} + \pi_L I_{MSHU} + \delta I_{MSLV} \\
dS_{FHV} =& -\mu S_{FHV} + (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSHV} + (\gamma_{bF} + \gamma_{iF}) I_{FAHV} - (1-\lambda_V)\lambda_{FH} S_{FHV} + \pi_H S_{FLV} \\
& - \pi_L S_{FHV} - \delta S_{FHV} + \rho\sigma\frac{\mu}{2} \\
dS_{FHU} =& -\mu S_{FHU} + (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSHU} + (\gamma_{bF} + \gamma_{iF}) I_{FAHU} - \lambda_{FH} S_{FHU} + \pi_H S_{FLU} \\
& - \pi_L S_{FHU} + \delta S_{FHV} + \rho(1-\sigma)\frac{\mu}{2} \\
dS_{FLV} =& -\mu S_{FLV} + (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSLV} + (\gamma_{bF} + \gamma_{iF}) I_{FALV} - (1-\lambda_V)\lambda_{FL} S_{FLV} - \pi_H S_{FLV} \\
& + \pi_L S_{FHV} - \delta S_{FLV} + (1-\rho)\sigma\frac{\mu}{2} \\
dS_{FLU} =& -\mu S_{FLU} + \gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSLU} + (\gamma_{bF} + \gamma_{iF}) I_{FALU} - \lambda_{FL} S_{FLU} - \pi_H S_{FLU} \\
& + \pi_L S_{FHU} + \delta S_{FLV} + (1-\rho)(1-\sigma)\frac{\mu}{2} \\
dI_{FAHV} =& -\mu I_{FAHV} - (\gamma_{bF} + \gamma_{iF}) I_{FAHV} + (1-\lambda_V)\lambda_{FH} S_{FHV}(1-\phi_F) + \pi_H I_{FALV} - \pi_L I_{FAHV} - \delta I_{FAHV} \\
dI_{FAHU} =& -\mu I_{FAHU} - (\gamma_{bF} + \gamma_{iF}) I_{FAHU} + \lambda_{FH} S_{FHU}(1-\phi_F) + \pi_H I_{FALU} - \pi_L I_{FAHU} + \delta I_{FAHV} \\
dI_{FALV} =& -\mu I_{FALV} - (\gamma_{bF} + \gamma_{iF}) I_{FALV} + (1-\lambda_V)\lambda_{FL} S_{FLV}(1-\phi_F) - \pi_H I_{FALV} + \pi_L I_{FAHV} - \delta I_{FALV} \\
dI_{FALU} =& -\mu I_{FALU} - (\gamma_{bF} + \gamma_{iF}) I_{FALU} + \lambda_{FL} S_{FLU}(1-\phi_F) - \pi_H I_{FALU} + \pi_L I_{FAHU} + \delta I_{FALV} \\
dI_{FSHV} =& -\mu I_{FSHV} - (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSHV} + (1-\lambda_V)\lambda_{FH} S_{FHV}\phi_F + \pi_H I_{FSLV} - \pi_L I_{FSHV} - \delta I_{FSHV} \\
dI_{FSHU} =& -\mu I_{FSHU} - (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSHU} + \lambda_{FH} S_{FHU}\phi_F + \pi_H I_{FSLU} - \pi_L I_{FSHU} + \delta I_{FSHV} \\
dI_{FSLV} =& -\mu I_{FSLV} - (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSLV} + (1-\lambda_V)\lambda_{FL} S_{FLV}\phi_F - \pi_H I_{FSLV} + \pi_L I_{FSHV} - \delta I_{FSLV} \\
dI_{FSLU} =& -\mu I_{FSLU} - (\gamma_t + \gamma_{bF} + \gamma_{iF}) I_{FSLU} + \lambda_{FL} S_{FLU}\phi_F - \pi_H I_{FSLU} + \pi_L I_{FSHU} + \delta I_{FSLV}
\end{aligned}
\tag{4}
$$

Symbol	Description (unit)	Bounds	Posterior (low)	Posterior (high)
β_M	Per act transmission probability, male-to-female	0.7*		
ϵ_β	Contagiousness of women compared to men	(0.5, 0.75)	(0.51, 0.67)	(0.51, 0.69)
β_F	Per act transmission probability, female-to-male	$\epsilon_\beta \beta_M$ †		
κ_{low}	Low activity class contact rate	(0.3, 3)	(2.72, 2.99)	(2.81, 2.99)
ϵ_κ	Proportionate increase in contact rate in the high activity class compared to the low	(10, 100)	(91.2, 99.5)	(93.9, 99.7)
κ_{high}	High activity class contact rate	$\epsilon_\kappa\ \kappa_{low}$ †		
ρ	High activity proportion	(0.05, 0.15)	(0.13, 0.15)	(0.14, 0.15)
π_L	Rate of shifting from high to low activity	0.2*		
π_H	Rate of shifting from low to high activity	$\frac{\rho}{1-\rho}\ \pi_L$ †		
μ	Population dynamics	0.1*		
ψ	Proportion of contacts reserved for within class sexual contact	(0, 1)	(0.22, 0.96)	(0.15, 0.94)
ϕ_M	Proportion of new male infections that are symptomatic	(0.3, 0.9)	(0.8, 0.9)	(0.8, 0.9)
ϵ_ϕ	Chance of symptoms in women compared to men	(0.1, 0.5)	(0.1, 0.4)	(0.1, 0.3)
ϕ_F	Proportion of new female infections that are symptomatic	$\epsilon_\phi\ \phi_M$ †		
γ_{bF}	Background screening rate, females	(0.1, 0.3)	(0.12, 0.28)	(0.12, 0.28)
ϵ_{γ_b}	Proportionate decreased background screening rate in men compared to women	(0.25, 0.75)	(0.26, 0.70)	(0.25, 0.71)
γ_{bM}	Background screening rate, males	$\epsilon_{bF}\ \gamma_{bF}$ †		
γ_{iM}	Natural clearance rate, males	(3.65, 6.08) (60-100d)	(5.42, 6.06)	(5.59, 6.06)
ϵ_{γ_i}	Natural clearance rate in women compared to men	(0.17, 0.67)	(0.17, 0.18)	(0.17, 0.18)
γ_{iF}	Natural clearance rate, females	$\epsilon_{\gamma_i}\ \gamma_{iM}$ †		
γ_t	Symptomatic treatment rate, males and females	(14.4, 43.2)	(19.6, 40.9)	(19.6, 40.9)

Table 1: Model parameters, descriptions, and bounds. *Unvaried parameter. †Composite parameters do not have bounds and take values based on the illustrated formulations. Posterior distributions reflect the first and third quartiles of either the low or high baseline prevalence model fitting parameter sets.

	Low coverage (20%)								High coverage (50%)							
Efficacy (%)	30	30	50	50	50	70	70	70	30	30	50	50	50	70	70	70
Protection Duration (y)	5	8	2	5	8	2	5	8	5	8	2	5	8	2	5	8
ϵ_β	-0.006	-0.004	-0.007	-0.008	-0.004	-0.009	-0.006	0.005	-0.005	0.008	-0.012	0.035	0.071	-0.002	0.093	0.141
ϕ_M	-0.004	0.002	-0.006	-0.010	0.002	-0.012	-0.007	0.030	-0.001	0.043	-0.024	0.138	0.255	0.016	0.330	0.537
ϵ_ϕ	0.044	0.047	0.043	0.043	0.049	0.041	0.047	0.062	0.049	0.068	0.042	0.113	0.162	0.067	0.204	0.287
γ_t	0.063	0.062	0065	0.070	0.063	0.070	0.068	0.046	0.064	0.037	0.074	-0.036	-0.116	0.034	-0.190	-0.353
ρ	0.306	0.309	0.305	0.310	0.315	0.305	0.315	0.322	0.317	0.324	0.309	0.327	0.325	0.313	0.315	0.267
κ_{low}	-0.074	-0.074	-0.074	-0.076	-0.075	-0.075	-0.077	-0.073	-0.077	-0.072	-0.081	-0.067	-0.056	-0.084	-0.057	-0.032
ϵ_κ	-0.020	-0.102	-0.102	-0.104	-0.104	-0.103	-0.106	-0.010	-0.106	-0.097	-0.109	-0.079	-0.056	-0.108	-0.051	-0.011
ψ	-0.907	-0.907	-0.907	-0.905	-0.904	-0.906	-0.903	-0.902	-0.904	-0.901	-0.903	-0.881	-0.829	-0.901	-0.759	-0.471
γ_{b_F}	-0.009	-0.008	-0.009	-0.010	-0.008	-0.010	-0.009	-0.004	-0.008	-0.002	-0.010	0.011	0.023	-0.003	0.033	0.058
ϵ_{γ_b}	-0.016	-0.015	-0.016	-0.016	-0.015	-0.016	-0.016	-0.013	-0.016	-0.012	-0.017	-0.002	0.008	-0.012	0.016	0.032
γ_{iM}	0.073	0.072	0.073	0.075	0.072	0.075	-0.073	0.063	0.071	0.059	0.073	0.019	-0.017	0.042	-0.070	-0.157
ϵ_{γ_i}	-0.063	-0.066	-0.062	-0.059	-0.066	-0.058	-0.061	-0.083	-0.064	-0.091	-0.053	-0.152	-0.218	-0.084	-0.267	-0.360

Table 2: Correlation between each fitted parameter and vaccine impact across vaccine candidates defined by vaccine efficacy and vaccine duration of protection. Low prevalence at baseline is assumed. Parameter descriptions available in Table 1.

2 Supplemental Results

2.1 Additional low prevalence baseline results

Our primary results assumed a baseline prevalence of of 1.125% in females and 0.75% in males. Table 2 illustrates how context in terms of parameter uncertainty affects vaccine impact across vaccine candidates defined by duration of protection and vaccine efficacy against infection acquisition.

2.2 High prevalence baseline results

As a sensitivity analysis, we reproduced all analyses assuming a higher baseline prevalence of 2.25% in females and 1.5% in males. First we illustrate the primary vaccine impact results across nine vaccine candidates (Figure 1). Second, we summarize the median relative improvements in vaccine impact given improvements in a vaccine candidate's duration of protection or vaccine efficacy, compared to a vaccine with only 2 years duration of protection and 30% efficacy (Figure 2). Finally, we show how context affects vaccine impact by showing the correlation between each varied parameter and vaccine impact for all nine vaccine candidates (Table 3).

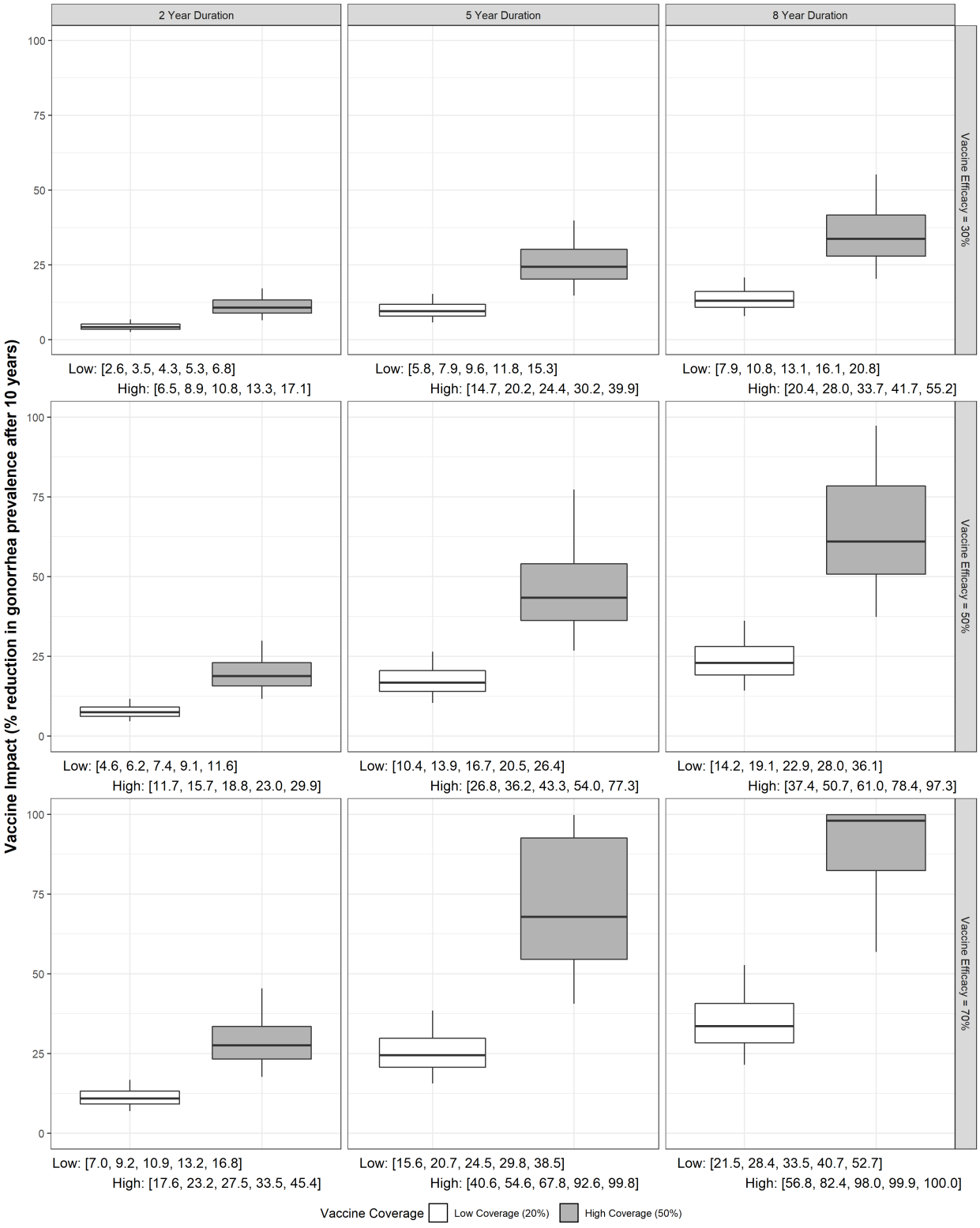

Figure 1: Distributions of predicted impact for a vaccine impact among low and high coverage levels when the baseline gonorrhea prevalence was 2.25% in females and 1.5% in males. Minimum, 25th percentile, median, 75th percentile, and maximum predicted impact values are listed below each panel for each coverage level.

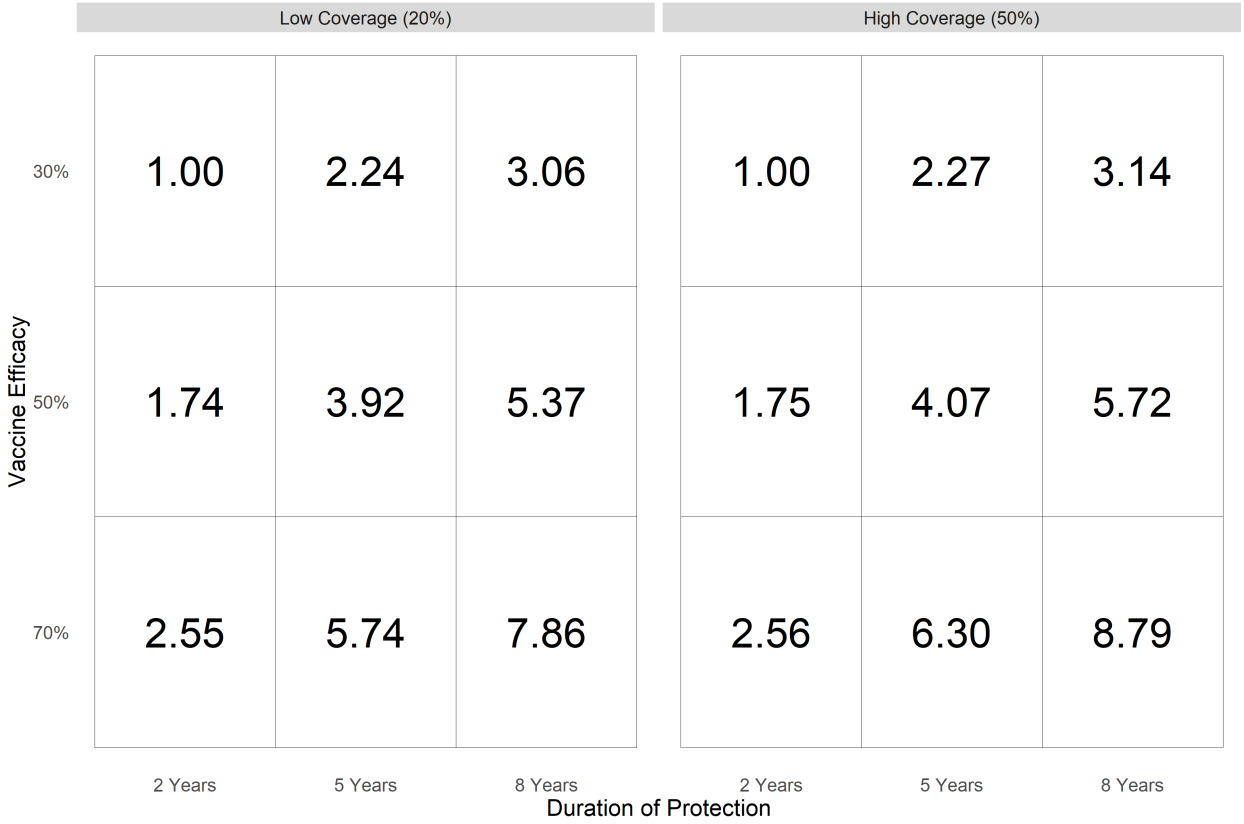

Figure 2: Median increased vaccine impact of improved vaccines compared to a vaccine with 30% efficacy and 2-year duration assuming either low (20%) or high (50%) coverage and assuming a high baseline NG prevalence (2.25% in females and 1.5% in males). "Increased vaccine impact" is calculated as the ratio of the reduction in prevalence in the improved vaccine compared to the reduction in prevalence of the vaccine with 30% efficacy and 2-year duration of protection.

	Low coverage (20%)									High coverage (50%)								
Efficacy (%)	30	30	30	50	50	50	70	70	70	30	30	30	50	50	50	70	70	70
Protection Duration (y)	2	5	8	2	5	8	2	5	8	2	5	8	2	5	8	2	5	8
ϵ_β	0.018	0.017	0.018	0.018	0.017	0.017	0.018	0.016	0.016	0.018	0.016	0.016	0.017	0.016	0.015	0.015	0.020	0.043
ϕ_M	-0.003	-0.035	-0.034	-0.032	-0.036	-0.034	-0.032	-0.038	-0.036	-0.003	-0.038	-0.036	-0.034	-0.049	-0.037	-0.039	-0.018	0.065
ϵ_ϕ	0.096	0.096	0.097	0.097	0.096	0.097	0.097	0.096	0.097	0.097	0.097	0.098	0.097	0.095	0.101	0.096	0.110	0.137
γ_t	0.017	0.010	0.018	0.017	0.021	0.021	0.018	0.024	0.024	0.018	0.024	0.024	0.020	0.035	0.028	0.025	0.012	-0.043
ρ	0.075	0.078	0.079	0.077	0.080	0.083	0.078	0.082	0.086	0.078	0.083	0.088	0.081	0.089	0.010	0.083	0.105	0.122
κ_{low}	-0.067	-0.067	-0.067	-0.067	-0.068	-0.068	-0.067	-0.069	-0.069	-0.067	-0.069	-0.070	-0.068	-0.074	-0.073	-0.070	-0.072	-0.058
ϵ_κ	-0.123	-0.123	-0.123	-0.123	-0.123	-0.123	-0.123	-0.124	-0.123	-0.123	-0.124	-0.123	-0.123	-0.124	-0.125	-0.124	-0.124	-0.104
ψ	-0.963	-0.962	-0.962	-0.963	-0.962	-0.961	-0.962	-0.961	-0.960	-0.962	-0.961	-0.960	0.962	-0.958	-0.957	-0.960	-0.956	-0.945
γ_{b_F}	0.034	0.034	0.034	0.034	0.034	0.034	0.034	0.033	0.034	0.034	0.033	0.036	0.034	0.032	0.034	0.033	0.037	0.047
ϵ_{γ_b}	-0.007	-0.008	-0.007	-0.007	-0.008	-0.008	-0.005	-0.008	-0.008	-0.008	-0.008	-0.008	-0.008	-0.009	-0.007	-0.008	-0.004	-0.003
γ_{iM}	0.088	0.089	0.089	0.088	0.089	0.090	0.088	0.090	0.091	0.088	0.090	0.091	0.089	0.093	0.092	0.090	0.084	0.076
ϵ_{γ_i}	-0.052	-0.051	-0.052	-0.052	-0.051	-0.052	-0.052	-0.050	-0.051	-0.052	-0.050	-0.051	-0.051	-0.046	-0.051	-0.050	-0.060	-0.091

Table 3: Correlation between each fitted parameter and vaccine impact across vaccine candidates defined by vaccine efficacy and vaccine duration of protection. High prevalence at baseline is assumed. Parameter descriptions available in Table 1.