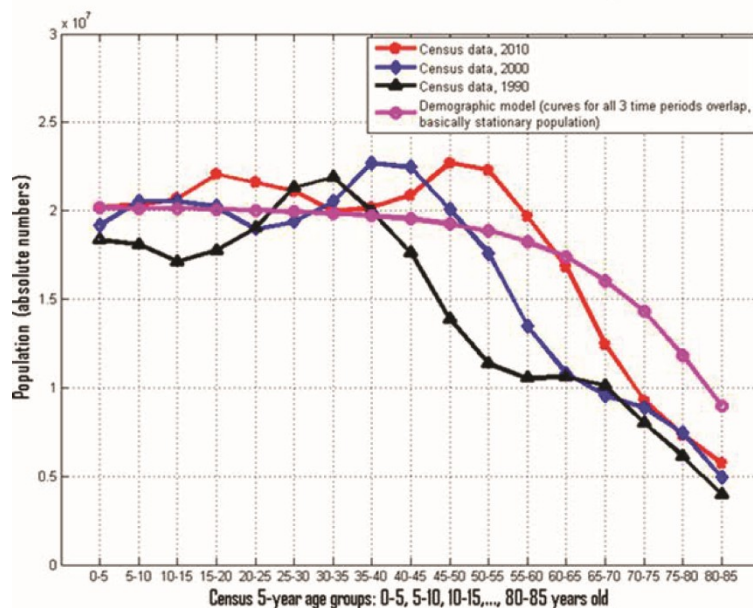


## Appendix 1.

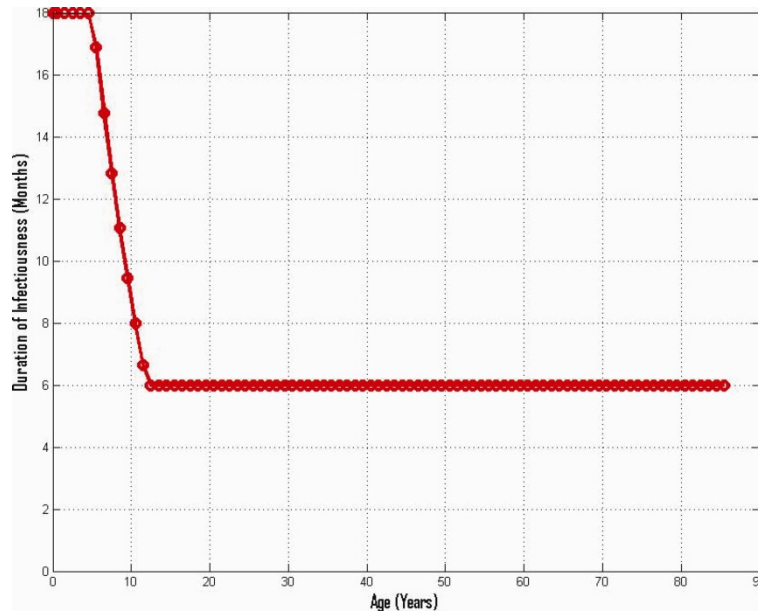
### Illustration of best-fit model underlying quantities



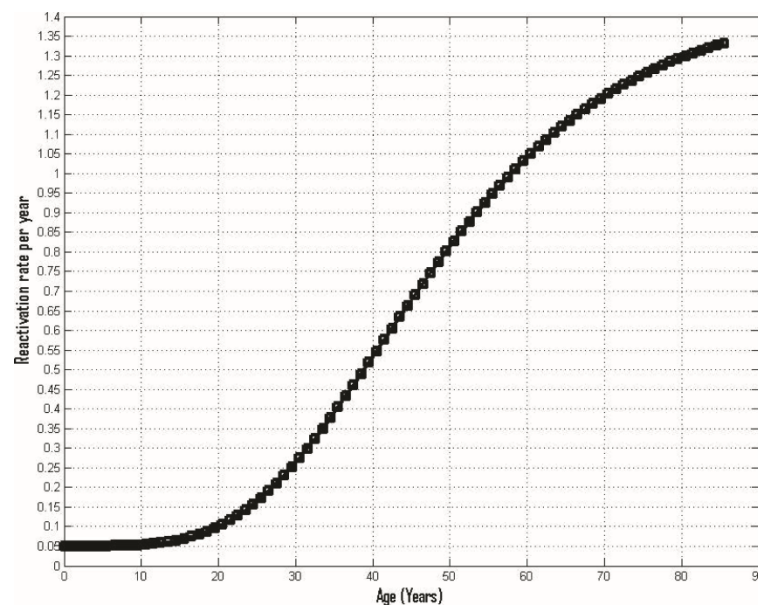
**Figure A1.** Illustration of the age-stratified population corresponding to the underlying demographic model with stable age distribution for the US population fitted against official US Census data

Model-estimated growth rate, based on a Lotka-McKendrick equation.<sup>49</sup> Corresponding number of births for the stable age distribution here is  $4.058 \times 10^6$  per year.

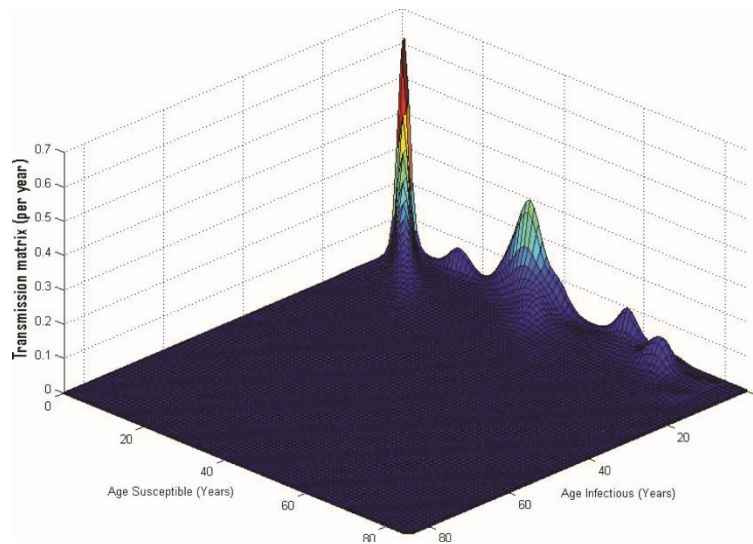
The age-dependent average duration of infectiousness, reactivation rate, and transmission matrix corresponding to the best-fit model here are illustrated in Figures A2, A3, and A4, respectively, for completeness.



**Figure A2.** Model-estimated age-specific average duration of infectiousness in months corresponding to best model-data fit in Figure 1 panel a



**Figure A3.** Model-estimated age-specific reactivation rate ( $\text{year}^{-1}$ ) corresponding to best model-data fit in Figure 1 panel a



**Figure A4.** Model-estimated transmission matrix ( $\text{year}^{-1}$ ) corresponding to best model-data fit in Figure 1 panel a

The main transmitters here are represented by the very young age groups (0–2 years of age). The shape of the full matrix across all age groups is difficult to visualize properly, due to large relative differences in values, but some diagonal transmission patterns can still be observed, more obvious up to the age of 20–30 years, reflecting the underlying social mixing employed as support for transmission.

## Appendix 2

### Illustration of mathematical modelling framework: a base-case

#### Notations:

$a$	Age
$t$	Time
$A$	Life span

#### Unvaccinated:

$s = s(a, t)$	Proportion of susceptible unvaccinated individuals of age $a$ at time $t$
$p = p(a, t)$	Proportion of primarily infected unvaccinated individuals of age $a$ at time $t$
$l = l(a, t)$	Proportion of latently infected unvaccinated individuals of age $a$ at time $t$
$r_{end} = r_{end}(a, t)$	Proportion of reactivated (endogenously) unvaccinated individuals of age $a$ at time $t$
$r_{ex} = r_{ex}(a, t)$	Proportion of re-infected (exogenously) unvaccinated individuals of age $a$ at time $t$
$r_{both} = r_{both}(a, t)$	Proportion of reactivated and re-infected unvaccinated individuals of age $a$ at time $t$

#### Vaccinated:

$s_v = s_v(a, t)$	Proportion of susceptible vaccinated individuals of age $a$ at time $t$
$p_v = p_v(a, t)$	Proportion of primarily infected vaccinated individuals of age $a$ at time $t$
$l_v = l_v(a, t)$	Proportion of latently infected vaccinated individuals of age $a$ at time $t$
$r_{v\_end} = r_{v\_end}(a, t)$	Proportion of reactivated (endogenously ) vaccinated individuals of age $a$ at time $t$
$r_{v\_ex} = r_{v\_ex}(a, t)$	Proportion of re-infected (exogenously) vaccinated individuals of age $a$ at time $t$
$r_{v\_both} = r_{v\_both}(a, t)$	Proportion of reactivated and re-infected vaccinated individuals of age $a$ at time $t$
$v_c^-$	Vaccination rate for seronegative individuals
$v_c^+$	Vaccination rate for seropositive individuals
$w_v$	Vaccine protection waning rate
$v_e$	Vaccine efficacy against infection
$\beta(a, a) = q(a, a)c(a, a)$	Transmission rate between people of age $a$ and $\tilde{a}$
$c(a, a)$	Rate at which an individual of age $\tilde{a}$ makes contact with an individual of age $a$ (from the POLYMOD contact data)
$q = q(a, a)$	Proportionality factor, related to likelihood of a susceptible of age $a$ to get infected with via an adequate contact with an infectious of age $\tilde{a}$ , $q a, a = (q_1 + q_2 a)e^{-q_3 a}$

The rest of the model parameters involved and related descriptions are outlined in the accompanying table below Figure 7 in the main text.

**Model governing equations:**

$$\frac{\partial}{\partial t} + \frac{\partial}{\partial a} = -\lambda(a,t)s - \nu_c^-(a,t)s + w_v(a,t)s_v$$

$$\frac{\partial \Phi}{\partial t} + \frac{\partial \Phi}{\partial a} = \lambda(a,t)s - \alpha(a)p$$

$$\frac{\partial \bar{l}}{\partial t} + \frac{\partial \bar{l}}{\partial a} = \alpha(a)p - \gamma(a)l - (1-k)\lambda(a,t)l + \alpha(a)r_{ex} + \alpha(a)r_{end} - \nu_c^+(a,t)l + w_v(a,t)l_v$$

$$\frac{\partial r_{end}}{\partial t} + \frac{\partial r_{end}}{\partial a} = \gamma(a)l - \alpha(a)r_{end} + \alpha(a)r_{both} - (1-k)\lambda(a,t)r_{end}$$

$$\frac{\partial r_{ex}}{\partial t} + \frac{\partial r_{ex}}{\partial a} = (1-k)\lambda(a,t)l - \alpha(a)r_{ex} + \alpha(a)r_{both} - \gamma(a)r_{ex}$$

$$\frac{\partial r_{both}}{\partial t} + \frac{\partial r_{both}}{\partial a} = (1-k)\lambda(a,t)r_{end} + \gamma(a)r_{ex} - \alpha(a)r_{both} - \alpha(a)r_{both}$$

$$\frac{\partial}{\partial t} + \frac{\partial}{\partial a} = \nu_c^-(a,t)s - (1-\nu_e)\lambda(a,t)s_v - w_v(a,t)s_v$$

$$\frac{\partial \Phi_v}{\partial t} + \frac{\partial \Phi_v}{\partial a} = (1-\nu_e)\lambda(a,t)s_v - \alpha(a)p_v$$

$$\frac{\partial \bar{l}_v}{\partial t} + \frac{\partial \bar{l}_v}{\partial a} = \nu_c^+(a,t)l_v + \alpha(a)p_v - \gamma(a)l_v - (1-\nu_e)(1-k)\lambda(a,t)l_v + \alpha(a)r_{v\_ex} + \alpha(a)r_{v\_end} - w_v(a,t)l_v$$

$$\frac{\partial r_{v\_end}}{\partial t} + \frac{\partial r_{v\_end}}{\partial a} = \gamma(a)l_v - \alpha(a)r_{v\_end} + \alpha(a)r_{v\_both} - (1-\nu_e)(1-k)\lambda(a,t)r_{v\_end}$$

$$\frac{\partial r_{v\_ex}}{\partial t} + \frac{\partial r_{v\_ex}}{\partial a} = (1-\nu_e)(1-k)\lambda(a,t)l_v - \alpha(a)r_{v\_ex} + \alpha(a)r_{v\_both} - \gamma(a)r_{v\_ex}$$

$$\frac{\partial r_{v\_both}}{\partial t} + \frac{\partial r_{v\_both}}{\partial a} = (1-\nu_e)(1-k)\lambda(a,t)r_{v\_end} + \gamma(a)r_{v\_ex} - \alpha(a)r_{v\_both} - \alpha(a)r_{v\_both}$$

$$\lambda(a,t) = \int_0^A \beta(a,\bar{a})(p(\bar{a},t) + r_{ex}(\bar{a},t) + r_{end}(\bar{a},t) + r_{both}(\bar{a},t) + p_v(\bar{a},t) + r_{v\_ex}(\bar{a},t) + r_{v\_end}(\bar{a},t) + r_{v\_both}(\bar{a},t))\bar{a}d\bar{a}$$

These equations are properly duplicated to reflect explicit gender stratification with a 1:1 female:male ratio solely for the purpose of further enabling proper simulation of the impact of female vaccination only. No other explicit (e.g. sexual) mixing patterns between males and females are considered besides the empirical social mixing pattern that applies to the whole population, irrespective of gender.

Appropriate boundary conditions at  $a=0$  reflect the assumptions that all newborns are susceptible, except for the small fraction with congenital primary infection, completing the mathematical formulation.

The underlying demographic model is consistently governed by a Lotka-McKendrick equation, where we assume a population with stable age distribution and a 1:1 female:male ratio,<sup>49</sup> with corresponding age-specific pregnancy/fertility rates and death rates based on

public US official government data.<sup>32,52</sup> The model-based population growth rate over time is estimated by fitting the resulting demographic model age distribution against longitudinal US Census age-specific demographic data from years 1990, 2000 and 2010 (Figure A1).