Supplementary Methods

Analytical outbreak risk derivation

We consider the generalised renewal equation transmission model outlined in the Methods section of the main text, and define the following additional quantities:

- $g(\alpha)$ is the probability density function of the distribution of possible individual infectiousness factors. For generality, we initially derive an equation satisfied by the outbreak risk for an arbitrary distribution (with mean value one), before considering a gamma distribution with shape (dispersion) parameter k as assumed in the main text.
- $q_{t,\tau}(\alpha)$ is the extinction probability (one minus the outbreak risk) if a single infected individual with infectiousness factor α, who was infected on calendar day t, is introduced into the population at (the start of) day since infection τ (i.e., on calendar day $(t+\tau)$), assuming there are no other infected individuals at the time of introduction (and no further external pathogen introductions into the population).
- $q_t = \int_0^\infty q_{t,1}(\alpha) g(\alpha) \mathrm{d}\alpha$ is the overall extinction probability (averaged over the distribution of possible infectiousness factors) following the introduction one day post infection (note that we assume transmission cannot occur on the day of infection, i.e., $w_0 = 0$) of an individual infected on day t. The outbreak risk is then $p_t = 1 - q_t$.

To derive an expression for $q_{t,\tau}(\alpha)$ (and therefore q_t), we condition on the number of transmissions generated by the first infected individual on the day of introduction, which follows a Poisson distribution with mean $\alpha R_{t+\tau} w_\tau$, to obtain

$$q_{t,\tau}(\alpha) = \sum_{j=0}^{\infty} \frac{(\alpha R_{t+\tau} w_\tau)^j e^{-\alpha R_{t+\tau} w_\tau}}{j!} q_{t,\tau+1}(\alpha) q_{t+\tau}^j . \qquad \text{(S1)}$$

Here, $q_{t,\tau+1}(\alpha) q_{t+\tau}^j$ gives the extinction probability conditional on j transmissions occurring (since infection lineages are assumed to be independent). This sum can be evaluated as

$$\begin{aligned} q_{t,\tau}(\alpha) &= q_{t,\tau+1}(\alpha) e^{-\alpha R_{t+\tau} w_\tau} \sum_{j=0}^{\infty} \frac{(\alpha R_{t+\tau} w_\tau q_{t+\tau})^j}{j!} \\ &= q_{t,\tau+1}(\alpha) e^{-\alpha R_{t+\tau} w_\tau (1-q_{t+\tau})}. \qquad \text{(S2)} \end{aligned}$$

Therefore, assuming $q_{t,\infty}(\alpha) = 1$, we have

$$\begin{aligned} q_{t,1}(\alpha) &= q_{t,2}(\alpha) e^{-\alpha R_{t+1} w_1 (1-q_{t+1})} \\ &= \cdots = q_{t,\infty}(\alpha) \prod_{\tau=1}^{\infty} e^{-\alpha R_{t+\tau} w_\tau (1-q_{t+\tau})} \\ &= \exp\left(-\alpha \sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau (1-q_{t+\tau})\right). \qquad \text{(S3)} \end{aligned}$$

Finally, we have

$$q_t = \int_0^\infty q_{t,1}(\alpha) g(\alpha) \mathrm{d}\alpha = \int_0^\infty \exp\left(-\alpha \sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau (1-q_{t+\tau})\right) g(\alpha) \mathrm{d}\alpha . \qquad \text{(S4)}$$

Therefore, the outbreak risk, $p_t = 1 - q_t$, satisfies

$$p_t = 1 - \int_0^\infty \exp\left(-\alpha \sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau p_{t+\tau}\right) g(\alpha) \mathrm{d}\alpha . \qquad \text{(S5)}$$

In the specific case where the infectiousness factors, α, follow a gamma distribution with shape parameter k and (to ensure a mean value of one) scale parameter $1/k$, we then have

$$
\begin{aligned}
p_t &= 1 - \int_0^\infty \frac{k^k}{\Gamma(k)} \alpha^{k-1} \times \exp\left(-\alpha\left(k + \sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau p_{t+\tau}\right)\right) \mathrm{d}\alpha \\
&= 1 - \left(1 + \frac{1}{k}\sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau p_{t+\tau}\right)^{-k}, \qquad (S6)
\end{aligned}
$$

where the second equality follows by noting that the integrand in the first expression is proportional to the probability density function of a gamma distribution with shape parameter k and scale parameter $(k + \sum_{\tau=1}^{\infty} R_{t+\tau} w_\tau p_{t+\tau})^{-1}$.

Outbreak risk with periodic transmissibility

We now suppose that the instantaneous reproduction number, R_t is a periodic function of time with period T (i.e., $R_{t+T} = R_t$), so that the outbreak risk, p_t, must also be periodic with the same period. For $1 \leq t \leq T$, equation S6 then gives

$$
\begin{aligned}
p_t &= 1 - \left(1 + \frac{1}{k}\sum_{j=0}^{\infty}\sum_{s=1}^{T} R_{t+jT+s} w_{jT+s} p_{t+jT+s}\right)^{-k} \\
&= 1 - \left(1 + \frac{1}{k}\sum_{s=1}^{T} R_{t+s} \nu_s p_{t+s}\right)^{-k}, \qquad (S7)
\end{aligned}
$$

where $\nu_s = \sum_{j=0}^{\infty} w_{jT+s}$. Note that if the generation time is always shorter than the period, T, then we simply have $\nu_s = w_s$. Now, equation S7 can be re-written as

$$
p_t = 1 - \left(1 + \frac{1}{k}\sum_{s=1}^{T} B_{t,s} p_s\right)^{-k}, \qquad (S8)
$$

where $B_{t,s}$ is the $(t,s)^{\mathrm{th}}$ entry of the $T \times T$ matrix,

$$
B = \begin{pmatrix}
\nu_T R_1 & \nu_1 R_2 & \cdots & \nu_{T-1} R_T \\
\nu_{T-1} R_1 & \nu_T R_2 & \cdots & \nu_{T-2} R_T \\
\vdots & \vdots & \ddots & \vdots \\
\nu_2 R_1 & \nu_3 R_2 & \cdots & \nu_1 R_T \\
\nu_1 R_1 & \nu_2 R_2 & \cdots & \nu_T R_T
\end{pmatrix} \qquad (S9)
$$

Equation S8 gives a closed system of T equations in T variables $(p_1, \ldots, p_T)$, which can be solved numerically. While equation S8 always has a solution with each p_t equal to zero, in all our numerical examples we obtained a (numerical) solution with each p_t strictly between zero and one, which was assumed to give the true outbreak risk values (this can be verified using model simulations, as in Figure 1E of the main text).

Calculation of COVID-19 susceptibility profile

Here, we provide details of the calculation of the expected susceptibility, $\bar{S}(\tau)$, of an individual included in annual vaccination campaigns, as a function of time since most recent vaccine dose, τ.

We considered a large synthetic cohort of $n = 10{,}000$ individuals, labelled $i = 1, \dots, n$. For each individual, we sampled each antibody dynamics model parameter, $\theta_i \in \{H_i, m_i, K_i, \mu_i, \tau_{d,i}, D_i, \delta_i\}$ as $\theta_i = \theta_{pop} \exp(\omega_\theta \varepsilon_{\theta,i})$, where θ_{pop} and ω_θ are the assumed population (median) parameter and standard deviation of random effect, respectively (as listed in Extended Data Table 1), and $\varepsilon_{\theta,i}$ is a random variate drawn from a normal distribution with mean zero and standard deviation one (independently for different parameters and individuals). The individual parameter values were then used to generate an individual antibody titre profile, $A_i(\tau)$, given by the periodic solution of the antibody dynamics model (equations 7-8 in the main text) with period $T = 365$ days. This periodic solution was generated by numerically solving equations 7-8 on $\tau \geq -5T$ with boundary condition $A_i(-5T) = 0$, and with vaccination assumed to occur at each time jT for integer $j \geq -5$, and then taking the resulting solution for $\tau \in [0, T)$. Equation 9 in the main text was then used to obtain the individual susceptibility profile, $S_i(\tau)$. We then calculated the expected susceptibility,

$$\bar{S}(\tau) = \frac{1}{n}\sum_{i=1}^{n} S_i(\tau). \tag{S10}$$

Additionally, we calculated 95% prediction intervals for individual antibody titres and susceptibility levels at each time τ (although these were not used in outbreak risk calculations).