Supplementary Data - Model equations and analytical derivations

1. Model equations

The model is described by the following set of partial differential equations:

$$\frac{\partial S}{\partial t} + \frac{\partial S}{\partial a} = -\lambda S - \mu(a)S - \kappa(t,a)S$$

$$\frac{\partial I}{\partial t} + \frac{\partial I}{\partial a} = \lambda S - \mu(a)I - \gamma I - \kappa(t,a)I$$

$$\frac{\partial R}{\partial t} + \frac{\partial R}{\partial a} = \gamma I - \mu(a)R - \kappa(t,a)R$$

$$\frac{\partial VS}{\partial t} + \frac{\partial VS}{\partial a} = -\lambda VS - \mu(a)VS + (1-\tau)\kappa(t,a)S - \tau\kappa_2(t,a)VS$$

$$\frac{\partial VI}{\partial t} + \frac{\partial VI}{\partial a} = \lambda VS - \mu(a)VI + \kappa(t,a)I - \gamma VI$$

$$\frac{\partial VR}{\partial t} + \frac{\partial VR}{\partial a} = \gamma VI - \mu(a)VR + \tau\kappa(t,a)S + \tau\kappa_2(t,a)VS$$

supplemented by the following conditions:

$$S(t,a) + I(t,a) + R(t,a) + VS(t,a) + VI(t,a) + VR(t,a) = N(t,a)$$

$$S(t,0) = \nu N(t,0)$$

t is the time (in years), a is the age (in years). S, I, R, VS, VI, VR are the numbers of susceptible, infected, recovered, vaccinated susceptible, vaccinated infected, and vaccinated recovered, within the total population N. $\kappa(t,a)$ is the coverage of measles immunization for individuals vaccinated for the first time in year t at age a: it can be through routine immunization (MCV1) (in which case $a < 1$) or through supplemental immunization activity (SIA) (in which case $a < 1$). $\kappa_2(t,a)$ is the coverage of measles immunization for individuals vaccinated for the second time in year t at age a: it is through SIA only (in which case $a < 1$). τ is the effectiveness of measles vaccine: $\tau = 0.85$ for individuals vaccinated once through MCV1, $\tau = 0.95$ for individuals vaccinated once through SIA, and $\tau = 0.98$ for individuals vaccinated twice. Finally, λ

represents the force of infection and is a function of I and VI; ν is the birth rate in the population, $\mu(a)$ is the mortality rate at age a, and γ is the infectiousness period of measles.

2. Analytical derivation

Assume routine coverage κ_R at effectiveness τ_R and SIA coverage κ_S at effectiveness τ_S. We use a standard SIR model [1]:

$$\frac{dS}{dt} = \upsilon(1 - \tau_R \kappa_R) - \beta IS - \mu S - \tau_S \kappa_S \sum_{n=0}^{\propto} S(nT_{-})\delta(t - nT)$$

$$\frac{dI}{dt} = \beta IS - \mu I - \gamma I$$

t is the time (in years). S and I are the numbers of susceptible and infected within the total population. β is the contact rate between two individuals; ν is the birth rate in the population, μ is the mortality rate, and γ is the infectiousness period of measles. δ is the Dirac delta function.

T is the inter-period between two SIAs, T_{-} depicts the instant just before which SIAs happen. We assume $I(t) = 0$ for $t \geq 0$ (there are no infections). Hence:

$$\frac{dS}{dt} = \upsilon(1 - \tau_R \kappa_R) - \mu S - \tau_S \kappa_S \sum_{n=0}^{\propto} S(nT_{-})\delta(t - nT)$$

so that:

$$\frac{dS}{dt} = \upsilon(1 - \tau_R \kappa_R) - \beta IS - \mu S - \tau_S \kappa_S S(nT_{-})\delta(t - nT)$$

for: $(n-1)T \leq t \leq nT$

which has the solution:

$$S(t) = S^{+}e^{-\mu(t-t_0)} + e^{-\mu t}\int_{t_0}^{t} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx - [S^{+}e^{-\mu T}$$

$$+ e^{-\mu nT}\int_{t_0}^{nT} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx]\tau_S\kappa_S\int_{t_0}^{t}\delta(u-nT)du$$

We define:

$$Q(t) = S^{+}e^{-\mu(t-t_0)} + e^{-\mu t}\int_{t_0}^{t} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx$$

hence:

$$S(t) = \begin{Bmatrix} Q(t), t_0 = (n-1)T \leq t < nT \\ (1-\tau_S\kappa_S)Q(t), t = nT \end{Bmatrix}$$

We then look for fixed points:

$$\Pi(S_n) = S_n$$

$$S^{+}e^{-\mu T} + e^{-\mu T}\int_{(n-1)T}^{nT} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx = S^{+}$$

hence:

$$S^{+} = \frac{(1-\tau_S\kappa_S)e^{-\mu T}}{1-(1-\tau_S\kappa_S)e^{-\mu T}}\int_{0}^{T} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx$$

Then, the stability of the fixed point is given by:

$$\left|\frac{\partial\Pi}{\eth S}(S = S^{+})\right| = |(1-\tau_S\kappa_S)e^{-\mu T}| < 1$$

Hence, there is convergence to S^{*}. Setting $S = S^{*}$, we obtain the periodic solution:

$$\tilde{S}(t) = S^{*}e^{-\mu t} + e^{-\mu t}\int_{0}^{t} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx - [S^{*}e^{-\mu T}$$

$$+ e^{-\mu T}\int_{0}^{T} e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx]\tau_S\kappa_S\int_{0}^{t}\delta(u-T)du$$

For stability, we need to have:

$$\int_0^T \widetilde{S(t)}dt < \frac{\mu+\gamma}{\beta}T$$

which leads to the following condition:

$$\frac{(1-\tau_S\kappa_S)e^{-\mu T}}{1-(1-\tau_S\kappa_S)e^{-\mu T}}\int_0^T e^{\mu x}\upsilon(1-\tau_R\kappa_R)dx\frac{1-e^{-\mu T}}{\mu} + \iint_{0\,0}^{T\,t} e^{-\mu(1-x)}\upsilon(1-\tau_R\kappa_R)\,dxdt < \frac{\mu+\gamma}{\beta}T$$

If we assume κ_R to be constant and we have $\mu T \ll 1$, we can do a Taylor expansion:

$$\upsilon(1-\tau_R\kappa_R)T[\frac{1}{2}+\frac{1-\tau_S\kappa_S}{\tau_S\kappa_S}] < \frac{\mu+\gamma}{\beta}$$

The maximum inter-period for SIAs is then:

$$T_{max} = \frac{\mu+\gamma}{\beta}\frac{1}{\upsilon}\frac{1}{1-\tau_R\kappa_R}\frac{\tau_S\kappa_S}{1-\tau_S\kappa_S/2}$$

As $\mu \ll \gamma$, we obtain:

$$T_{max} \sim \frac{\gamma}{\beta}\frac{1}{\upsilon}\frac{1}{1-\tau_R\kappa_R}\frac{\tau_S\kappa_S}{1-\tau_S\kappa_S/2}$$

We now try to estimate what would be the effective coverage of vaccinating SIA coverage of under-five children in the simulation model (SIA_{0-4}) and find the equivalent coverage in the analytical model. The effective coverage corresponding to SIA_{0-4} in the analytical model is given by:

$$\kappa_{S,eff} = SIA_{0-4}d_{0-4}$$

where d_{0-4} is the fraction of measles cases among the under-fives (as estimated based on routine immunization coverage and as estimated by Global Burden of Disease region by Simons and colleagues [2]). $\kappa_{S,eff} = 0.70$ for Mali and Nigeria; $\kappa_{S,eff} = 0.56$ for Ethiopia, Madagascar, and Niger; $\kappa_{S,eff} = 0.52$ for Burkina Faso; $\kappa_{S,eff} = 0.47$ for

Afghanistan and India; $\kappa_{S,eff} = 0.45$ for Indonesia; $\kappa_{S,eff} = 0.63$ for the Indian states of Bihar and Utter Pradesh.

In addition, population grows and in that sense the birth rate needs to be adjusted every 5 years:

$$\tilde{\upsilon} = \upsilon \frac{p_{0-4}}{p_{5-9}}$$

where p_{0-4} and p_{5-9} are the populations of under-fives and five-nine year-olds, respectively.

Therefore, the maximum inter-period for SIAs is given by:

$$T_{max} \sim \frac{\gamma}{\beta}\frac{1}{\tilde{\upsilon}}\frac{1}{1-\tau_R\kappa_R}\frac{\tau_S\kappa_{S,eff}}{1-\tau_S\kappa_{S,eff}/2}$$

As $\frac{1}{R_0} = \frac{\gamma}{\beta}$, we then obtain:

$$T_{max} \sim \frac{1}{R_0}\frac{1}{\tilde{\upsilon}}\frac{1}{1-\tau_R\kappa_R}\frac{\tau_S\kappa_{S,eff}}{1-\tau_S\kappa_{S,eff}/2}$$

References

1. Shulgin B, Stone L, Agur Z. Pulse vaccination in the SIR epidemic model. Bulletin of Mathematical Biology 1998; 60:1123-1148.
2. Simons E, Ferrari M, Fricks J, et al. Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data. Lancet 2012; 379:2173-2178.