Vaccination Strategies for Epidemic Models

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27 May 1999

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S I R Model

- Assumptions
  - constant population size ($N = S + I + R = 1$)
  - mass-action kinetics for infection
  - exponentially distributed mean time to recovery and natural death
  - no death from infection
  - no vaccination

Ref: Shulgin, Stone, and Agur, *Bull Math Bio* (1998) **60**, 1123–1148.

S I R Model — No Vaccination

$$
\begin{aligned}
\dot{S} &= \mu - \mu S - \beta S I \\
\dot{I} &= - \mu I + \beta S I - \gamma I \\
\dot{R} &= - \mu R + \gamma I \\
\dot{N} &= 0
\end{aligned}
$$

S I R Model — No Vaccination

- Equilibria

	S	I
infection-free	1	0
endemic	$1/R_0$	$\frac{\mu}{\beta}(R_0 - 1)$

- Reproduction Rate: $R_0 = \frac{\beta}{\mu+\gamma}$
- Stability

	$R_0 < 1$	$R_0 > 1$
infection-free	globally stable	unstable
endemic	unstable	globally stable

S I R Model — Constant Vaccination

- Assumptions
  - life-long immunization at birth

$$\begin{aligned}
\dot{S} &= (1-\rho)\mu - \mu S - \beta S I \\
\dot{I} &= - \mu I + \beta S I - \gamma I \\
\dot{R} &= \rho\mu - \mu R + \gamma I \\
\dot{N} &= 0
\end{aligned}$$

S I R Model — Constant Vaccination

- Equilibria

	S	I
infection-free	$1-\rho$	0
endemic	$1/R_0$	$\frac{\mu}{\beta}(R_0-1)-\frac{\mu}{\mu+\gamma}\rho$

- Reproduction Rate: $R_\rho = (1-\rho)\,R_0$
- Critical Vaccination Rate: $\rho_0 = 1 - \frac{1}{R_0}$
- Stability

	$R_\rho < 1\ (\rho > \rho_0)$	$R_\rho > 1\ (\rho < \rho_0)$
infection-free	globally stable	unstable
endemic	unstable	globally stable

S I R Model — Pulse Vaccination

- Assumptions
  - fixed portion of susceptibles vaccinated every T years

$$\begin{aligned}
\dot{S} &= \mu - \mu S - \beta S I - \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t-nT) \\
\dot{I} &= -\mu I + \beta S I - \gamma I \\
\dot{R} &= -\mu R + \gamma I + \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t-nT) \\
\dot{N} &= 0
\end{aligned}$$

S I R Model — Pulse Vaccination

- Infection-Free Equilibrium
  - initial value problem:

$$\dot{S} = \mu - \mu S - \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t - nT), \qquad S(0) = S_0$$

  - solution:

$$\begin{aligned} S(t) &= \begin{cases} S^{(n)}(t), & t \in [nT, (n+1)T) \\ S_{n+1}, & t = (n+1)T \end{cases} \\ S^{(n)}(t) &= 1 - (1 - S_n)e^{-\mu(t-nT)} \\ S_{n+1} &= S((n+1)T^+) \\ &= (1-\rho)S^{(n)}((n+1)T^-) \end{aligned}$$

S I R Model — Pulse Vaccination

– construction of periodic equilibrium solution:

* if $S_\infty = \lim_{n\to\infty} S_n$ exists, then S_∞ is a fixed point of

$$F(x) = (1-\rho)(1-(1-x)e^{-\mu T})$$

* unique fixed point is locally stable

$$S_\infty = \frac{(1-\rho)(e^{\mu T}-1)}{e^{\mu T}-(1-\rho)}$$

* periodic equilibrium solution:

$$S^{(\infty)}(t) = 1-(1-S_\infty)e^{-\mu(t \bmod T)}$$

S I R Model — Pulse Vaccination

– local stability:

$$\frac{1}{T}\int_0^T S\,dt \quad < \quad S_c$$

where $S_c = 1/R_0$ is the endemic equilibrium with no vaccination

– maximum vaccination period:

$$\frac{(\mu T - \rho)(e^{\mu T} - 1) + \mu\rho T}{\mu T(e^{\mu T} - (1 - \rho))} \quad = \quad \frac{\mu + \gamma}{\beta}$$

Application: Rubella (Measles)

- Parameters

mean infectious period	3.5 days	$\gamma = 100$
mean lifespan	50 years	$\mu = 0.02$
contact rate		$\beta = 1800$

- No Vaccination:
  - $R_0 \approx 18 \Longrightarrow$ endemic state is stable
  - endemic equilibrium: $S \approx 0.05$
- Constant Vaccination:
  - $\rho_0 \approx 0.95$
  - reasonable for school age, but not pre-school (35-50%)

S E I R Model

- Assumptions
  - exposed period prior to becoming infectious
  - non-constant population size ($N = S + E + I + R$)
    - immigration
    - birth
    - death from infection
  - mass-action kinetics for infection
  - exponentially distributed mean time to recovery and natural death
  - no vaccination

S E I R Model — No Vaccination

$$
\begin{aligned}
\dot{S} &= \Lambda + \mu_0 N - \mu_1 S - \beta S I \\
\dot{E} &= - \mu_1 E + \beta S I - \delta E \\
\dot{I} &= - \mu_1 I + \delta E - \gamma I - \epsilon I \\
\dot{R} &= - \mu_1 R + \gamma I \\
\dot{N} &= \Lambda - (\mu_1 - \mu_0) N - \epsilon I
\end{aligned}
$$

Note:

- all parameters are positive
- to prevent exponential growth in total population, assume death-dominant ($\mu_1 > \mu_0$)
- S I R model obtained with $\epsilon = 0$, $\delta = \infty$, $\frac{\Lambda}{\mu_1 - \mu_0} = 1$

S E I R Model — No Vaccination

- Equilibria

	infection-free	endemic
S	$\frac{\Lambda}{\mu_1-\mu_0}$	$\frac{(\mu_1+\delta)(\mu_1+\gamma+\epsilon)}{\beta\delta}$
E	0	$\frac{\mu_1(\mu_1+\gamma+\epsilon)}{\beta\delta}\frac{A_0}{B_0}$
I	0	$\frac{\mu_1}{\beta}\frac{A_0}{B_0}$
R	0	$\frac{\gamma}{\beta}\frac{A_0}{B_0}$
N	$\frac{\Lambda}{\mu_1-\mu_0}$	$\frac{(\beta\Lambda+\epsilon\mu_1)(\mu_1+\delta)(\mu_1+\gamma+\epsilon)-\epsilon\delta\beta\Lambda}{\beta B_0}$

where

$$A_0 = \beta\delta\Lambda - (\mu_1 - \mu_0)(\mu_1 + \delta)(\mu_1 + \gamma + \epsilon)$$

$$B_0 = \epsilon\delta\Lambda + (\mu_1 - \mu_0)(\mu_1 + \delta)(\mu_1 + \gamma + \epsilon)$$

S E I R Model — No Vaccination

- Reproduction Rate: $R_0 = \frac{\Lambda}{\mu_1 - \mu_0} \frac{\delta}{\mu_1 + \delta} \frac{\beta}{\mu_1 + \gamma + \epsilon}$

- Stability

	$R_0 < 1$	$R_0 > 1$
infection-free	globally stable	unstable
endemic	unstable	globally stable

S E I R Model — Constant Vaccination

- Assumptions
  - life-long immunization at birth

$$
\begin{aligned}
\dot{S} &= \Lambda + (1-\rho)\mu_0 N - \mu_1 S - \beta S I \\
\dot{E} &= -\mu_1 E + \beta S I - \delta E \\
\dot{I} &= -\mu_1 I + \delta E - \gamma I - \epsilon I \\
\dot{R} &= \rho\mu_0 N - \mu_1 R + \gamma I \\
\dot{N} &= \Lambda - (\mu_1 - \mu_0) N - \epsilon I
\end{aligned}
$$

S E I R Model — Constant Vaccination

- Equilibria

	infection-free	endemic
S	$\frac{\Lambda}{\mu_1 - \mu_0}\left(1 - \frac{\mu_0}{\mu_1}\right)$	$\frac{(\mu_1+\delta)(\mu_1+\gamma+\epsilon)}{\beta\delta}$
E	0	$\frac{\mu_1(\mu_1+\gamma+\epsilon)}{\beta\delta}\frac{A_\rho}{B_\rho}$
I	0	$\frac{\mu_1}{\beta}\frac{A_\rho}{B_\rho}$
R	$\frac{\Lambda}{\mu_1 - \mu_0}\frac{\mu_0}{\mu_1}$	$\frac{\gamma}{\beta}\frac{A_\rho}{B_\rho} + \frac{\mu_0}{\mu_1}\rho N$
N	$\frac{\Lambda}{\mu_1 - \mu_0}$	$\frac{(\beta\Lambda+\epsilon\mu_1)(\mu_1+\delta)(\mu_1+\gamma+\epsilon)-\epsilon\delta\beta\Lambda}{\beta B_\rho}$

where

$$A_\rho = A_0 - \frac{\mu_0}{\mu_1}\rho\beta\delta\Lambda, \qquad B_\rho = B_0 + \frac{\mu_0}{\mu_1}\rho\epsilon\delta\mu_0$$

S E I R Model — Constant Vaccination

- Reproduction Rate: $R_\rho = \left(1 - \frac{\mu_0}{\mu_1}\rho\right) R_0$
- Critical Vaccination Rate: $\rho_0 = \frac{\mu_1}{\mu_0}\left(1 - \frac{1}{R_0}\right)$
- Stability

	$R_\rho < 1$ $(\rho > \rho_0)$	$R_\rho > 1$ $(\rho < \rho_0)$
infection-free	globally stable	unstable
endemic	unstable	globally stable

S E I R Model — Pulse Vaccination

- Assumptions
  - fixed portion of susceptibles vaccinated every T years

$$
\begin{aligned}
\dot{S} &= \Lambda + \mu_0 N - \mu_1 S - \beta S I \\
&\quad - \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t - nT) \\
\dot{E} &= -\mu_1 E + \beta S I - \delta E \\
\dot{I} &= -\mu_1 I + \delta E - \gamma I - \epsilon I \\
\dot{R} &= -\mu_1 R + \gamma I \\
&\quad + \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t - nT) \\
\dot{N} &= \Lambda - (\mu_1 - \mu_0) N - \epsilon I
\end{aligned}
$$

S E I R Model — Pulse Vaccination

- Infection-Free Equilibrium
  - initial value problem:

$$\begin{aligned}
\dot{S} &= \Lambda + \mu_0 N - \mu_1 S - \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t-nT) \\
\dot{R} &= - \mu_1 R + \sum_{n=0}^{\infty} \rho S(nT^-)\delta(t-nT) \\
\dot{N} &= \Lambda - (\mu_1 - \mu_0)N
\end{aligned}$$

S E I R Model — Pulse Vaccination

– solution:

$$S(t) = \begin{cases} S^{(n)}(t), & t \in [nT, (n+1)T) \\ S_{n+1}, & t = (n+1)T \end{cases}$$

where, for all n=0, 1, 2, . . .,

$$\begin{aligned} S^{(n)}(t) &= \frac{\Lambda}{\mu_1 - \mu_0} + \left(S_n - \frac{\Lambda}{\mu_1 - \mu_0}\right) e^{-\mu_1(t-nT)} \\ &\quad + \left(N_0 - \frac{\Lambda}{\mu_1 - \mu_0}\right)\left(1 - e^{-\mu_0(t-nT)}\right) e^{-(\mu_1-\mu_0)t} \\ S_{n+1} &= S((n+1)T^+) \\ &= (1-\rho)S^{(n)}((n+1)T^-) \end{aligned}$$

S E I R Model — Pulse Vaccination

– construction of periodic equilibrium solution:

* if $S_\infty = \lim_{n\to\infty} S_n$ exists, then S_∞ is a fixed point of

$$F(x) \quad = \quad (1-\rho)\left(\frac{\Lambda}{\mu_1-\mu_0} + \left(x - \frac{\Lambda}{\mu_1-\mu_0}\right)e^{-\mu_1 T}\right)$$

* unique fixed point is locally stable

$$S_\infty \quad = \quad \frac{\Lambda}{\mu_1-\mu_0}\,\frac{(1-\rho)(e^{\mu T}-1)}{e^{\mu T}-(1-\rho)}$$

S E I R Model — Pulse Vaccination

∗ asymptotically periodic equilibrium solution:

$$\begin{aligned} S^{(\infty)}(t) &= \frac{\Lambda}{\mu_1 - \mu_0} + \left(S_\infty - \frac{\Lambda}{\mu_1 - \mu_0} \right) e^{-\mu_1 (t \bmod T)} \\ &\quad + \left(N_0 - \frac{\Lambda}{\mu_1 - \mu_0} \right) \left(1 - e^{-\mu_0 (t \bmod T)} \right) \\ &\quad \times e^{-(\mu_1 - \mu_0) t} \end{aligned}$$

– . . .

Application: Rubella (Measles)

- Parameters

mean exposed period	9 days	$\delta = 40$
mean infectious period	6 days	$\gamma = 60$
mean lifespan	80 years	$\mu = 0.0125$
contact rate	“high”	$\beta =$
immigration rate	???	$\Lambda =$
net birth rate	???	$\mu_0 =$
net death rate	???	$\mu_1 =$