Infectious Disease Management

Insights from simple models

The Anatomy of an Epidemic

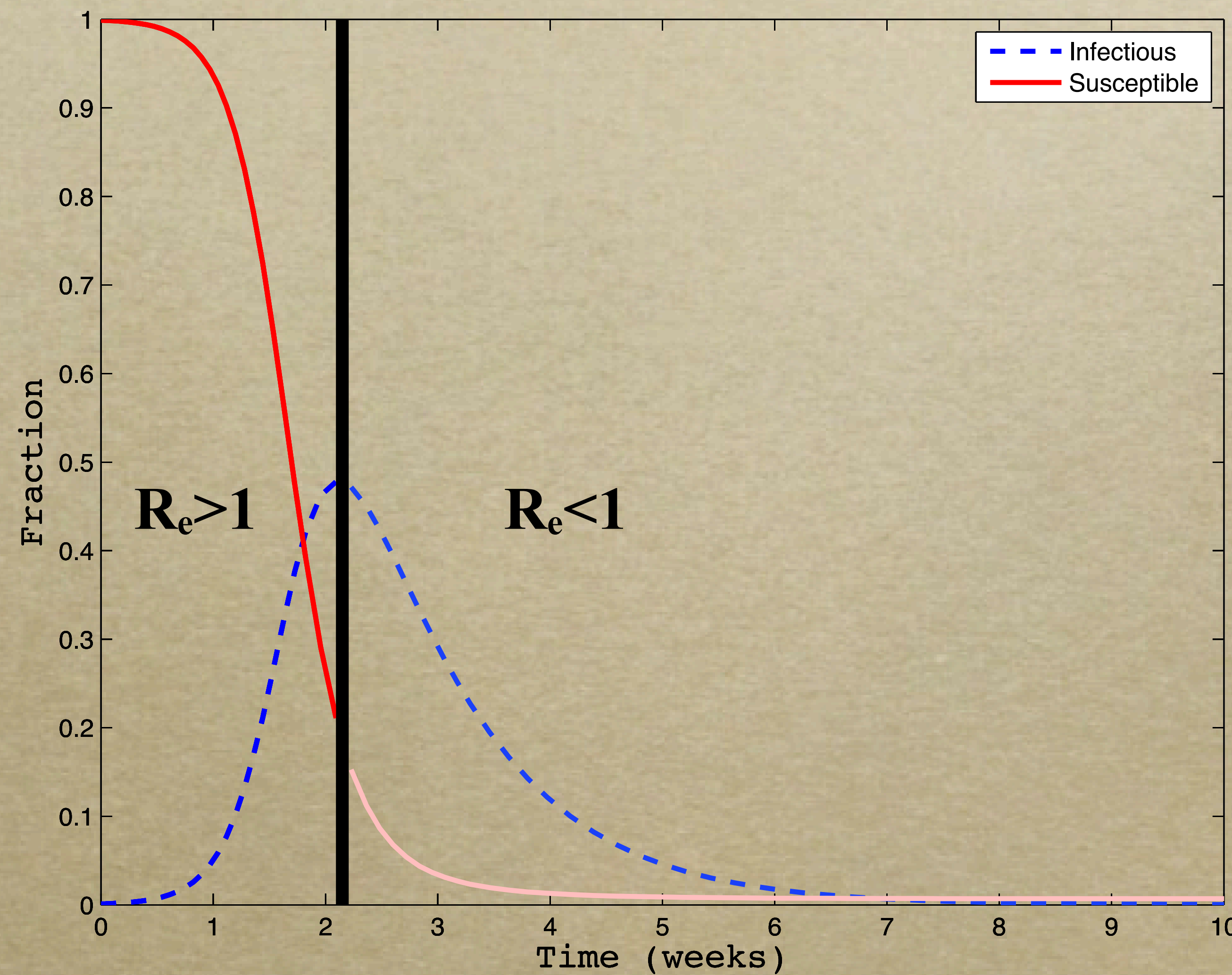
Initially, exponential growth (proportional to R_0)

But, depletes susceptibles, so R_0 no longer useful

Instead, define effective value of R_0 (call it R_e)

R_e scales with proportion of susceptibles in population ($s=X/N$), ie $R_e = R_0 s$

when $R_e<1$, each infectious individual infects fewer than one new person, breaking transmission chain



Vaccination

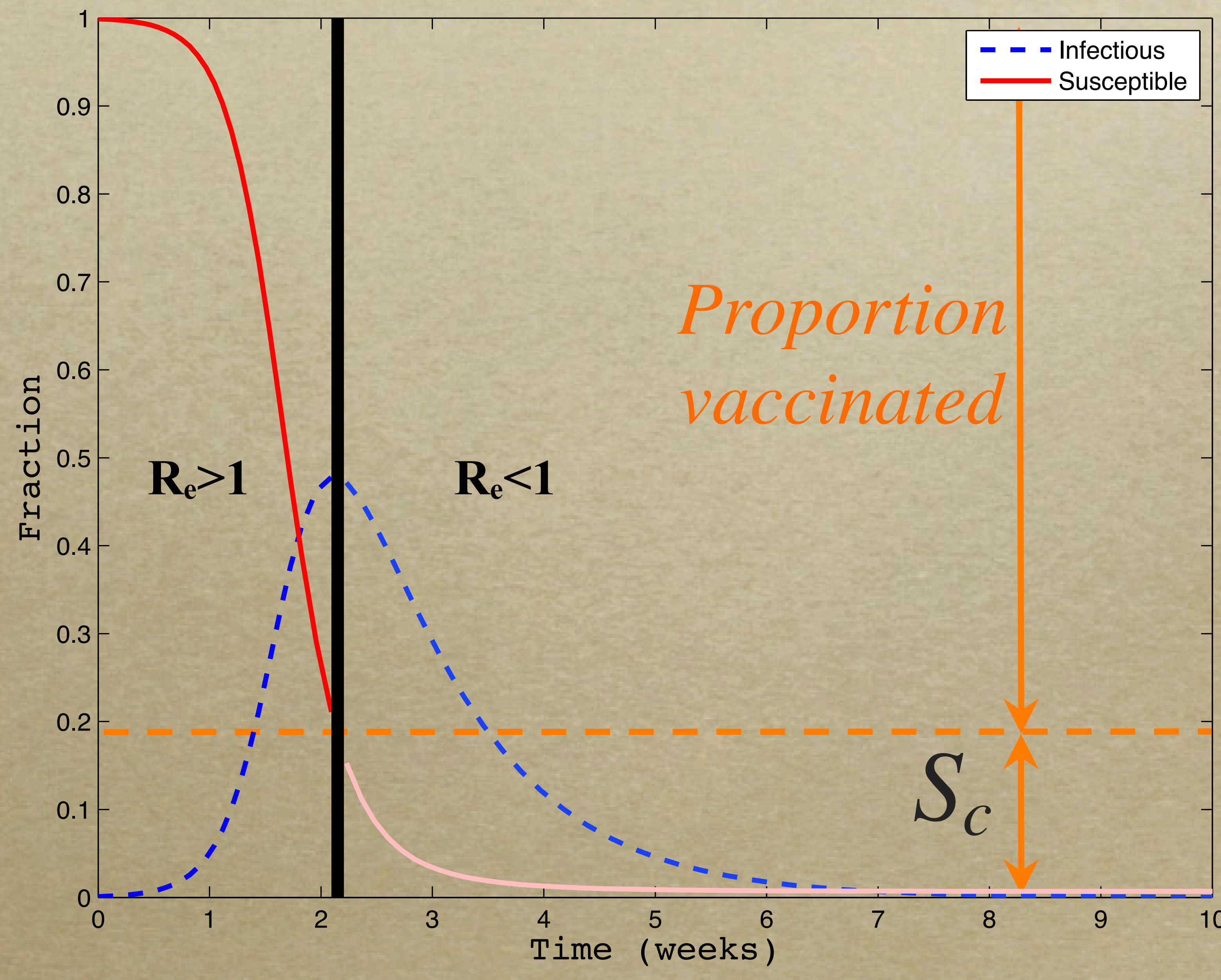
If, by vaccination, we can reduce proportion of susceptibles below a critical level, S_c, then $R_e<1$ and infection can never 'invade'

Recall: $R_{e_e} = R_0X/N$

So, $S_c=1/\mathbf{R_0}$ represents $R_{e_e}=1$ and will achieve our goal

So, critical vaccination proportion to eradicate is

$$p_c = 1-S_c = 1-1/\mathbf{R_0}$$



Mathematically ...

- Consider rate of change of invectives:

$$\frac{dY}{dt} = \beta X \frac{Y}{N} - \gamma Y$$

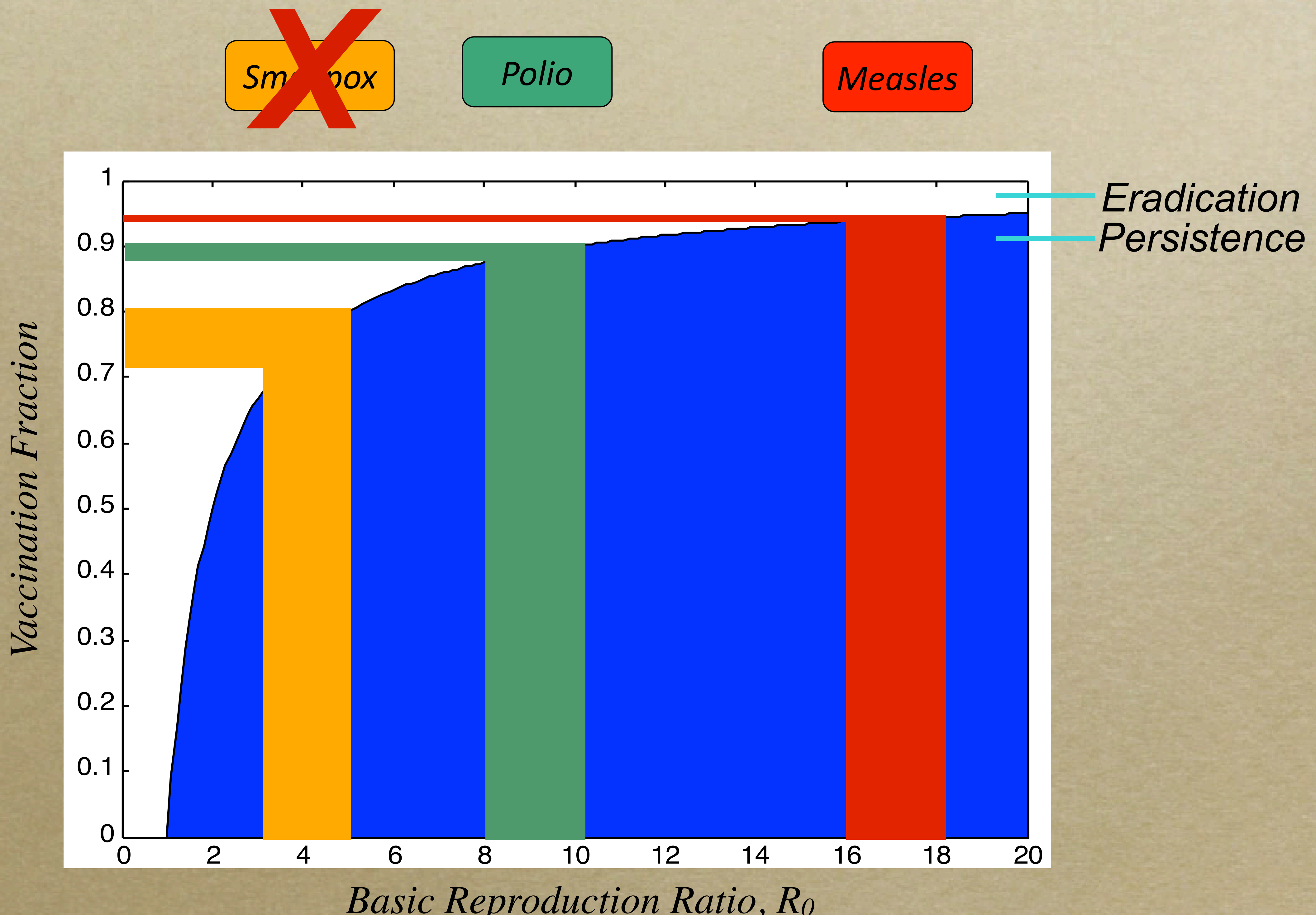
- Hence, preventing initial spread (dY/dt <0) requires

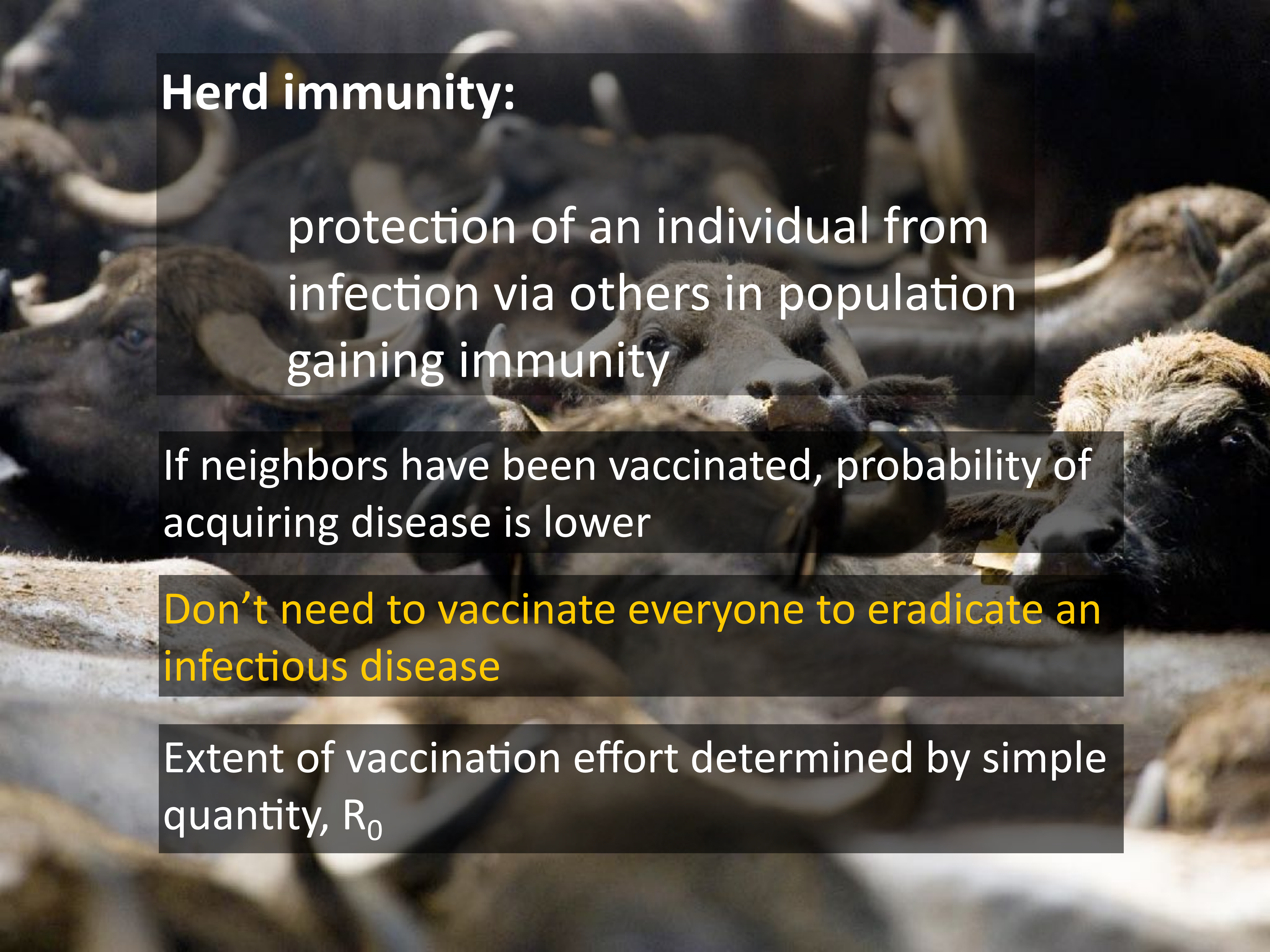
$$\beta \frac{X}{N} < \gamma$$

$$\implies \frac{X}{N} < \frac{\gamma}{\beta} = \frac{1}{R_0}$$

Eradication Criterion

$$p_c = 1 - \frac{1}{R_0}$$





Herd immunity:

protection of an individual from infection via others in population gaining immunity

If neighbors have been vaccinated, probability of acquiring disease is lower

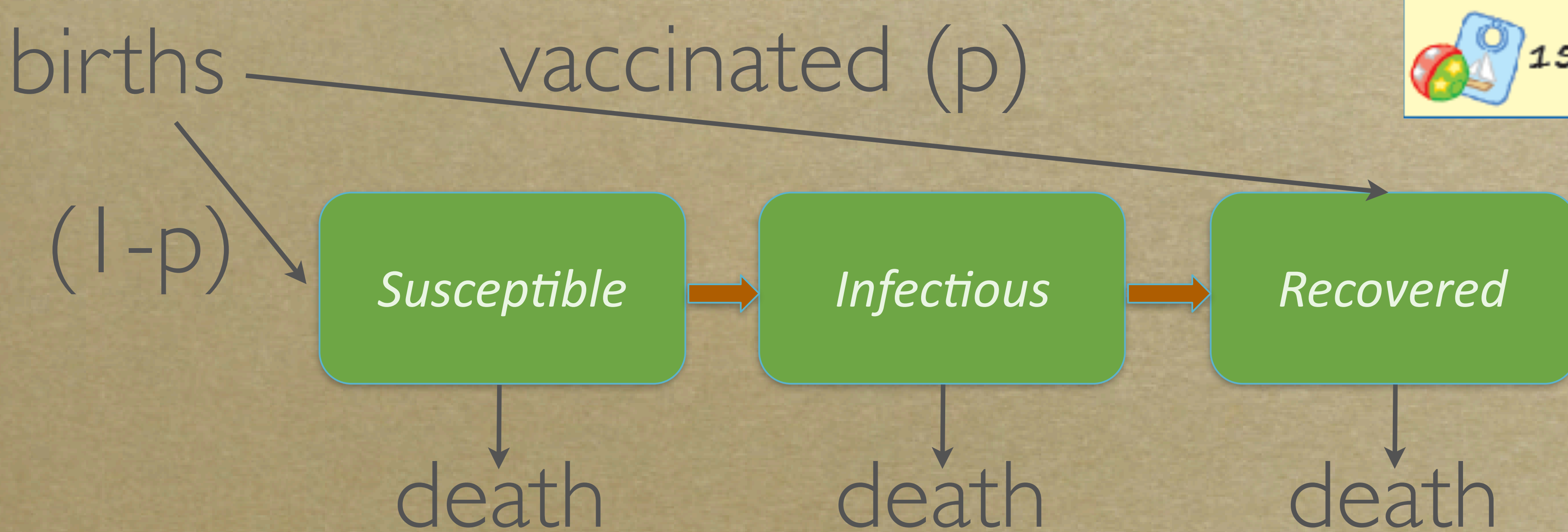
Don’t need to vaccinate everyone to eradicate an infectious disease

Extent of vaccination effort determined by simple quantity, R_0

1. “Paediatric immunization”

- *Familiar with infant immunization*
- *Generally treated as fraction, p, of newborns vaccinated*

at birth	HepB
2 months	HepB (1-2 mos) + DTaP + PCV13 + Hib + Polio + RV
4 months	DTaP + PCV13 + Hib + Polio + RV
6 months	HepB (6-18 mos) + DTaP + PCV13 + Hib + Polio (6-18 mos) + RV
12 Months	MMR (12-15 mos) + PCV13 (12-15 mos) + Hib (12-15 mos) + Varicella (12-15 mos) + HepA (12-23 mos)
15 months	DTaP (15-18 mos)



1. "Paediatric immunization"

- *Model this (as one time event)*

$$\frac{dS}{dt} = \mu(1-p) - \beta SI - \mu S$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

$$\frac{dR}{dt} = \mu p + \gamma I - \mu R$$

- *Now what?*
- *Let's derive expression for I**

“Paediatric immunization”

- *After some algebra:*

$$\frac{dS}{dt} = \mu(1 - p) - \beta SI - \mu S$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

$$\frac{dR}{dt} = \mu p + \gamma I - \mu R$$

  - $I^* = \mu/\beta\ (R_0(1\text{-}p) - 1)$

- *Eradication implies $I^*=0$*
- *Requires $p = 1-1/R_0$*

- *This is **fraction** of newborns to be immunized for (eventual) control*

2. Random Immunization

- *Consider wildlife diseases*
- *How would you vaccinate newborns?*
- *Pragmatically, will need continuous vaccination instead*

"Random immunization"

- *After some algebra:*
  - $I^* = \mu/\beta\,(R_0 - 1 - \rho/\mu)$
- *Again, eradication → I*=0*
- *Requires* $\rho \geq \mu(R_0-1)$
- *This is* ***rate*** *of susceptibles to be immunized for (eventual) control*
- *What does criterion tell us, biologically?*

$$\frac{dS}{dt} = \mu - \beta SI - \mu S - \rho S$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

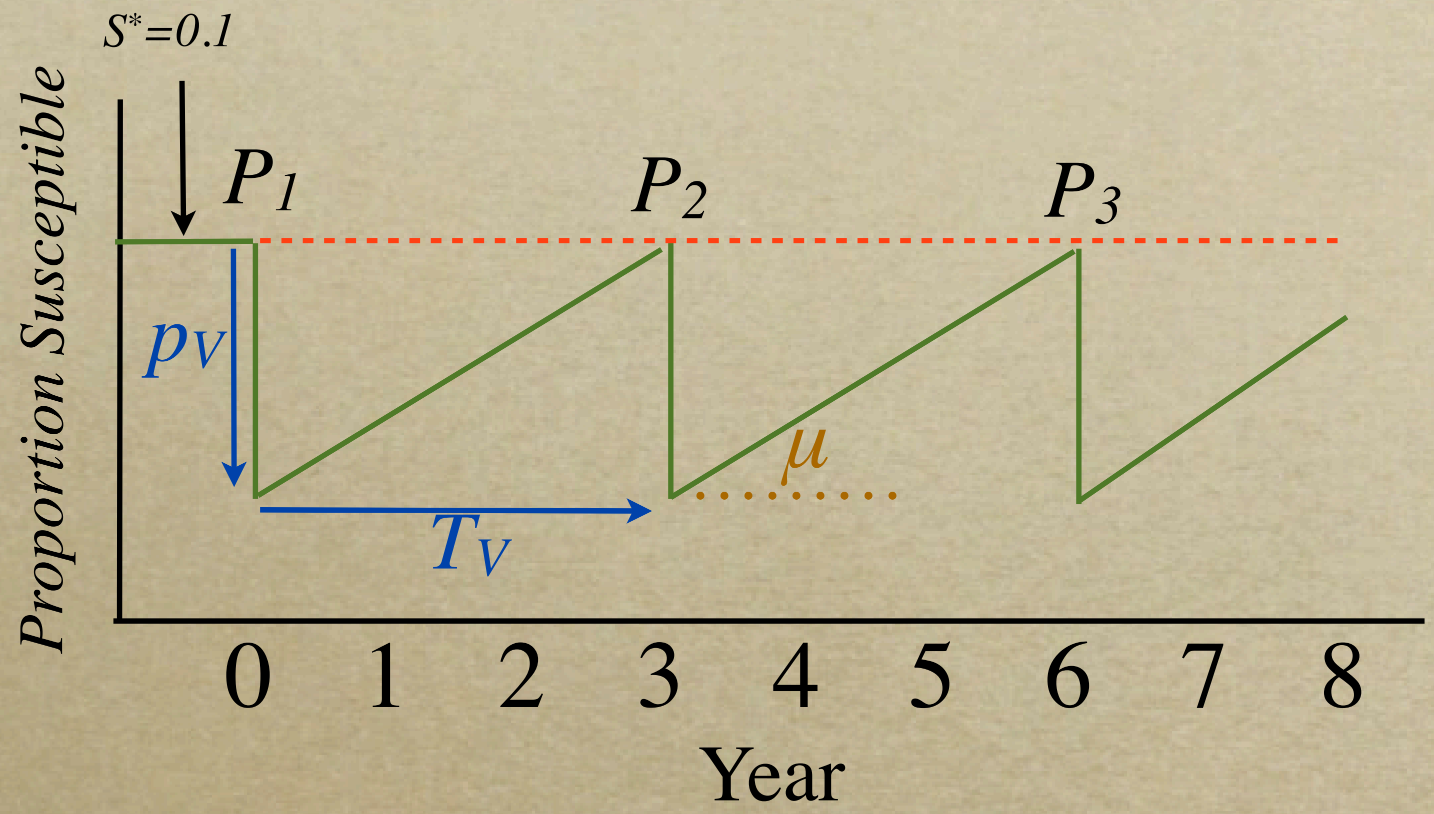
$$\frac{dR}{dt} = \rho S + \gamma I - \mu R$$

3. "Pulsed" Vaccination

- *Infant & Continuous vaccinations require sound infrastructure for vaccine delivery*
    - *may be challenging in many developing nations*

- *Alternative, perhaps more economic and logistically efficient strategy may be pulsed vaccination: immunize specific age cohorts at specified intervals*

Pulsed Vaccination



- *Assume $R_0 = 10$*
- *p_V = 60% and per capita annual birth rate = 2%*
- *For $dI/dt<0$, need to ensure $S < 1/10$*
- *After any pulse, $S = 1/10 * 0.4 = 0.04$*
- *Since $\mu=0.02$, it'll take 3 years for S to reach 0.1*
- *So, pulse period = 3 yrs*

More formally …

- *For an SIR model:*

$$\frac{dS}{dt} = \mu - \beta SI - \mu S - p_V \sum_{n=0}^{\infty} S(nT^-)\delta(t - nT)$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

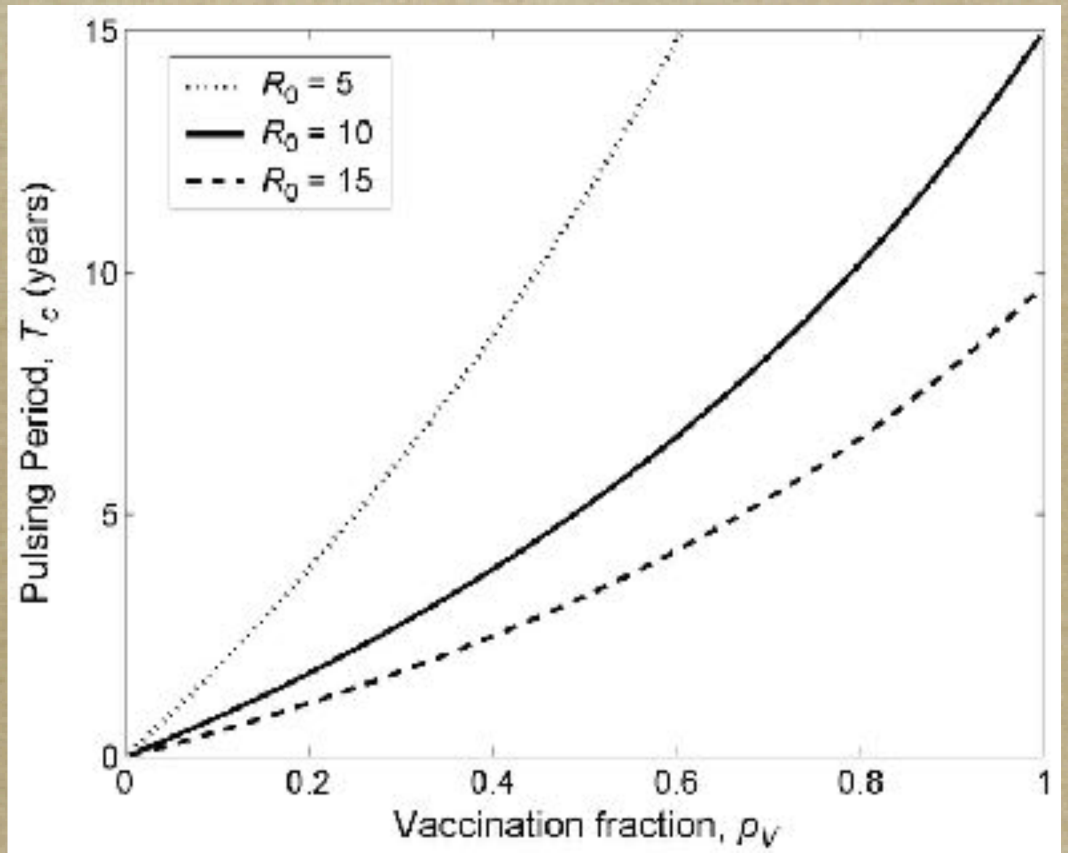
Vaccination fraction

Susceptibles prior to PV

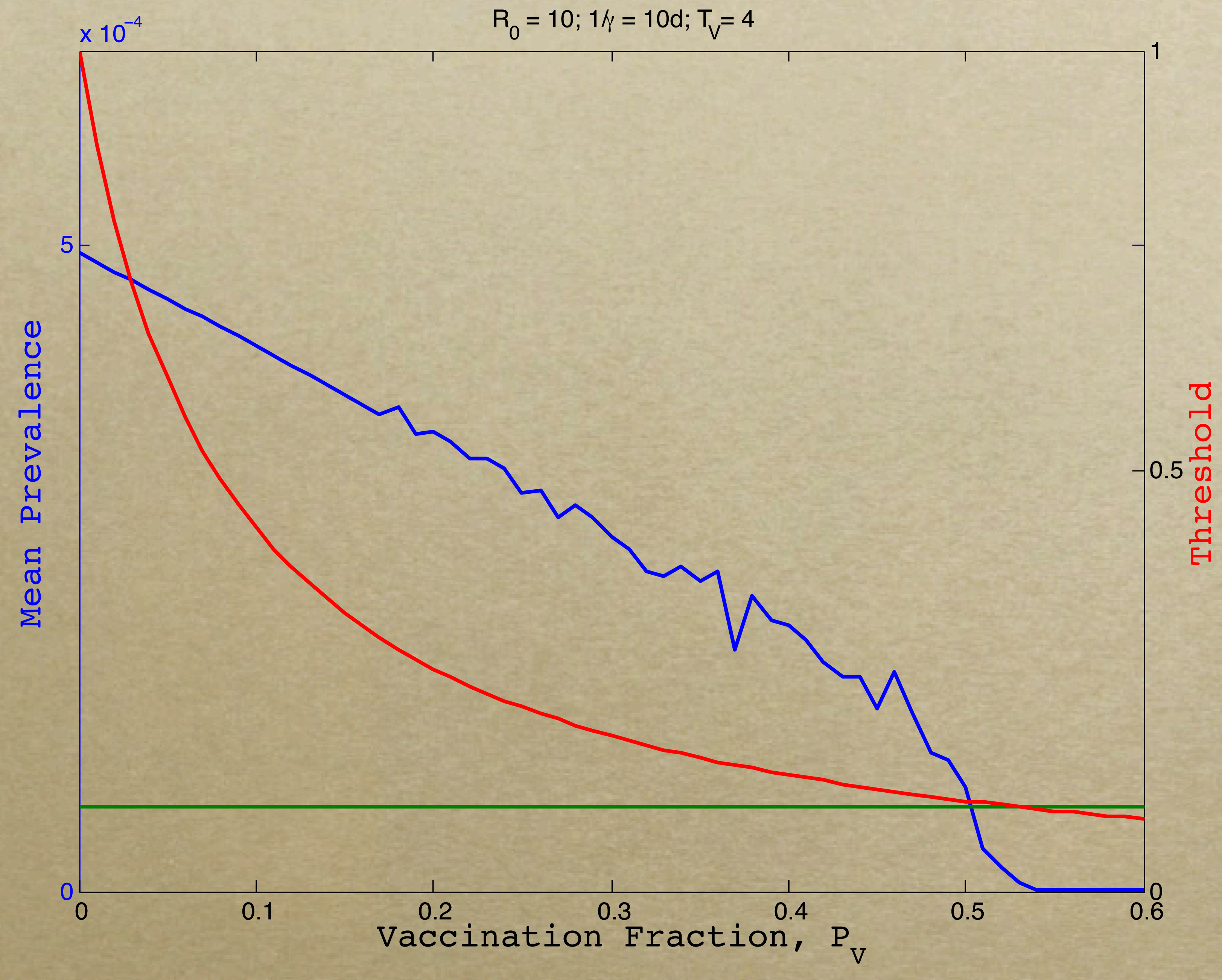
Dirac delta function

- *Shulgin et al. (1998; Bull Math Biol): Linear stability analysis reveals eradication criterion*

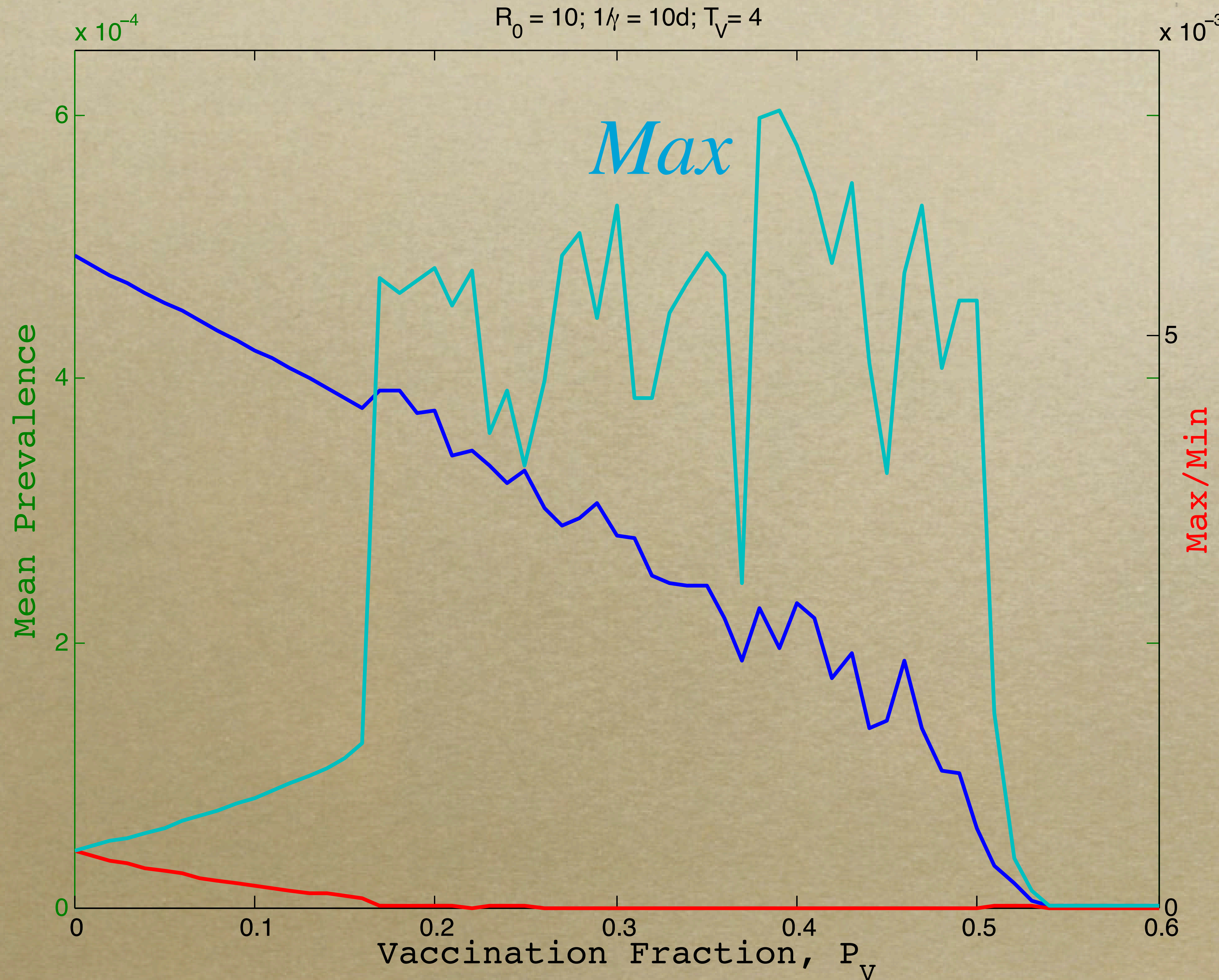
$$\frac{(\mu T - p_V)(e^{\mu T} - 1) + \mu p_V T}{\mu T(p_V - 1 + e^{\mu T})} < \frac{1}{R_0}$$



Programming:

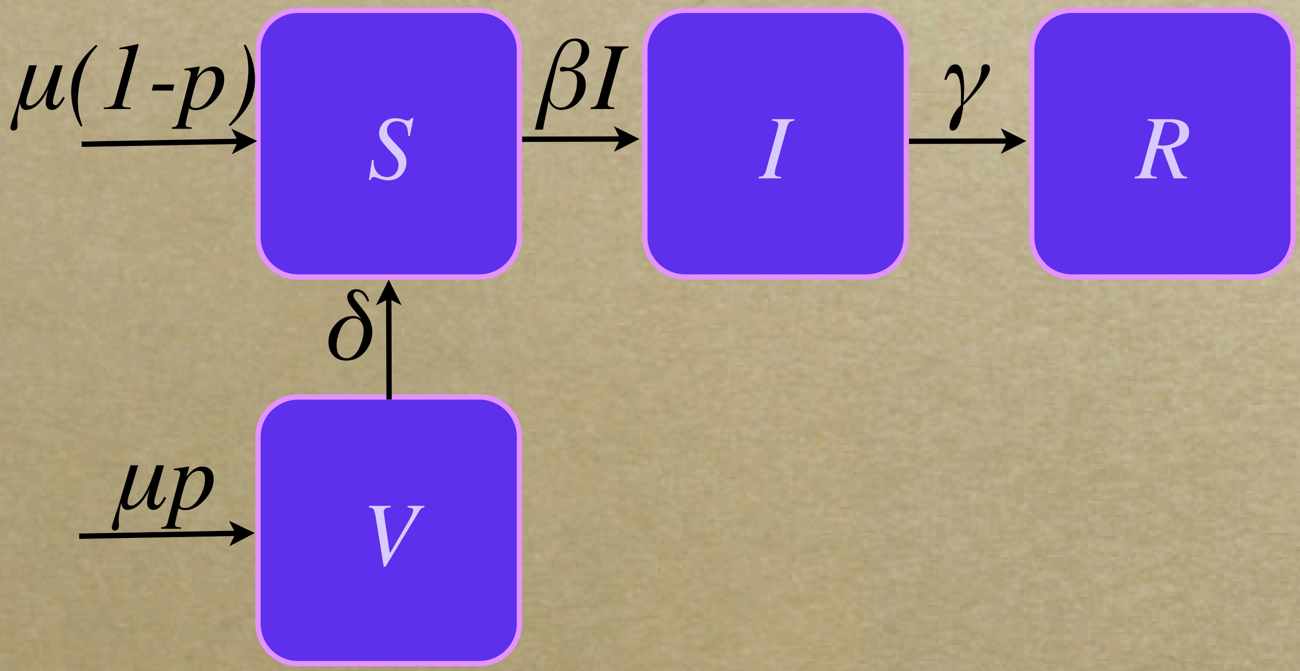


Programming Challenge:



Aside: Imperfect Vaccines

- *What if –as is at times the case– immunity derived from a vaccine wanes over time?*



$$\frac{dS}{dt} = \mu(1 - p) - \beta SI - \mu S + \delta V$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

$$\frac{dV}{dt} = \mu p - (\mu + \delta)V$$

Aside: Imperfect Vaccines

- *What if –as is at times the case– immunity derived from a vaccine wanes over time?*

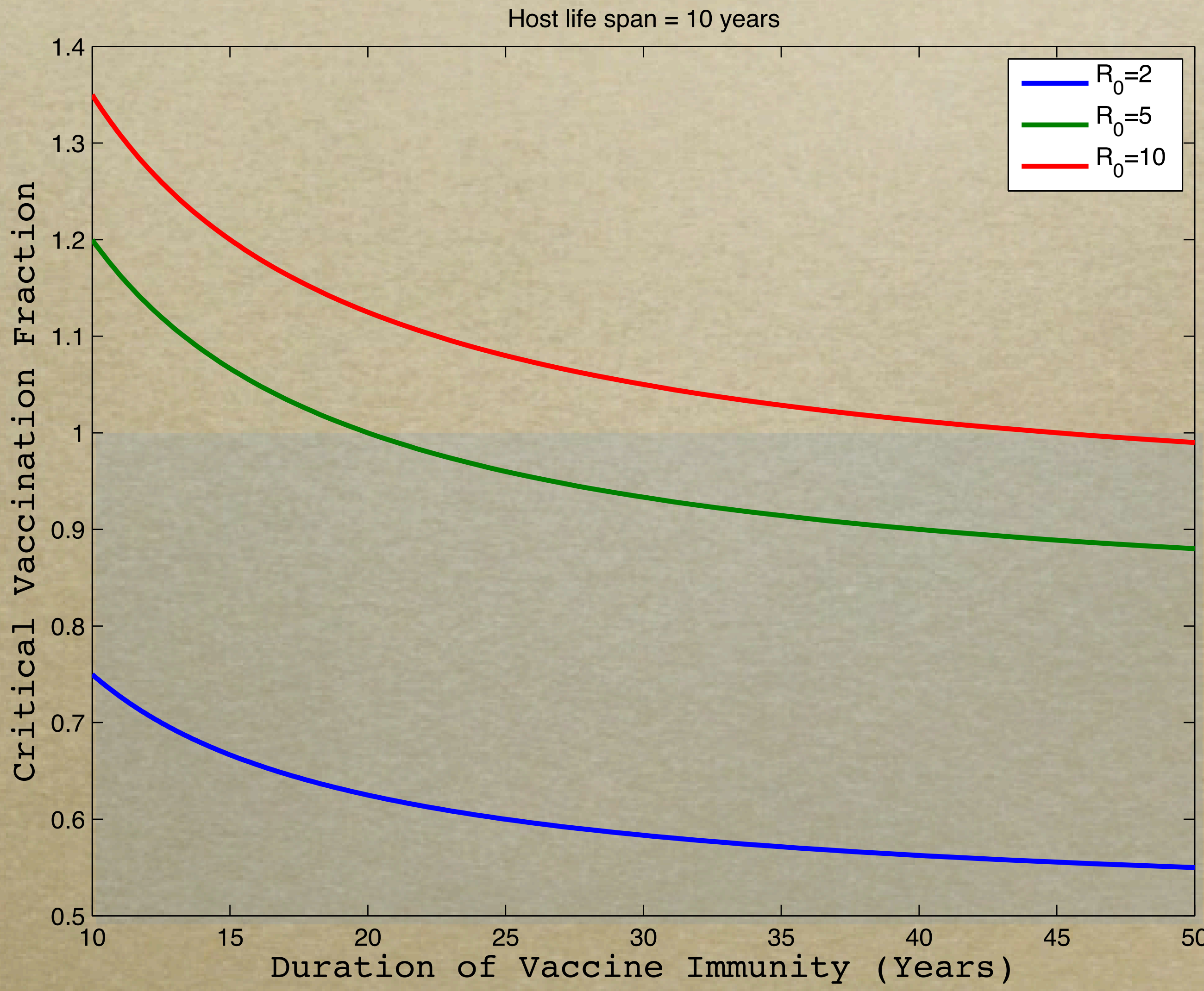
$$\frac{dS}{dt} = \mu(1-p) - \beta SI - \mu S + \delta V$$

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

$$\frac{dV}{dt} = \mu p - (\mu + \delta)V$$

Eradication requires (Check this)

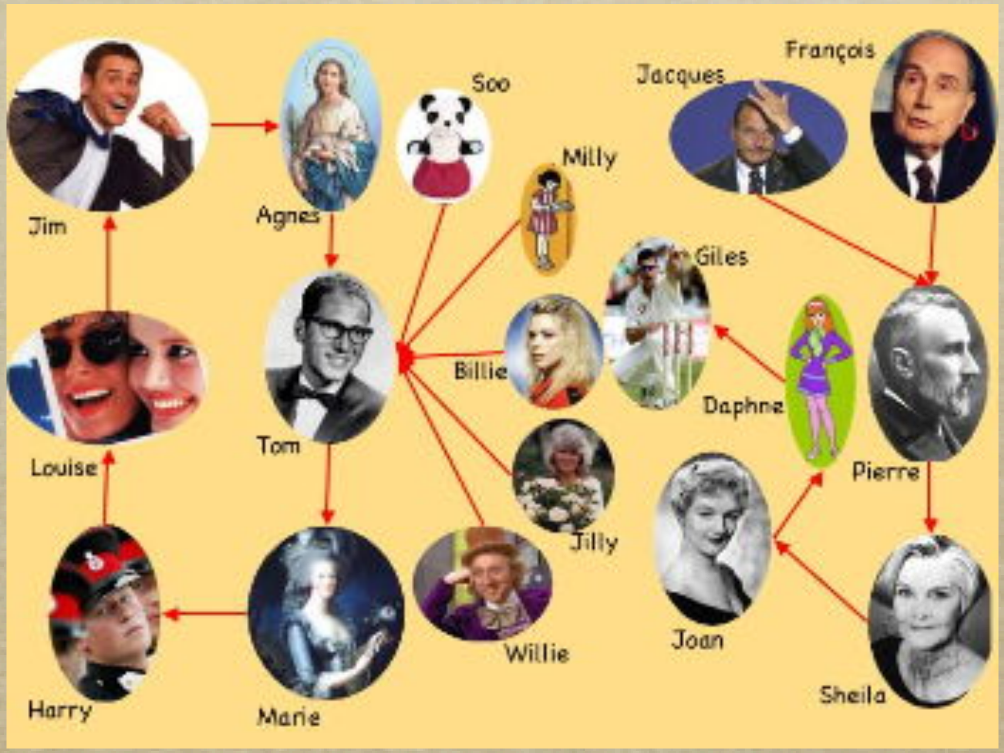
$$p = \left(1 - \frac{1}{R_0}\right)\left(1 + \frac{\delta}{\mu}\right)$$

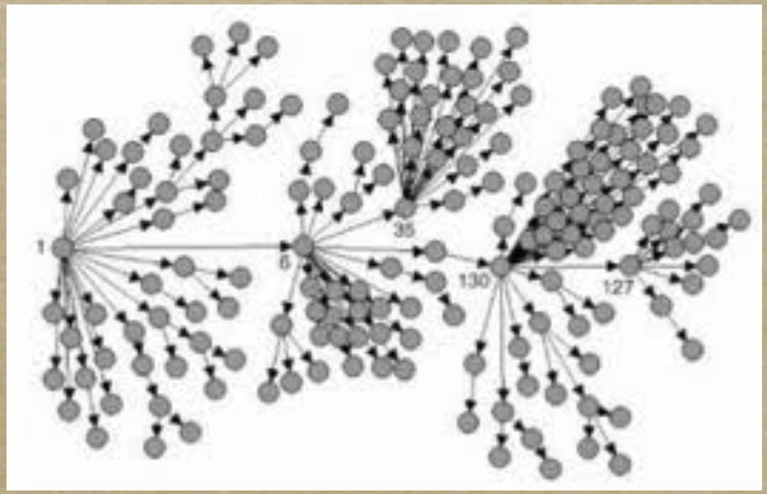


Eradication will require boosters

4. Non-Pharmaceutical Interventions

- *"Social distancing"*
- *Isolation and quarantining*
- *We should also find (or trace) their contacts*





Background

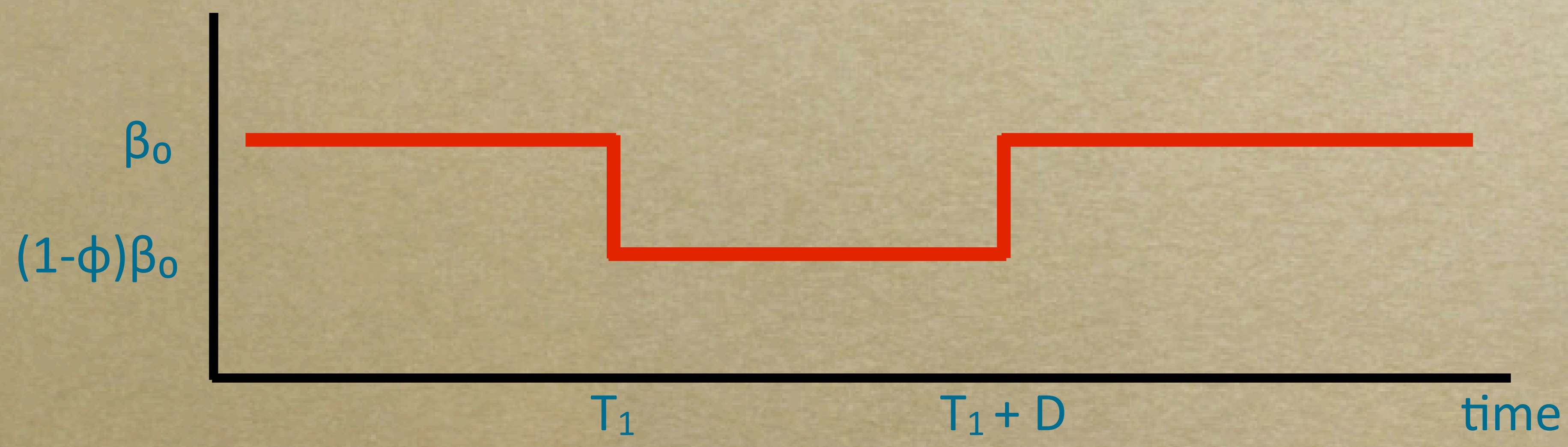
- Pandemic planning

    Consider emerging pathogen
    Everyone susceptible
    No pharmaceutical defense (drugs/vaccines)
    Only Non-Pharmaceutical Interventions would work

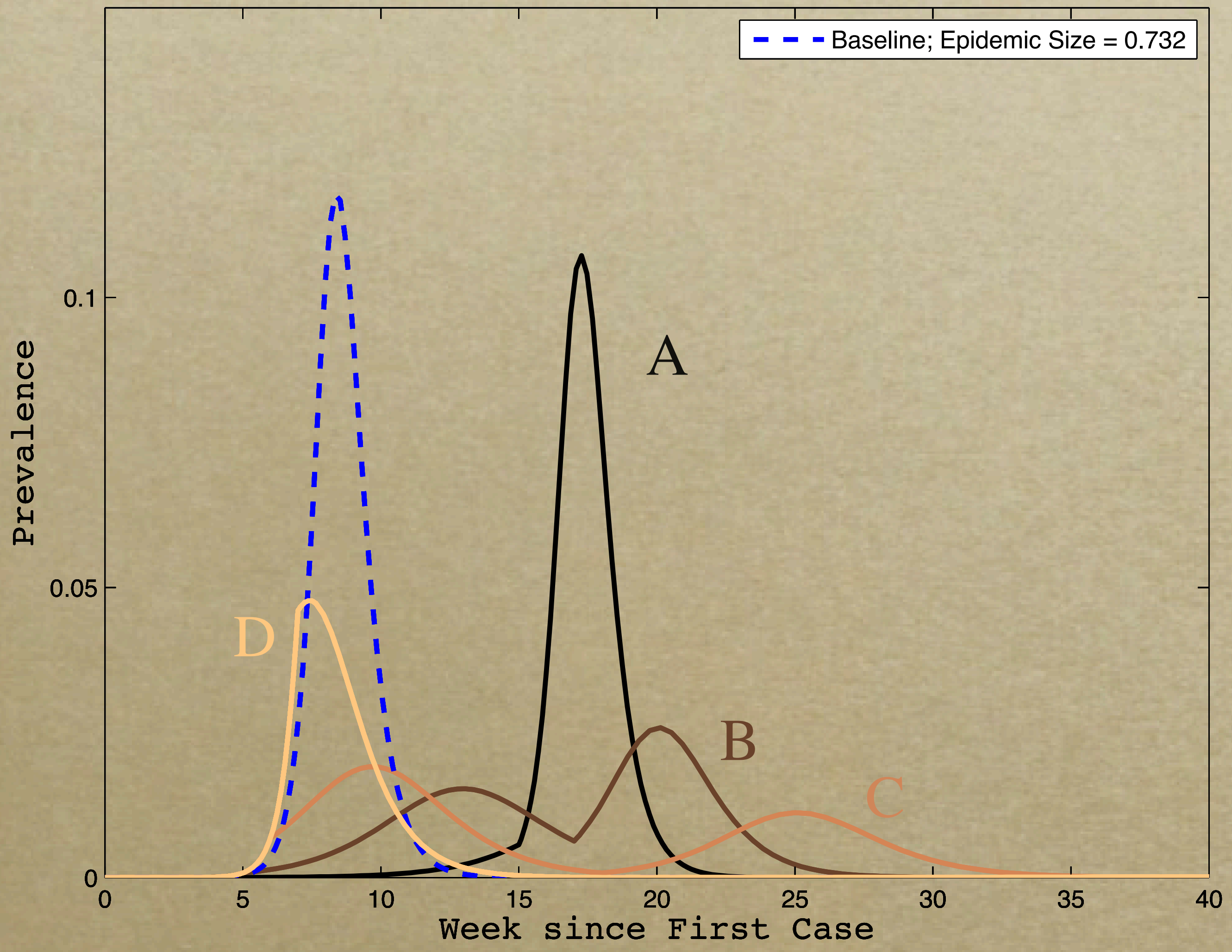
  Social distancing
    How long?
    What extent?

Protocol

- Basic reproduction ratio $R_0 = 1.8$
- Recovery rate $\gamma = 1/2.6$ day^{-1}
    - Generation time 2.6 days
- Baseline transmission rate $\beta_0 = R_0\,\gamma$
- Population size $n = 58.1$ million (UK)



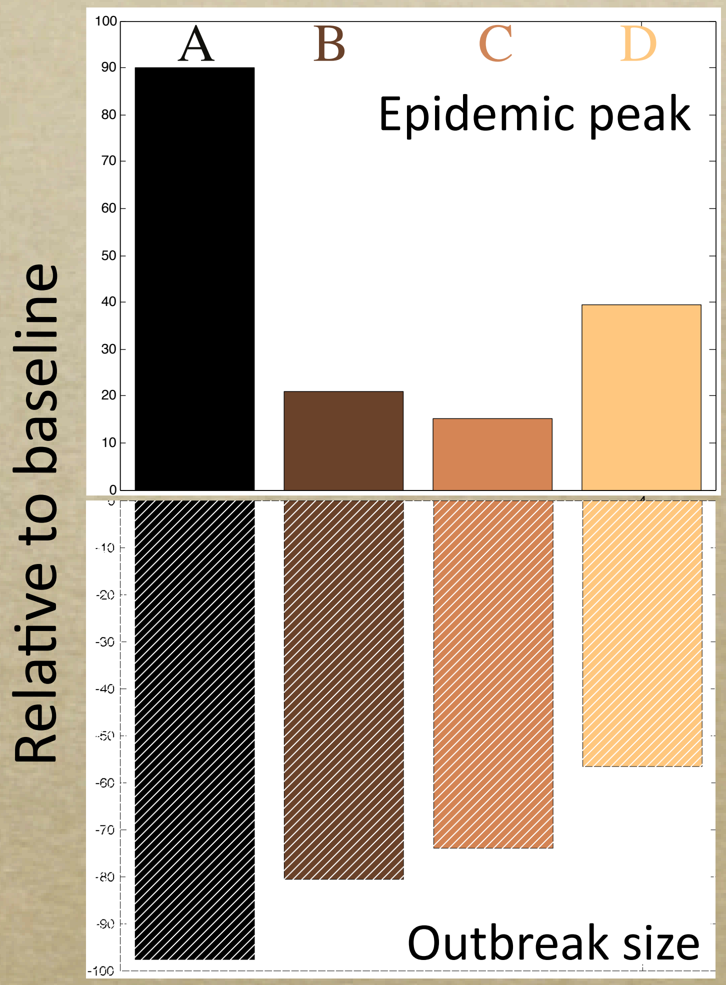
Intervention D=12 weeks



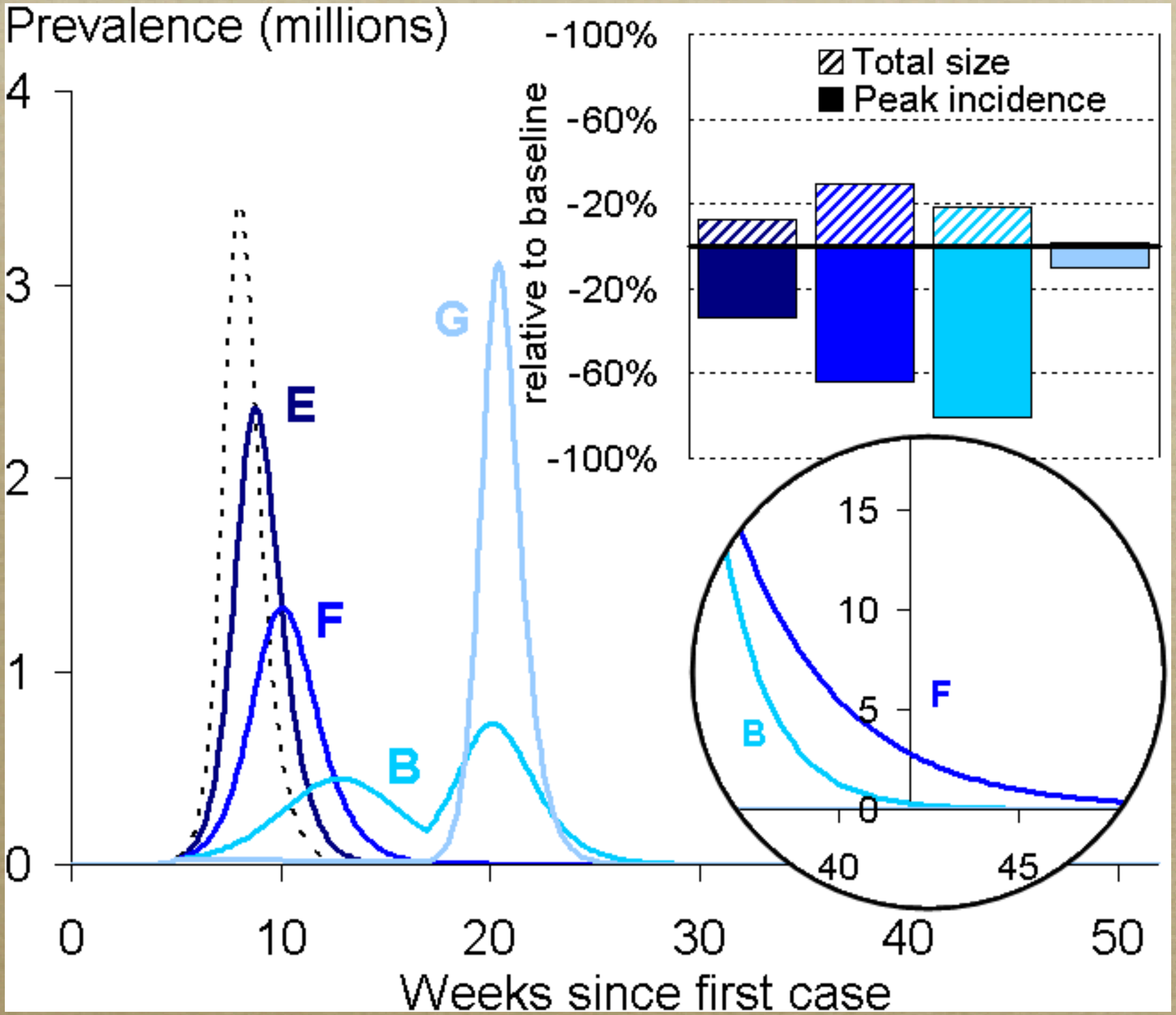
Intervention ϕ = 0.333

Start (week)

- A: T_1 = 3
- B: T_1 = 5
- C: T_1 = 6
- D: T_1 = 7



Intervention D=12 weeks



- Start (week) $T_1 = 5$
- Intervention

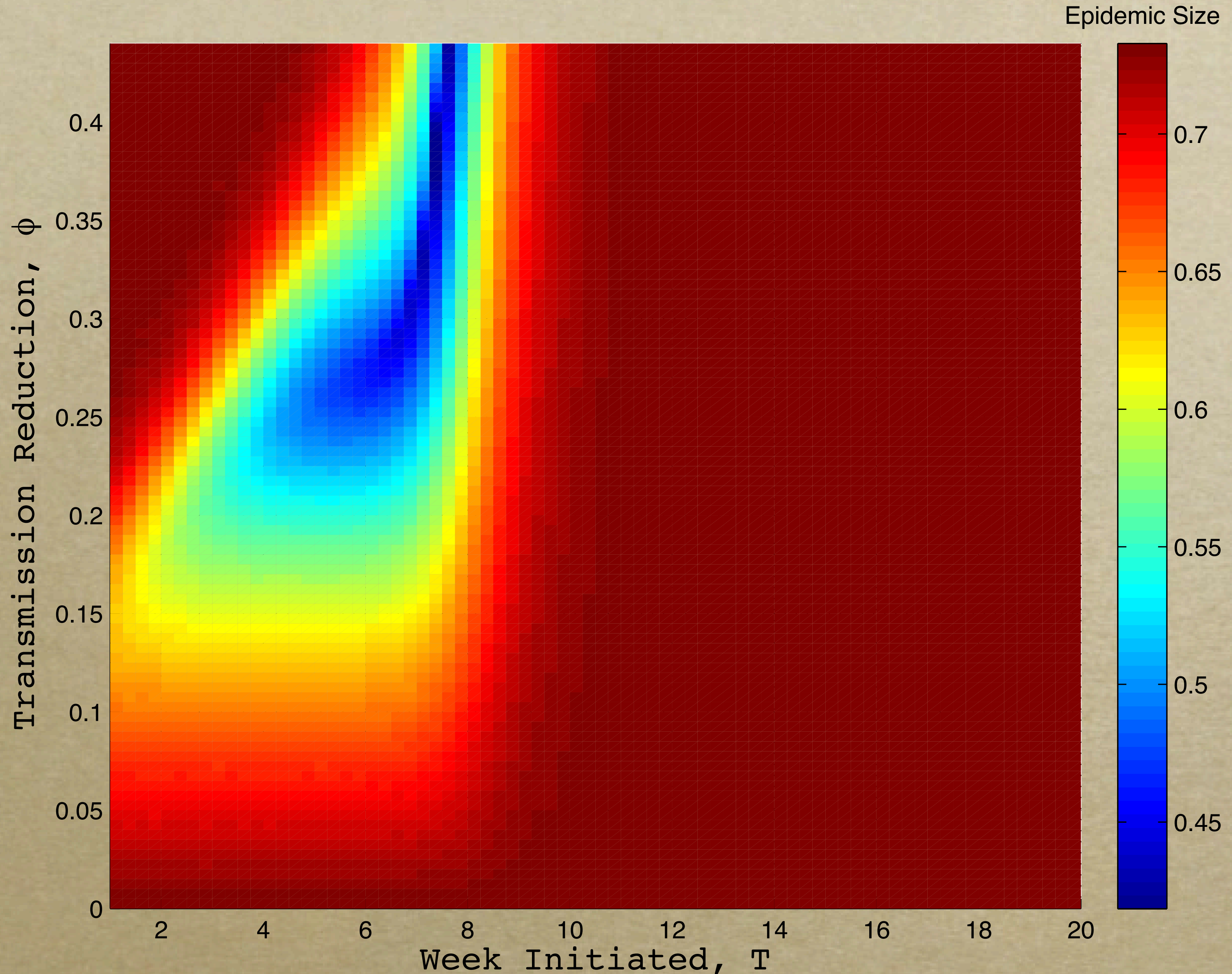
E: $\phi = 0.111$

F: $\phi = 0.222$

B: $\phi = 0.333$

G: $\phi = 0.444$

Intervention D=12 weeks



Depending on aims of control, efforts that are too early or too severe may be counter-productive

Lecture Summary …

- *Models can generate predictions about immunization levels required for eradication*
- *Similarly, extent of non-pharmaceutical interventions can be gauged*
- *NPIs leave many susceptibles behind*
  - *Important for re-introductions*
- *Infections with much silent transmission very difficult to control with NPIs*