Controlling Infectious Diseases

(vaccination, isolation & quarantine, & physical distancing)

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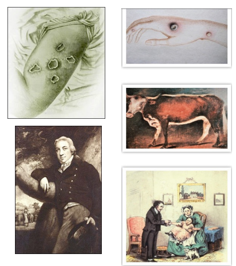
Edward Jenner



Source: National Library of Medicine & the Jenner Museum

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Smallpox Eradication

- Intensive global campaign by WHO results in smallpox eradication in 1977 (last case, Somalia).
- Key factors: human reservoir, effective (live) vaccine, cases easily identified.

Image source: CDC Public Health Image Library. http://phil.cdc.gov

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Vaccination: Concept

- Vaccines are biological substances or microorganisms that confer **immunity** to infectious disease that could otherwise only be obtained through natural infection.
  - Move directly to immune state without having to risk morbidity and (sometimes) mortality associated with natural infection.
  - **Utilitarian** framework:
    - Vaccines not risk free, societal adoption of vaccination presumes **net** reduction in mortality & morbidity (and sometimes costs).

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What Are We Trying To Achieve Through Vaccination?

- Protection of an **individual** who encounters a source of infection.
  - Modification of clinical illness, if vaccination fails.
- Elimination of conditions that permit **disease transmission** in the population ("herd immunity").
  - Elimination (from geographic area) or eradication (extinction) of infectious disease.

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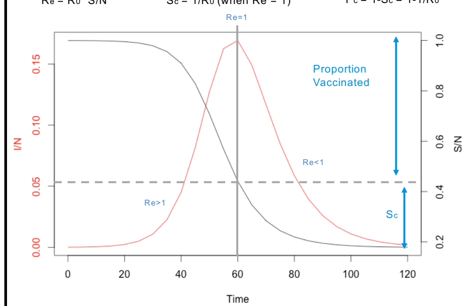
$R_e = R_0 * S/N$ $S_c = 1/R_0$ (when $R_e = 1$) $P_c = 1 - S_c = 1 - 1/R_0$



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Conditions for Herd Immunity (Vaccine with 100% Efficacy)

For no epidemic, Re < 1

$Re = (1-P_c) \times R0$

$(1-P_c) \times R0 < 1$

$1-P_c < (1/R0)$

$1 – (1/R0) < P_c$

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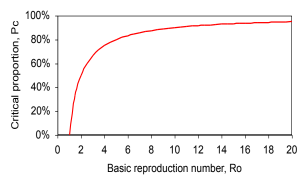
Example: Critical Fraction to Vaccinate

- For a disease with $R_0 = 3$
- $1-1/R_0 = 1-0.33 = 0.67$
- $R_e<1$ when $P_c > 0.67$ or 67%.



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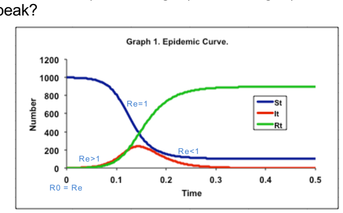
Why does the incidence of an immunizing infection cycle over time?

1. What can we say about the Re when the disease incidence is 1) increasing, 2) decreasing, 3) at the peak?



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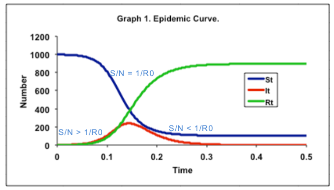
1. Given that Re is related to the proportion of the population susceptible

Re = R0 * (proportion Susceptible)

What can we say about the proportion of the population susceptible when disease incidence is 1) increasing, 2) decreasing, and 3) at the peak?



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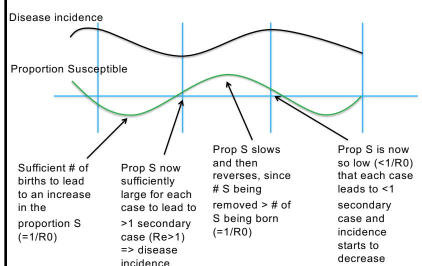
Entry of new susceptibles



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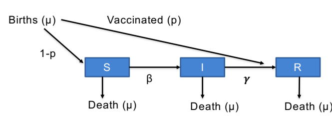
Measures to reduce S/N

- Pediatric immunization (treated as fraction, p, of newborns vaccinated)



Write out the equations!

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

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

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

Eradication requires that $p = 1-1/R_0$
This is the fraction of newborns to be immunized for (eventual) control.

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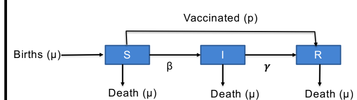
Measures to reduce S/N

- What if we can't/don't vaccinate newborns? Need continuous vaccination instead. Is there anything this figure doesn't account for? Simplifying assumptions?



Write out the equations!

14

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

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

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

Eradication requires that $p \geq \mu(R_0-1)$
This is the rate of susceptibles to be immunized for (eventual) control.

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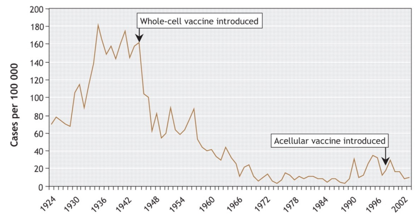
Fig. 1: Pertussis incidence rate, Canada, 1924-2002



Galanis, E. et al. CMAJ 2006;174:451-452

CMAJ·JAMC

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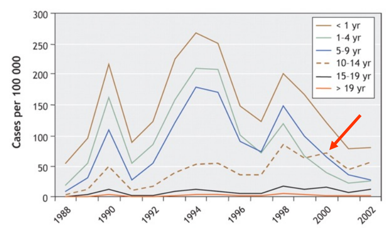
Fig. 2: Age-specific pertussis incidence rates, Canada, 1988-2002



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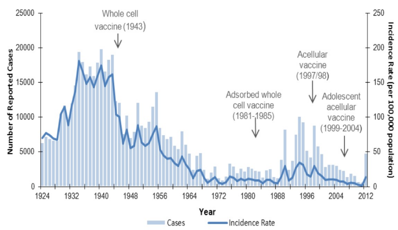

*Case data from 1924 to 2011 were obtained from the Canadian Notifiable Diseases Surveillance System. Case data for 2012 were obtained directly from provinces and territories by CIRID and are preliminary. PEI did not report 1924-1928; Newfoundland did not report until 1949; Yukon did not report 1924-1955; Northwest Territories did not report 1924-1958; Nunavut data for 1999 are only partial, for 2007 & 2009 are missing, and for 2008, 2010-2011 are preliminary. Population data (July 1st annual estimates) were obtained from Statistics Canada.

CCDR, Feb. 2014

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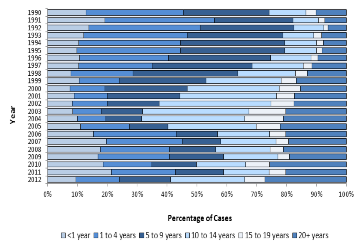
Figure 4. Age distribution of pertussis cases in Canada, 1990 to 2012*



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CCDR, Feb. 2014

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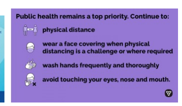
How do we control SARS-CoV-2 with a vaccine?

$R_0 = c \times p \times D$

c = contact rate

p = probability of transmission given an infected contact

D = duration of infectiousness



Combined with rapid test, trace, isolate

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And now some vaccine math…

The effective reproduction number (R_e) varies depending on the basic reproduction number (R_0), the proportion of the population that is fully vaccinated (x), and the effectiveness of the vaccine (V).

$$R_e = R_0 * (1 - x * V)$$

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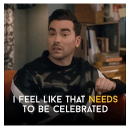
R_e for **OG** = 2.50*(1-0.76*0.94)
R_e (vaccine alone) = 0.73



R_e for **alpha** = 3.75*(1-0.76*0.94)
R_e (vaccine alone) = 1.1

R_e for **delta** = 7.5*(1-0.76*0.85)
R_e (vaccine alone)= 2.6

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R_e for **omicron (25 weeks after dose 2)** = 12*(1-0.76*0.09)
R_e (vaccine alone) = 11.6

R_e for **omicron (10 weeks after dose 3)** = 12*(1-0.76*0.46)
R_e (vaccine alone) = 7.8

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Age Structure and Partial Vaccination

- Can build **age-structured** models by subdividing model "compartments" to reflect different age-groups.
- Using age-structured model can derive the relationship:

$$R_0 \approx L/A$$

- L=life expectancy, and A = average age at infection.

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With Vaccination

↓R ≈ L/A↑

- When might age at first infection be relevant?
- How might partial vaccination of the herd be **harmful**?

$$A \approx \frac{1}{\mu R_0} \quad \Rightarrow A \approx \frac{L}{R_0} \quad \Rightarrow R_0 \approx \frac{L}{A}$$

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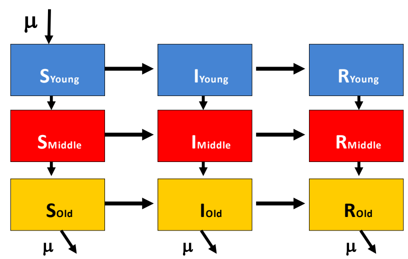
Simple Age-Structured Model



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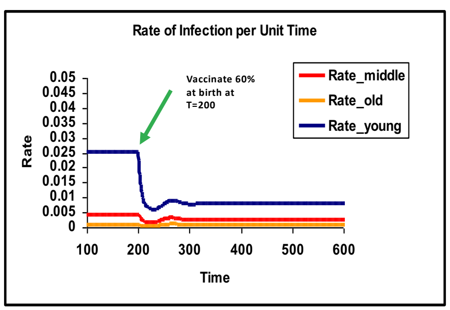

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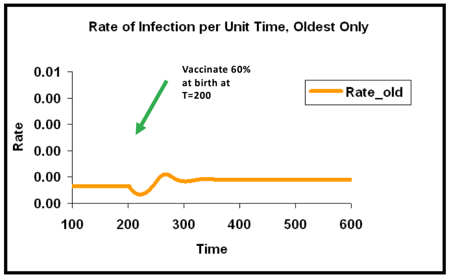

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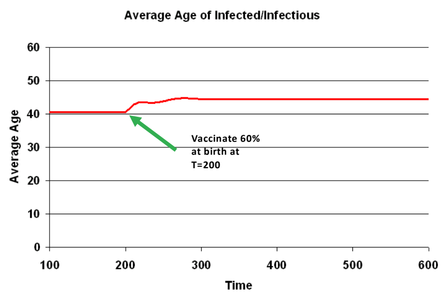

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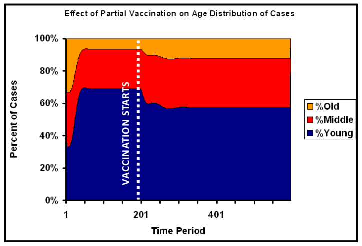
Proportion of Cases in Older Age Groups



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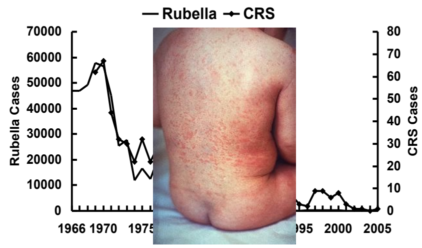
Rubella - United States, 1966-2005*



Source: US CDC, National Immunization Program

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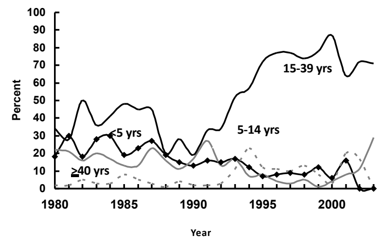
Rubella - United States, 1980-2003
Age Distribution of Reported Cases



Source: US CDC, National Immunization Program

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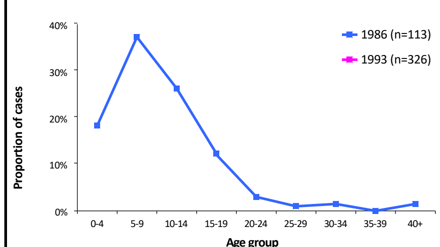
Age distribution of outpatient rubella cases, Athens



Source: Panagiotopoulos et al, BMJ, 1999, slide courtesy of Dr. John Edmunds

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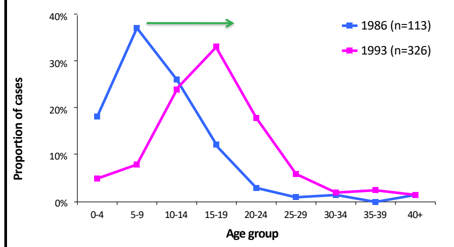
Age distribution of outpatient rubella cases, Athens



Source: Panagiotopoulos et al, BMJ, 1999, slide courtesy of Dr. John Edmunds

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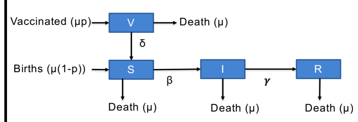
Imperfect vaccines

- In some cases, vaccine induced immunity wanes over time.



Write out the equations!

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

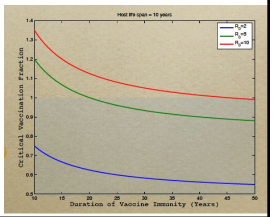
$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I$$

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

Eradication requires that:

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

Eradication is going to require boosters!



From Rohani and Drake

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"Catch Up" Vaccination and Boosting

- **Catch-up vaccination**: Means of overcoming increased age at infection due to decreased FOI when new vaccine introduced.
  - E.g., U.K. introduces rubella vaccine *simultaneously* for infants and 12 year-olds.
    - No late spike in CRS in U.K. following rubella vaccination, unlike U.S.
- **Boosting** when immunity wanes: diminished secondary failures.
  - E.g., pertussis boosting now advocated for pre-teens in Canada.

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Summary

- Partial vaccination of herd predicted to increase average age at infection via decreased FOI, cohort effect, and advanced age at secondary failure.
  - May be desirable if disease is more dangerous to young, undesirable if more dangerous to older individuals.
- Overcome through "**catch-up**" vaccination and **boosting**.

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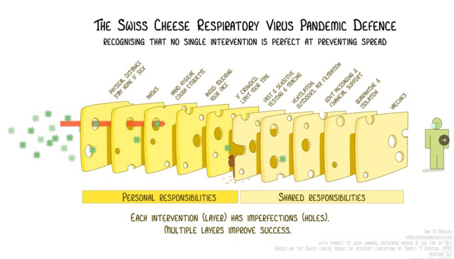

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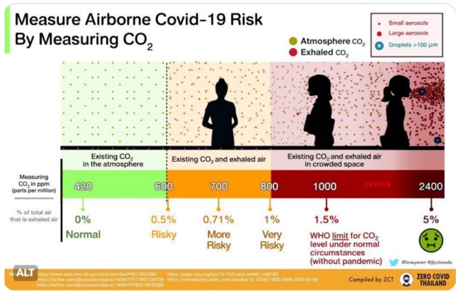

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Non-pharmaceutical interventions

- Physical distancing
- Test, trace, isolate
- Quarantine

What are some of the challenges with these types of interventions?

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Pandemic planning as a case study

- Emergence of a novel pathogen
- Entire population is Susceptible
- No pharmaceutical interventions
- NPI are the only option

- How long?
- To what extent?

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Table 1 Parameter values and assumptions used for the Canadian antiviral stockpile model

Item	Strain	Value (range)	Reference(s)
Transmissibility			
R0	1957/1958	1.6 (attack rate = 37%)	[8,26,34-36]
	1968/1969	1.8 (attack rate = 41%)	[8,26,34,35,37,38]
	1918	2.0 (attack rate = 45%)	[8,26,34,35,39,40]
Natural history			
Latent period	Seasonal	2.1 days	[41]
Duration of infection	Seasonal	4.8 days	[41]
Pre-existing immunity in individuals > years		0% (0 – 40%)	Assumption
Clinical characteristics			
Proportion symptomatic	1957	60%	[8]
Proportion of symptomatic cases seeking medical attention	1957	70%	[8]

Table 2 Parameter values and assumptions for implementing social distancing into the model

Social distancing parameters

Item	Experience	Value (range examined)	Reference
Proportion of the population *intending* to engage in social distancing	1. Avoiding crowded places	56% (31-81%)	[1,2,51-55]
	2. Avoiding public transportation		
	3. Avoiding public places		
	4. Changing school / work arrangements		
Magnitude of behaviour change	Percent reduction in contacts	38% (7 – 69%)	[13]
Start of social distancing behaviours	Assumption	2 weeks after first imported case	Assumption
Number of weeks that behaviour change is maintained	Assumption	16 weeks (12 – 24 weeks)	[53]
Effect of age on behaviour change	Assumption	No effect	[2,56]

Greer, 2013

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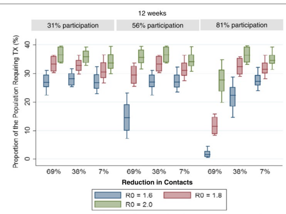

Figure 1 The median (line within the shaded box), 25th and 75th percentile values (top and bottom of shaded box), and upper and lower adjacent values (error bars) proportion of the Canadian population expected to require antiviral treatment (Y-axis) during a severe pandemic as a function of viral transmissibility and the magnitude of change maintained for 12 weeks. Each box represents 9 individual simulation runs using a range of pre-existing immunity values from 0-40%. We examined three different levels of behaviour change uptake where between 31% and 81% of the Canadian population engages in social distancing behaviour. The magnitude of the behaviour change ranged from only a 7% reduction in contacts to a 69% reduction in contacts for all scenarios.

Greer, 2013

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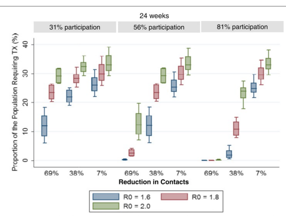

Figure 3 The median (line within the shaded box), 25th and 75th percentile values (top and bottom of shaded box), and upper and lower adjacent values (error bars) proportion of the Canadian population expected to require antiviral treatment (Y-axis) during a severe pandemic as a function of viral transmissibility and the magnitude of change maintained for 24 weeks. Each box represents 9 individual simulation runs using a range of pre-existing immunity values from 0-40%. We examined three different levels of behaviour change uptake where between 31% and 81% of the Canadian population engages in social distancing behaviour. The magnitude of the behaviour change ranged from only a 7% reduction in contacts to a 69% reduction in contacts for all scenarios.

Greer, 2013

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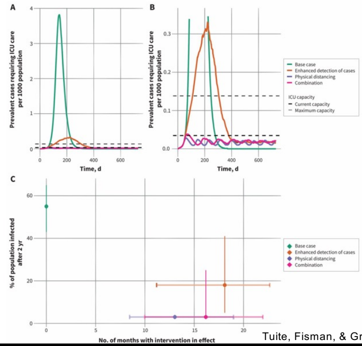

Tuite, Fisman, & Greer, 2020

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Contact Tracing and Isolation

- Assume average contact rate, κ
- Transmission probability, v
- Infectious individuals immediately symptomatic
- Infectious isolated at rate d_1
- Fraction q of contacts with infectious individuals quarantined
- Kept in quarantine for average τQ

From Rohani and Drake

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We now have 5 compartments

- Susceptible
- Susceptible in Quarantine
- Infectious
- Infectious in Isolation
- Recovered

Based on the previous slide, draw out the compartment model and write the associated equations

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Contact, transmission

$$\frac{dS}{dt} = -(\kappa v + q\kappa(1-v))SI + \tau_Q S_Q$$

Contact, no transmission, quarantine

Released quarantine

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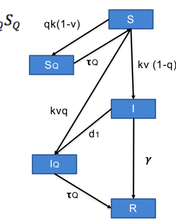
$$\frac{dS}{dt} = -(\kappa v + q\kappa(1-v))SI + \tau_Q S_Q$$

$$\frac{dS_Q}{dt} = q\kappa(1-v)SI - \tau_Q S_Q$$

$$\frac{dI}{dt} = \kappa v(1-q))SI - d_1 I - \gamma I$$

$$\frac{dI_Q}{dt} = \kappa v q SI + d_1 I - \tau_Q I_Q$$

$$\frac{dR}{dt} = \gamma I + \tau_Q I_Q$$



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What does this tell us?

- Can show that control requires

$$S < \frac{d_1 + \gamma}{\kappa v(1-q)}$$

$$\kappa v(1-q) > d_1 + \gamma$$

- If $R_0 = 5$, then $\tau_Q = 21$ days

From Rohani and Drake

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But there are some challenges...

- Assumed infected individuals are immediately symptomatic
- Uncertainties and delays with identifying and isolating potential contacts
- How do these factors work to complicate our ability to control SARS-CoV-2?

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