Epidemiologic Concepts for the Control and Prevention of Infectious Diseases

Tomás Aragón, MD, DrPH

Center for Infectious Disease Preparedness
UC Berkeley School of Public Health
URL: http://www.idready.org
Email: aragon@berkeley.edu

July 28, 2007

Overview/Summary

Learning objectives

At the end of this presentation, attendees will be able to:

- Describe the transmission of microbial agents from an infectious source to a susceptible human host;
- Describe the natural history of infection and infectiousness;
- Describe how humans and microbes interact with each other and their environment to produce infectious disease epidemics.
- Describe characteristics of infectives that $\uparrow$ transmission;
- Describe characteristics of susceptibles that $\uparrow$ transmission;
- Describe six control strategies for interrupting transmission;
- Design control measures based on the six control strategies

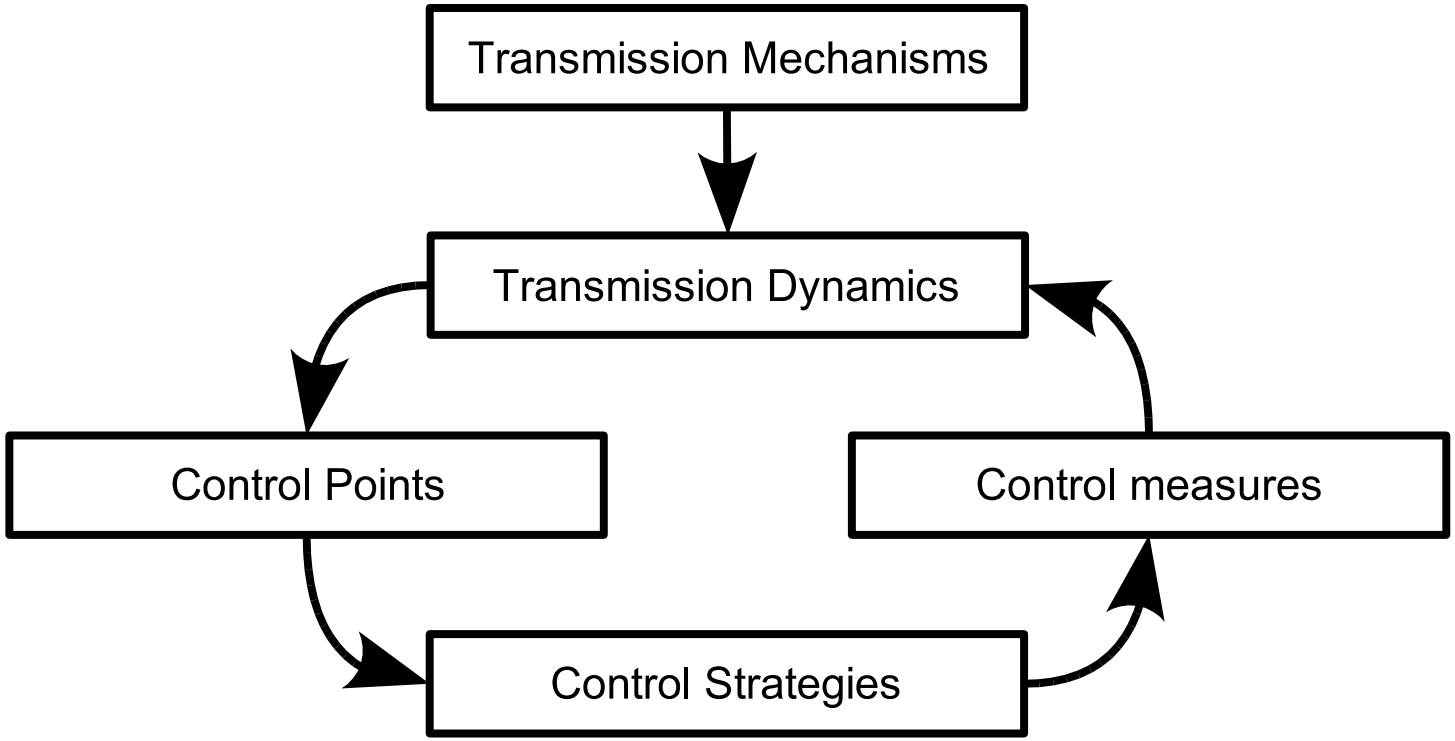
Understanding interventions to control infectious diseases

- Alter risk factors (e.g., behavior)
- Post-exposure prophylaxis
- Diagnosis, treatment
- Vaccination, immune globulin
- Infection control practices
- Case finding and isolation
- Contact tracing and quarantine
- Environmental disinfection
- Identify and control infectious sources

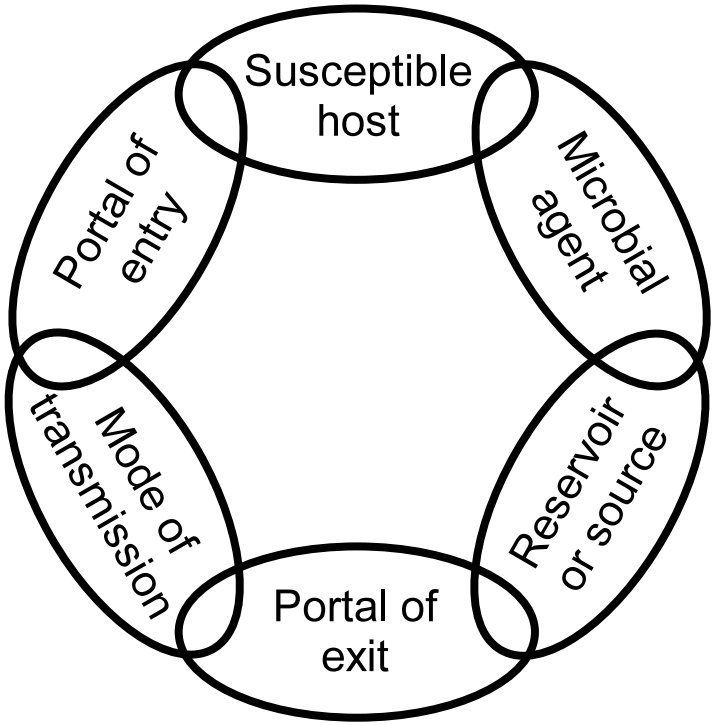
Use of epidemiologic concepts

- Control of acute microbial threats
- Prevention of infectious diseases
- Outbreak investigations
- Diagnosis & treatment
- Research

How are epidemiologic concepts related?



Chain model of infectious diseases



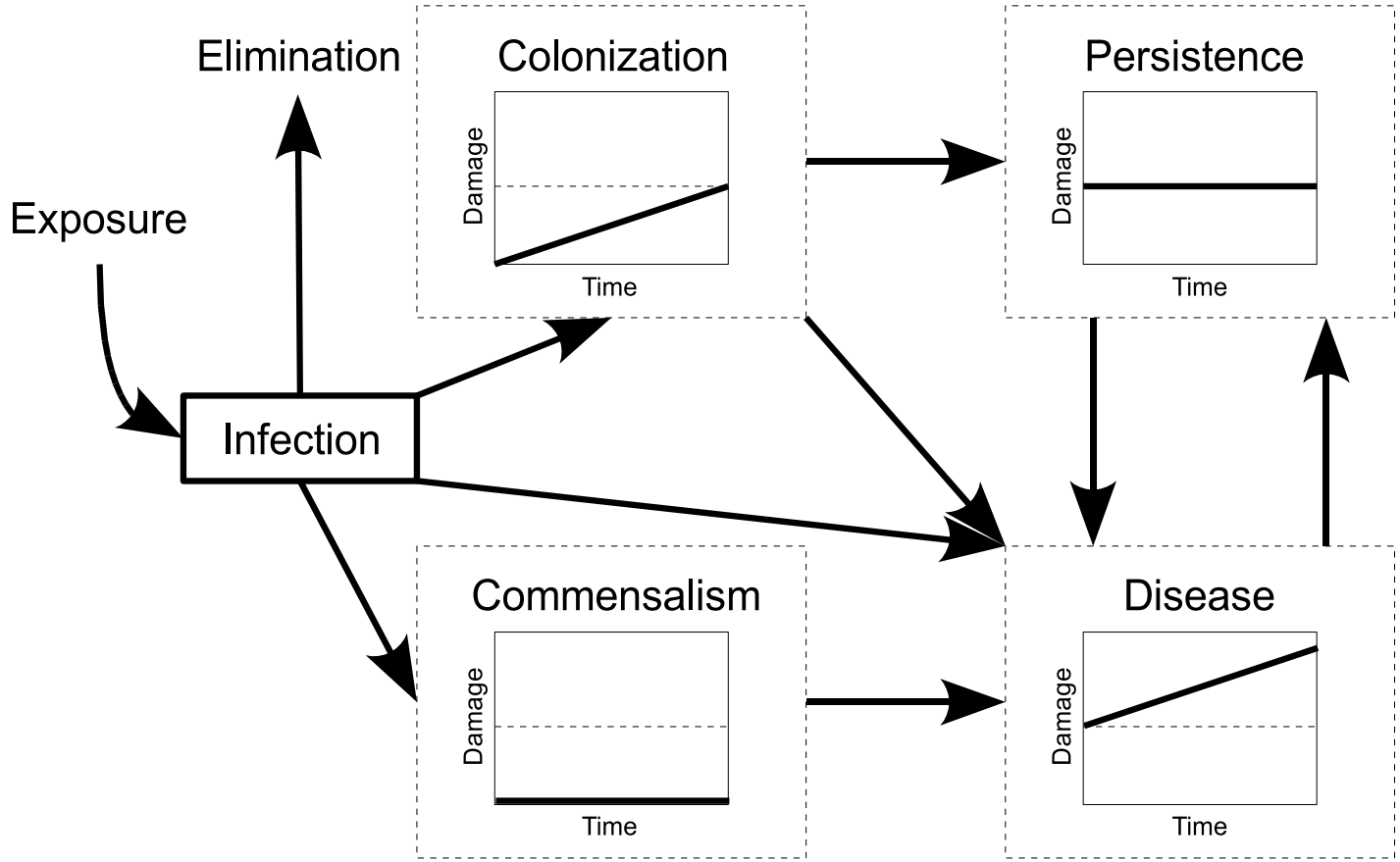
Source: Epidemiologic Methods for the Study of Infectious Diseases, Oxford University Press 2001

Causative agents

Transmissible microbe, microbe-like, or microbial toxin

- Bacteria
- Viruses
- Fungi
- Parasites (protozoa, multicellular)
- Prions

Damage-response framework of microbial pathogenesis



PMID: 12383613

Some definitions

- Infectivity
- Transmissibility
- Pathogenicity
- Virulence

Reservoirs

- Human
  - Symptomatic illness
  - Carrier states
    - Asymptomatic (no illness during infection)
    - Incubatory (pre-illness)
    - Convalescent (post-illness recovery)
    - Chronic (persistent infection)
- Animal (zoonoses)
- Environmental

Modes of transmission

- Contact
  - Direct contact (e.g., touch, kissing, sex)
  - Indirect contact (e.g., intermediate objects, fomites)
- Respiratory droplets/secretions (e.g., cough, sneeze)
- Airborne (e.g., droplet nuclei, dust)
- Vehicle-borne (e.g., ingestion, instrumentation, injection, infusion)
- Vector-borne (e.g., mechanical, biologic)
- Vertical transmission (e.g., before, during, and after birth)

Good infection control starts with common sense: Cover the source!

Source: American Society of Microbiology

Disease scare at San Jose airport: 5 on flight from Asia examined—none found with SARS I

San Francisco Chronicle, Wednesday, April 2, 2003

In a false alarm heard 'round the world, the Santa Clara County health system jumped into high alert Tuesday morning when an American Airlines flight from Tokyo radioed that it might have five cases of the mysterious flulike illness known as SARS on board.

[Joan] Krizman said she had no hard feelings about being treated as a potential health threat. The couple had just completed an exhausting, monthlong journey that included stops in Vietnam, Thailand and Hong Kong—three Southeast Asian hot spots for SARS.

"There were four fire trucks and eight police cars and four or five ambulances," she recalled. "I couldn't believe it. I thought, 'Wow!

Disease scare at San Jose airport: 5 on flight from Asia examined—none found with SARS II

What's going on here?' Little did I know that we were to be the 'victims.' "

The couple were asked twice to go to Valley Medical Center, and twice they politely declined. "And then," Krizman said, "they soon opened up the ambulance doors and said, sorry, we're taking you to the hospital."

At the hospital, according to Krizman, "we were the only ones there not wearing masks." When word got out just who they were, she said, "People started running like crazy, like we were the bubonic plague. They put us in a room full of people with plastic boots and face shields and masks."

Nurse wearing N-95 respirator outside of intensive care unit

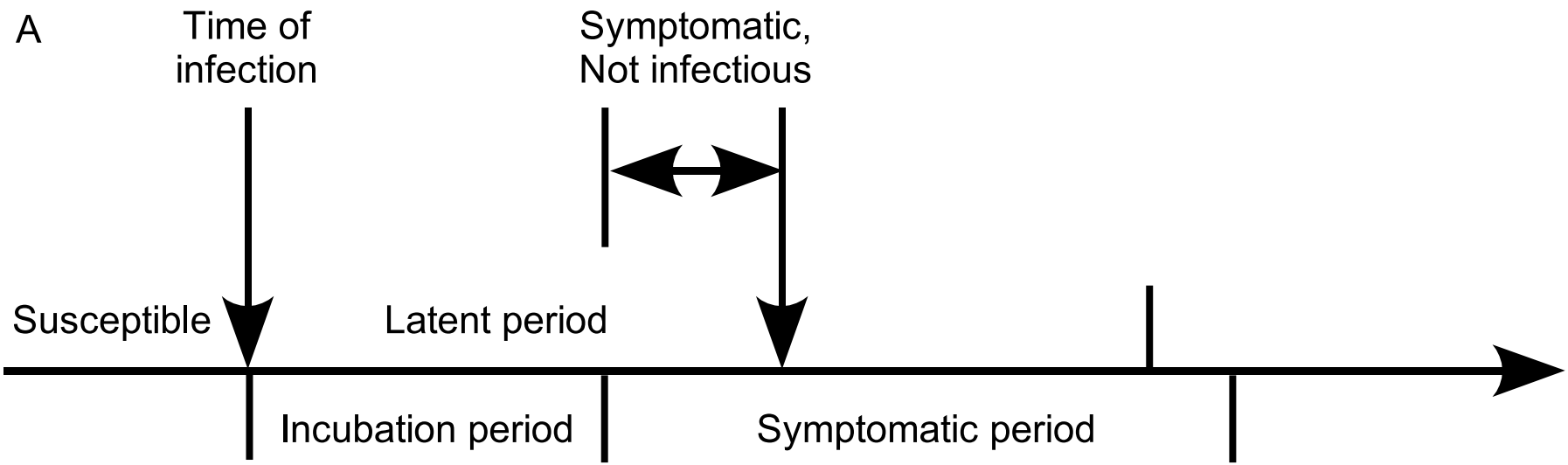
Associated Press: In a ward at Sunnybrook and Womens Hospital in Toronto, a nurse waits outside the door of a patient diagnosed with the illness [SARS].

Public-devised infection control, SARS outbreak, 2003

Inappropriate infection control, SARS outbreak, 2003

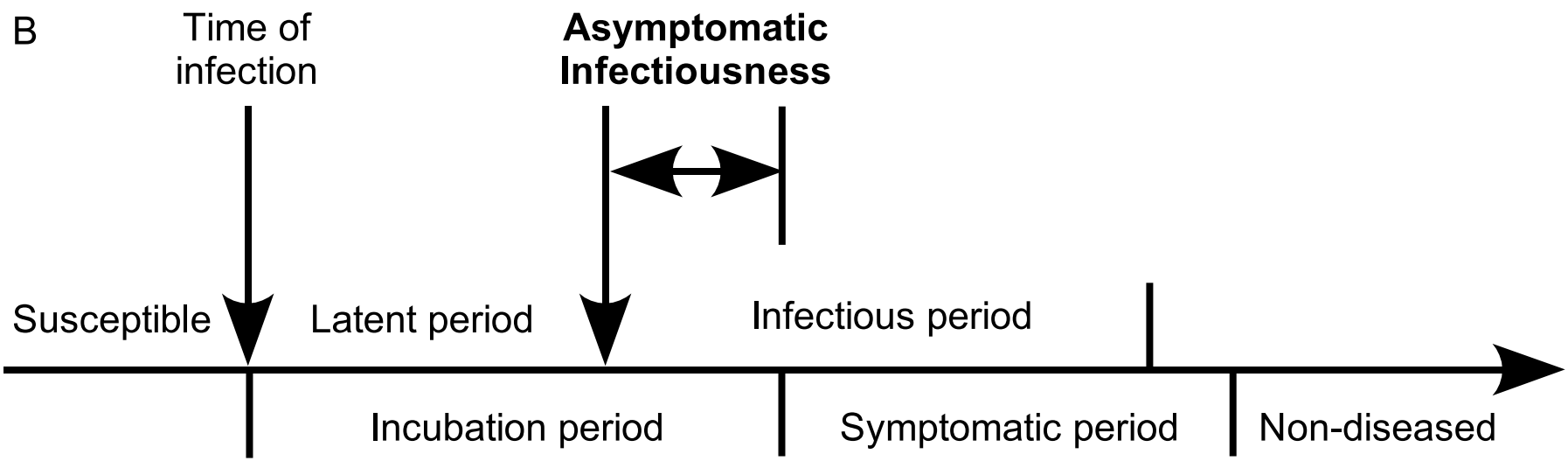
Reuters: An Indian woman diagnosed with SARS sits on her bed at the Doctor Naidu Infectious Diseases Hospital in the western city of Pune. Doctors reported India's first case of the disease in a marine engineer from the western coastal state of Goa on Friday, April 18, 2003.

Figure A: Latent period *longer* than incubation period



When the latent period is *longer* than the incubation period, an infected person becomes infectious *after* symptom onset.

Figure B: Latent period *shorter* than incubation period

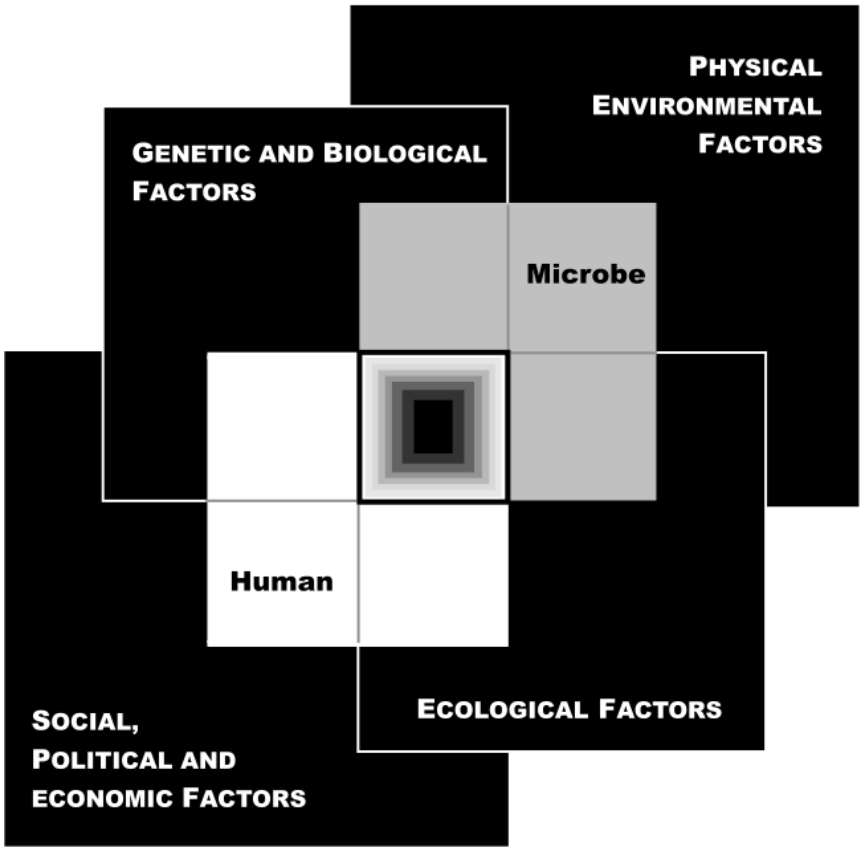


When the latent period is *shorter* than the incubation period, an infected person becomes infectious *before* symptom onset.

Distribution of infectiousness of selected infectious diseases

- Severe acute respiratory syndrome (SARS)
- Human immunodeficiency virus (HIV)
- Smallpox
- Influenza

Convergence model for human-microbe interaction



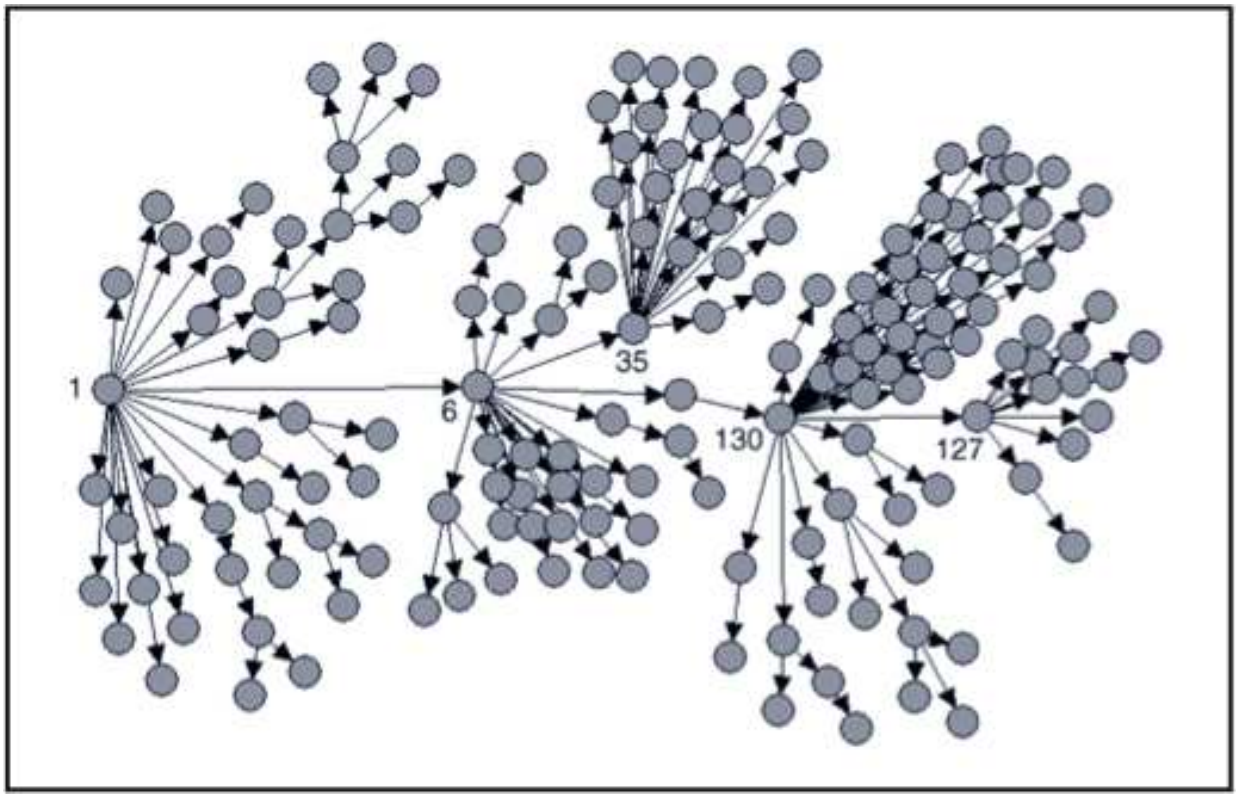
Institute of Medicine. *Microbial threats to health: Emergence, Detection, and Response*. National Academy Press, 2003

Convergence model for human-microbe interaction

- Microbial adaptation and change;
- Human susceptibility to infection;
- Climate and weather;
- Changing ecosystems;
- Economic development and land use;
- Human demographics and behavior;
- Technology and industry;
- International travel and commerce;
- Breakdown of public health measures;
- Poverty and social inequality;
- War and famine;
- Lack of political will; and
- Intent to harm.

Institute of Medicine. *Microbial threats to health: Emergence, Detection, and Response*. National Academy Press; 2003

Reproductive number in action, SARS outbreak, 2003



Probable cases of severe acute respiratory syndrome, by reported source of infection, Singapore, Feb 25-Apr 30, 2003 [PMID: 12807088]

The reproductive number

Effective reproductive number (R)

Average number of secondary infectious cases produced by infectious cases

Basic reproductive number (R_0)

Average number of secondary infectious cases produced by an index case in a susceptible population in the absence of control measures

Control reproductive number (R_c)

The effective reproductive number in the presence of control measures

Basic reproductive number (R_0)

Definition

Average number of secondary infectious cases produced by an index case in a susceptible population in the absence of control measures

Equation

$$R_0 = cpd,$$

where c is the contact rate between and infectious source and a susceptible case, p is the transmission probability, and d is the duration of infectiousness. R_0 is from the perspective of an infectious source.

Effective reproductive number (R)

Definition

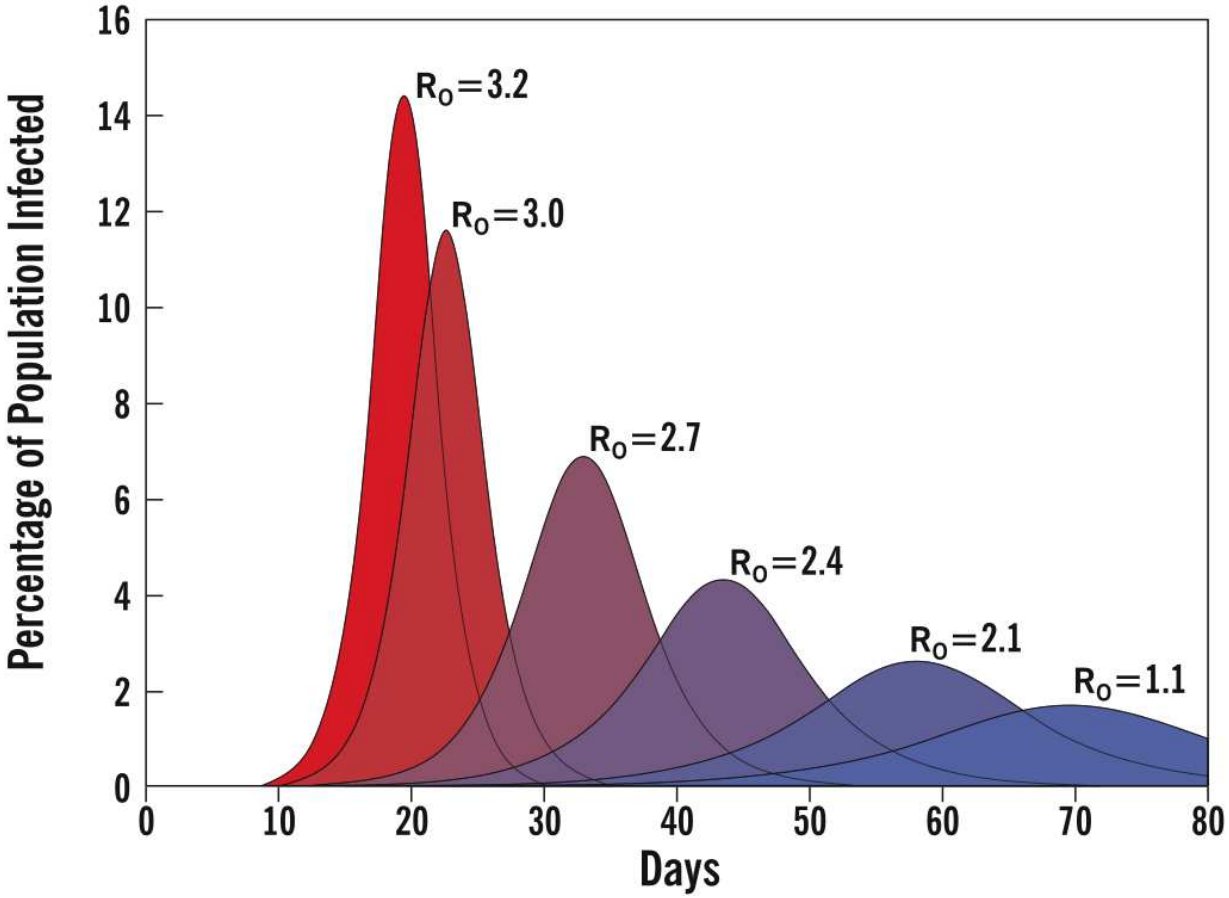
Average number of secondary infectious cases produced by infectious cases

Equation

$$R = R_0 x,$$

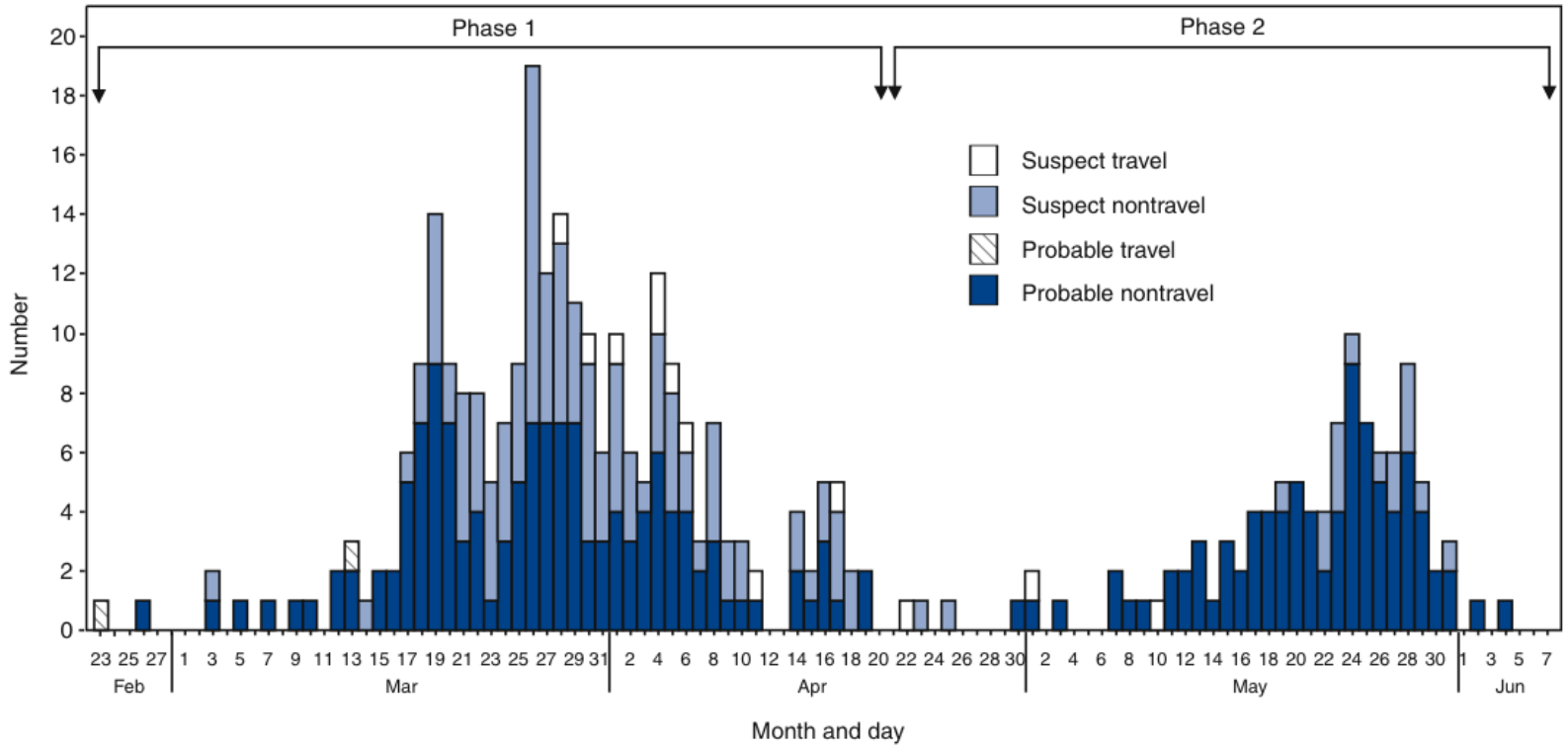
where x is the population fraction that is susceptible at time t.

Effect of R_0 on epidemic curves



Source: Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the U.S. CDC, 2007

SARS epidemic curves—Toronto, Canada, 2003



Number of reported cases ($N = 361$) of severe acute respiratory syndrome, by classification and date of illness onset—Ontario, February 23–June 7, 2003 [PMID: 12803194]

Control reproductive number (R_c): Vaccination example

Definition

The effective reproductive number in the presence of control measures

Equation

$$R_c = R_0(1 - hf),$$

where f is the fraction of population that has been vaccinated (vaccine coverage), and h is the fraction of those vaccinated that have complete protection (vaccine efficacy).

Control reproductive number (R_c): Vaccination example

To achieve our goal

$$R_c < 1$$

Fraction to vaccinate must be

$$f > \frac{1 - (1/R_0)}{h}$$

where f is the fraction of population that should be vaccinated (vaccine coverage), and h is vaccine efficacy.

Herd immunity thresholds for vaccine-preventable diseases

Disease	R_0	Herd Immunity	Immunization levels	
			1999 19–35 months	1997–1998 Pre-school levels
Diphtheria	6–7	85%	83%	9?%
Measles	12–18	83–94%	92%	96%
Mumps	4–7	75–86%	92%	97%
Pertussis	12–17	92–94%	83%	97%
Polio	5–7	80-86%	90%	97%
Rubella	6–7	83–85%	92%	97%
Smallpox	5–7	80-85%	n/a	n/a

Source: `http://www.bt.cdc.gov/agent/smallpox/training/overview/pdf/eradicationhistory.pdf`

Infection rate among susceptible hosts

Standard definition

$$I(\Delta t) = \frac{\text{Number of new infections during} \Delta t}{\text{Person-time at risk during} \Delta t}$$

Definition by components

$$I(t) = cpP(t),$$

where c is the average contact rate of susceptible hosts with a potentially infectious source, $P(t)$ is the probability that the potential source is infectious, and p is the probability of transmission to the susceptible host given contact with the infectious source.

Example: HIV infection rate among susceptibles

Definition by components

$$I(t) = cpP(t)$$

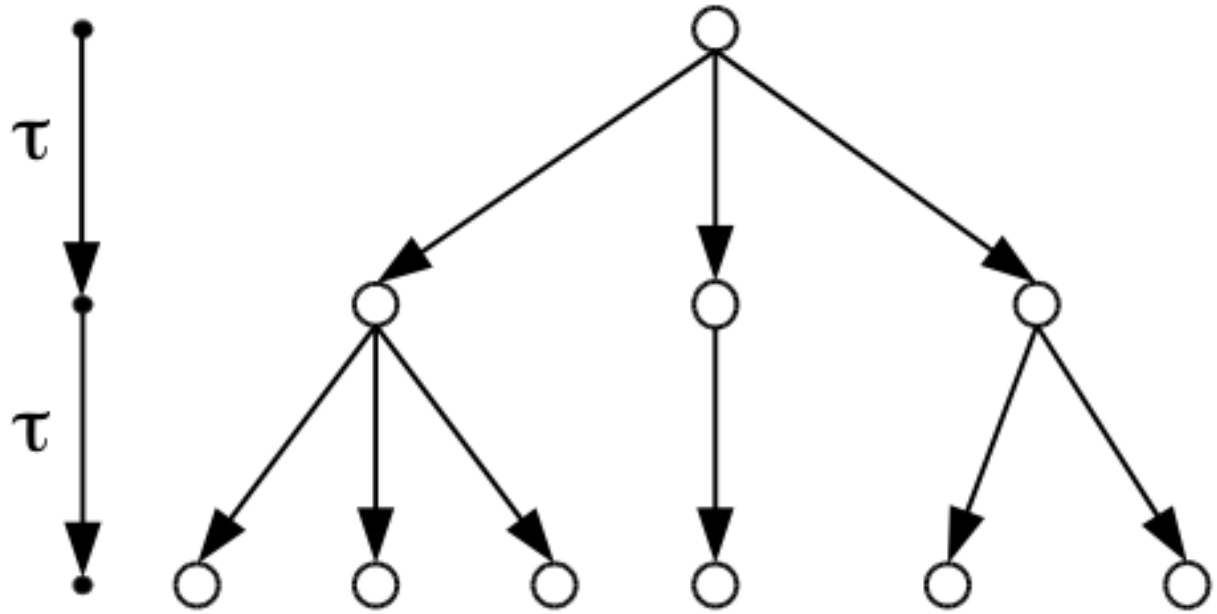
- $c =$ contact rate
  - Unprotected sex
  - Homogeneous mixing
  - Heterogeneous mixing (sexual sorting, risk factor sorting, agesorting, serosorting)
- $p =$ transmission probability
  - Infectiousness (anti-viral therapy)
  - Susceptibility (ulcerative STDs)
  - Interrupt transmission (condoms)
- $P(t) =$ probability potential source is infectious
  - Reduce Prevalence (counseling, testing, and referral)

Estimated per-act risk for acquisition of HIV, by exposure route to an infectious source

Exposure route	Risk per 10,000 exposures
Blood transfusion	9,000
Needle-sharing injection-drug use	67
Receptive anal intercourse	50
Percutaneous needle stick	30
Receptive penile-vaginal intercourse	10
Insertive anal intercourse	6.5
Insertive penile-vaginal intercourse	5
Receptive oral intercourse on penis	1
Insertive oral intercourse with penis	0.5

PMID: 15660015

Generation time



The generation time (τ) is the average time between the onset of symptoms in a given infectious individual and the onset of symptoms in individuals that person has infected. Communicable diseases with shorter generation times require more rapid detection and implementation of control measures. [PMID: 16756684]

Transmission dynamics and control points

Effective reproductive number

$$R = R_0 x = cpdx$$

Infection rate among susceptibles

$$I(t) = cpP(t)$$

Control points	Control strategies
Contact rate (c)	1. Reduce contact rate
Prob. source infectious (P)	2. Reduce P(source infectious)
Transmission prob. (p)	3. Reduce infectiousness
	4. Reduce susceptibility
	5. Interrupt transmission
Duration infectiousness (d)	(see #3)
Fraction susceptible (x)	6. Increase herd immunity

Control strategies

1. Reduce contact rate
2. Reduce P(source infectious)
3. Reduce infectiousness
4. Reduce susceptibility
5. Interrupt transmission
6. Increase herd immunity

Control measures ...

are interventions designed to address control strategies. Always consider mutliple perspectives: host, agent, infectious sources, and environment (physical, social, economic, political, etc.)

Control measures (examples)

1. Reduce contact rate

- Behavior change (host and/or source)
- Case finding for intervention (e.g., isolation)
- Contact tracing for intervention (e.g., quarantine)
- Case isolation
- Quarantine of exposed (individual, community, geographic boundary [Cordon sanitaire])
- Reverse isolation (isolation of non-exposed)
- Reduce number of infectious sources
- Social distancing (school closures, restrict mass gatherings, travel restrictions, etc.)

Control measures (examples)

2. Reduce probability sources are infectious

- Case finding for intervention (isolation, treatment, etc.)
- Identify and control infectious sources
- Vaccination

3. Reduce infectiousness (magnitude and duration)

- Treatment of cases
- Vaccination (Pre- and post-exposure)

4. Reduce susceptibility

- Pre/post-exposure vaccine, immune globulin, or drug
- Treatment of co-factor (e.g., ulcerative STD)

Control measures (examples)

5. Interrupt transmission

- Physical methods (barriers: maks, googles, condoms,, etc.)
- Engineering controls (HEPA filters, negative pressure rooms)
- Environmental controls (eg., disinfection)

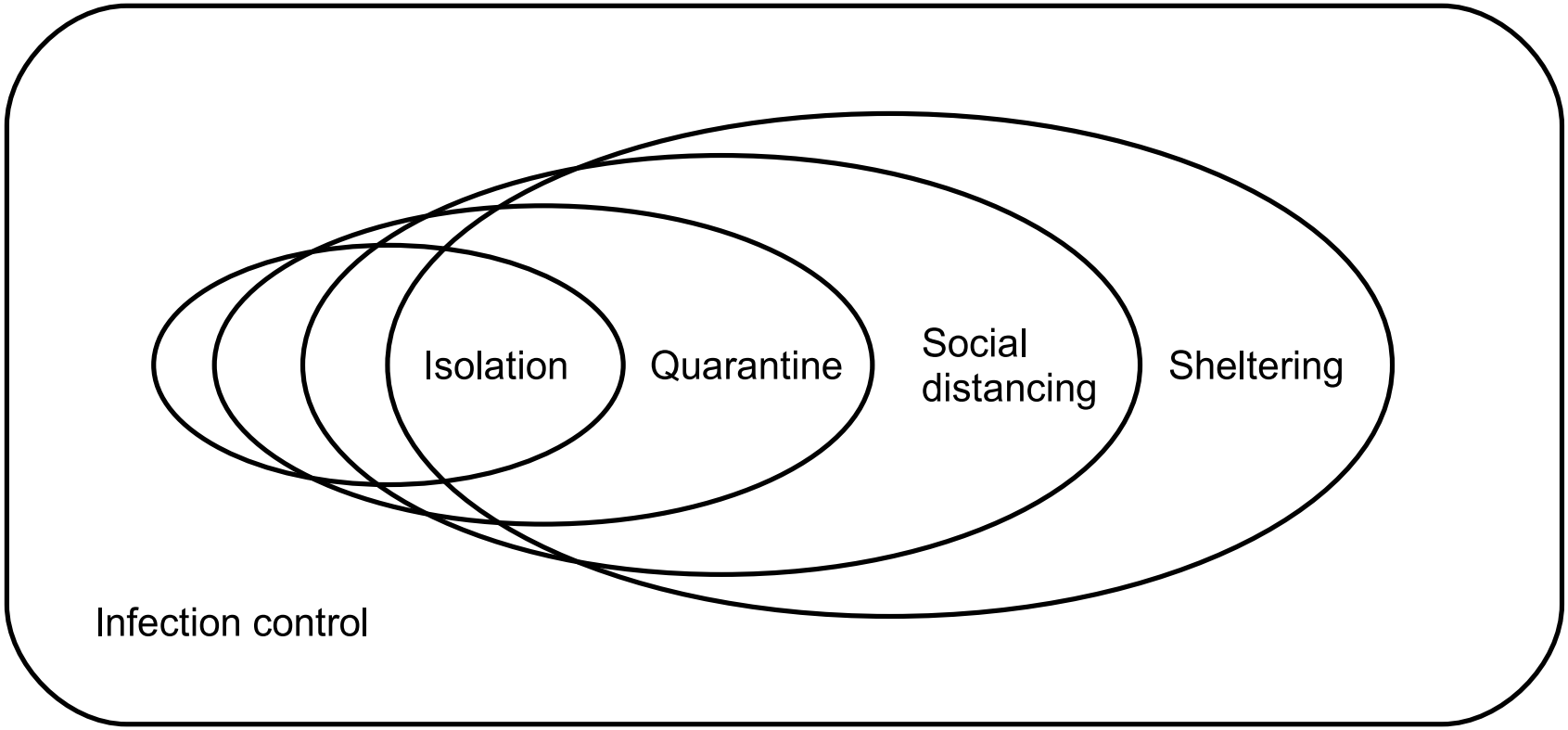
6. Increase herd immunity

- Vaccination, consider the following
  - Naturally acquired immunity
  - Fraction vaccinated
  - Vaccine efficacy

Public health response to human pandemic influenza

1. Surveillance and epidemiology
2. Laboratory diagnostics
3. Transmission containment
   - Community mitigation measures
     - Isolation (of cases)
     - Quarantine (of exposed)
     - Social distancing
     - Sheltering (of non-exposed)
   - Vaccine distribution and use
   - Antiviral drug distribution and use
4. Infection control and clinical guidelines
5. Medical & mental health care, and surge capacity
6. Public health communications (media, public, clinicians, facilities)

Summary of community mitigation measures



Source: http://www.csis.org/component/option,com_csis_pubs/task,view/id,2504/type,1/

Overview/Summary

1. Introduction
2. Transmission mechanisms
   - Chain model of infectious diseases
   - Natural history of infection and infectiousness
   - Convergence model for human-microbe interaction
3. Transmission dynamics
   - Reproductive number
   - Infection rate among susceptibles
   - Generation time
4. Transmission containment
   - Control points
   - Control strategies
   - Control measures