# Concepts for the prevention and control of microbial threats – 1

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# 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



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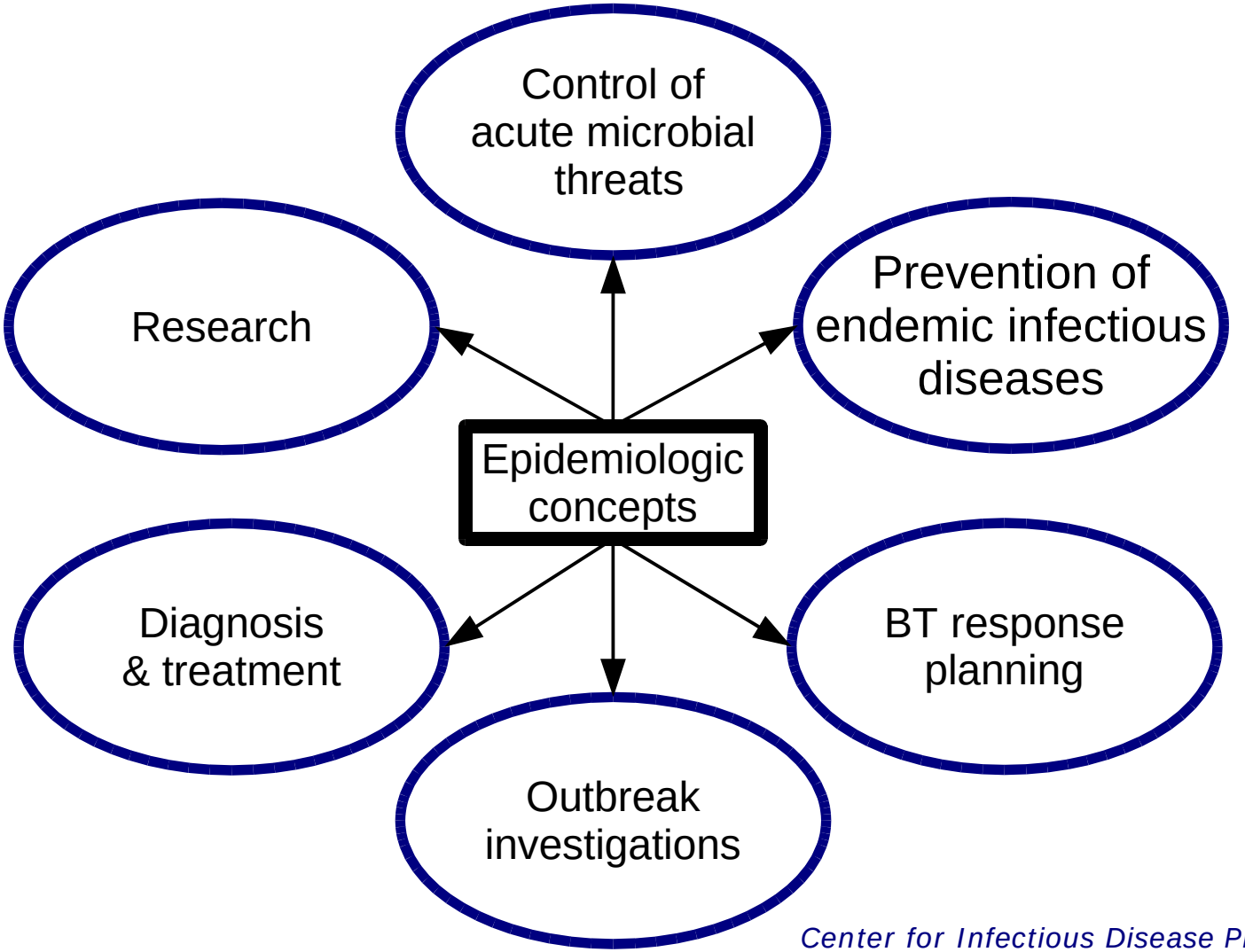
# Use of epidemiologic concepts



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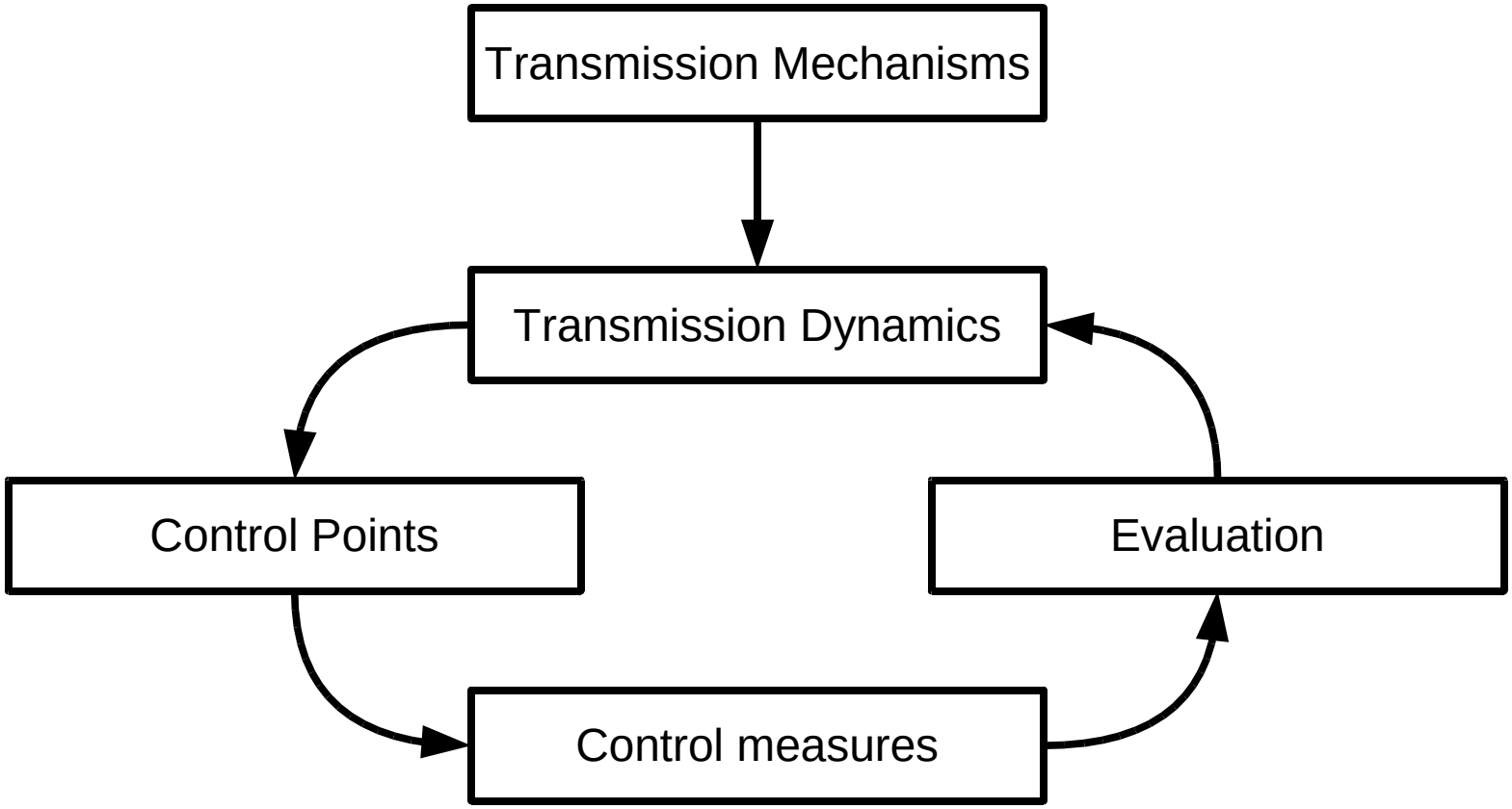
# Epidemiologic concepts for the control of microbial threats



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# Infectious disease epidemiology concepts – Overview

- Mechanisms (Part 1)
  - Chain model of infectious diseases
  - Natural history of infection/infectiousness
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- Dynamics (Part 2)
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- Control points and Control measures



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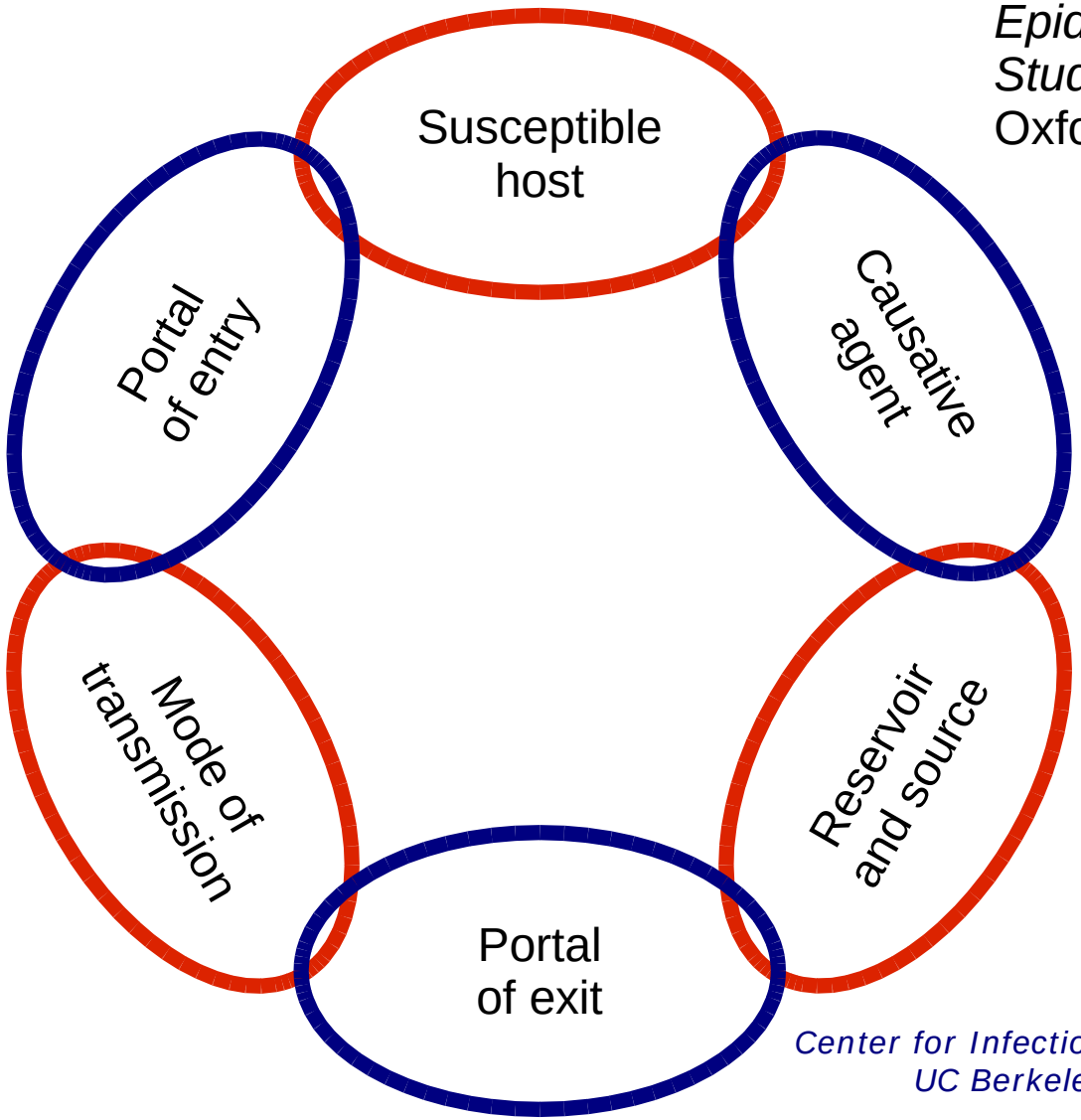
# Chain model of infectious diseases

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



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# Chain model of ID: Causative agent

- Transmissible microbe, microbe-like, or microbial toxin
  - Bacteria
  - Viruses
  - Fungi
  - Parasites (protozoa, multicellular)
  - Prions





# Chain model of ID: Agent transmission and infection

- Transmissibility = P(transmission|exposure[a])
- Infectivity = P(Infection|transmission[b])
- Pathogenicity = P(Disease|Infection)
- Virulence = P(Complication|Disease)

a. Exposure to external source; could be within species (e.g., human influenza to humans) or between species (e.g., avian influenza to humans)
b. Or colonization; could be endogenous



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# Chain model of infectious diseases: Reservoir

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





# Modes of transmission for an exogenous agent

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



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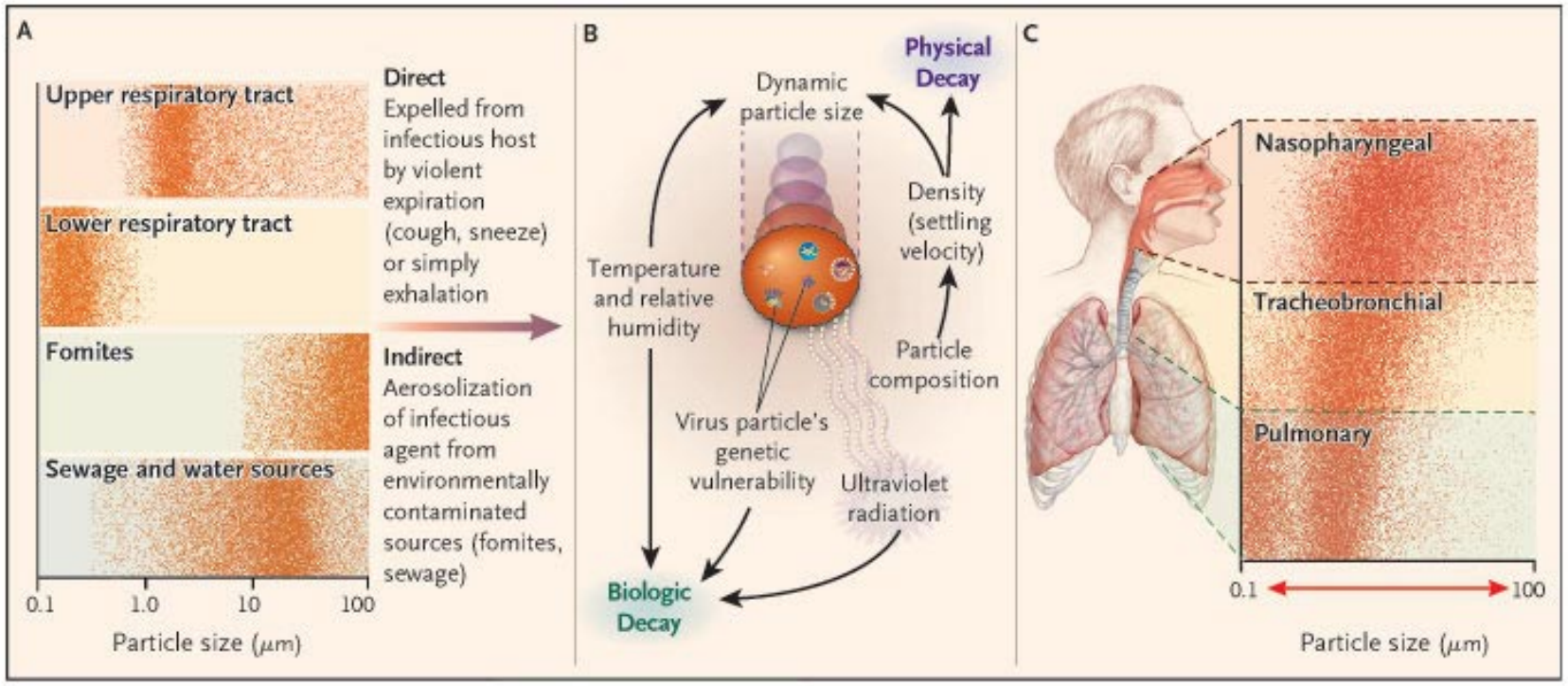
# Aerobiologic transmission of a respiratory microbial agent






PMID: 15102996

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# Good infection control starts with common sense

American Society for Microbiology

*Cover the source!*

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# Disease scare at San Jose airport 5 on flight from Asia examined -- none found with SARS, SF Chronicle 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! What's going on here?' Little did I know that we were to be the 'victims.' "

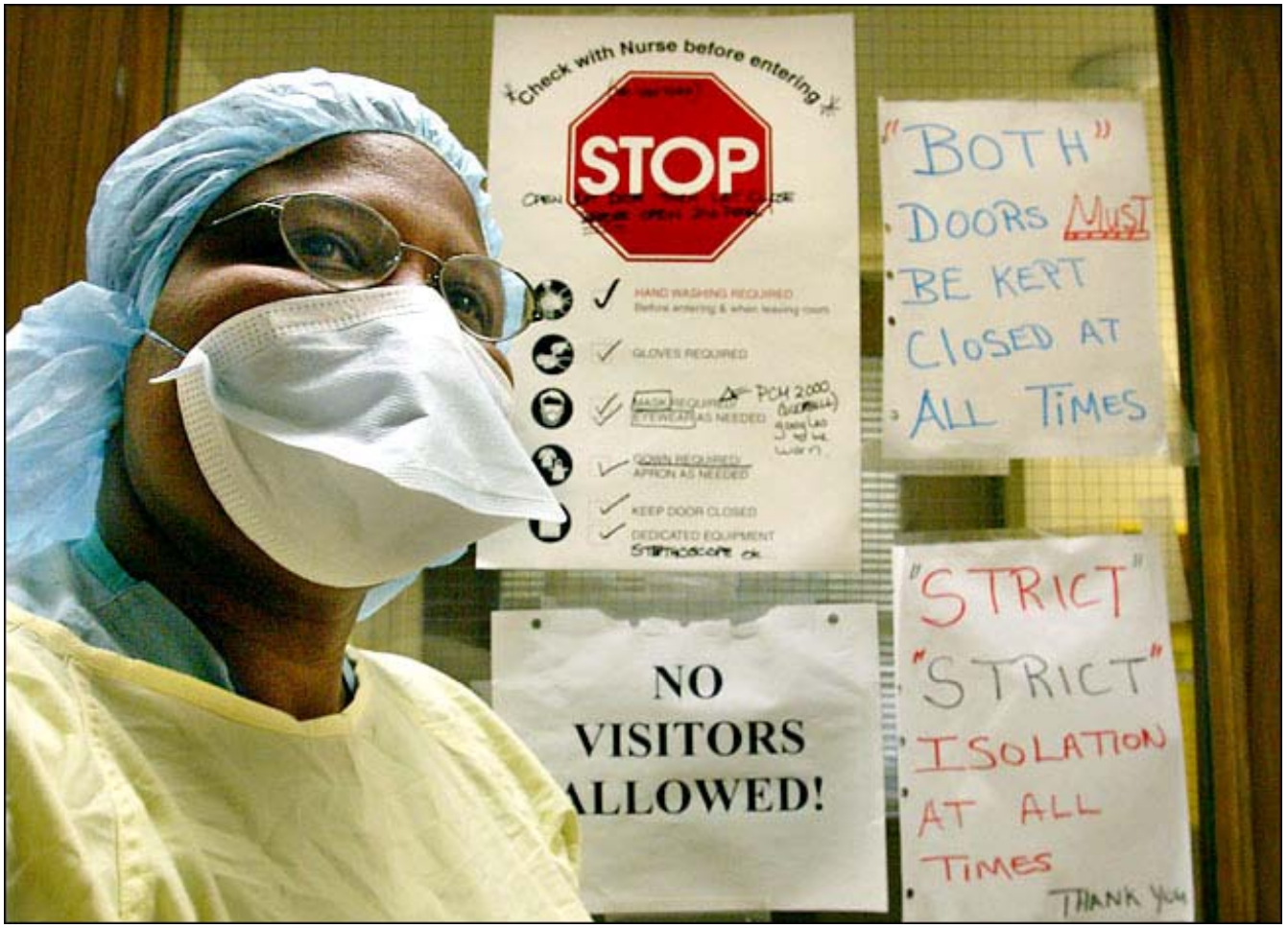
The couple were asked twice to go to Valley Medical Center, and twice they politely declined. "And then," Krizman said, "they soon opened up the ambulance doors and said, sorry, we're taking you to the hospital."

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."



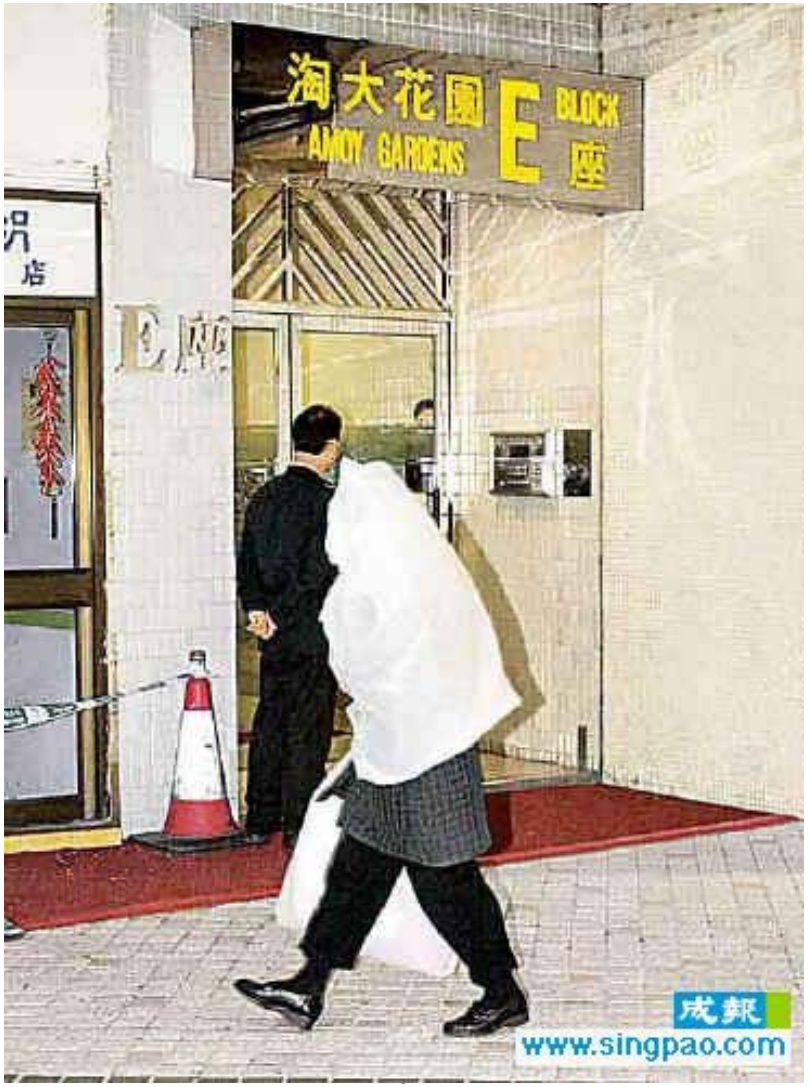


# Nurse wearing N-95 respirator outside of intensive care unit




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].

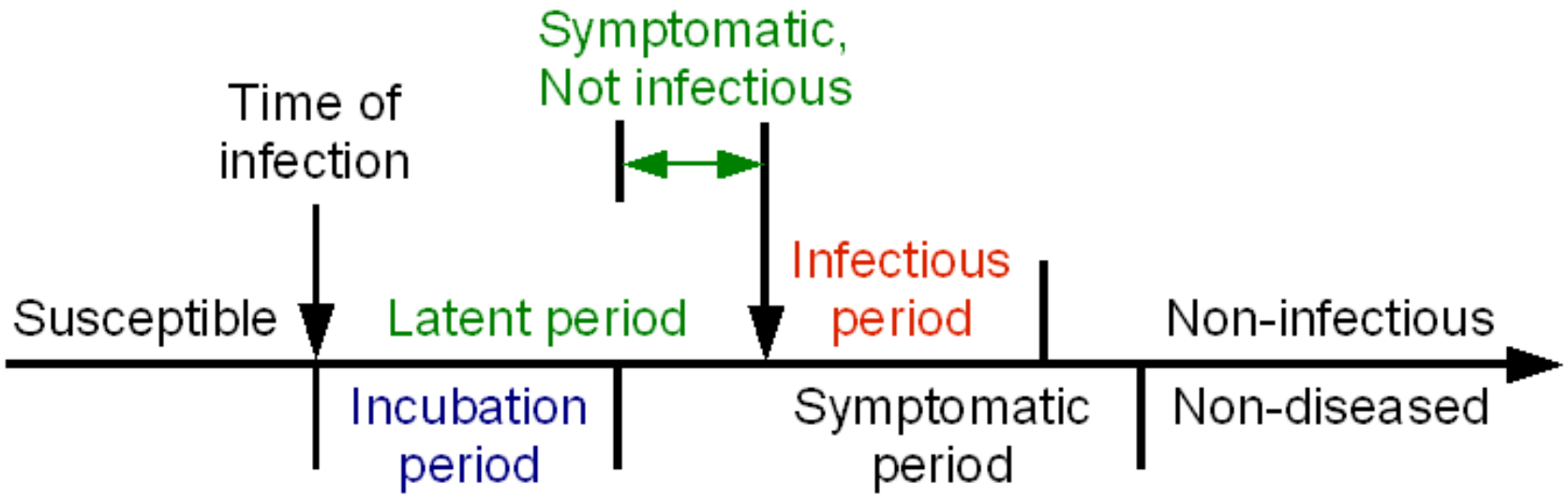
# Public devised infection control during SARS outbreak, 2003

# Inappropriate infection control during 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

# Natural history of infection: Latent period>Incubation period




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



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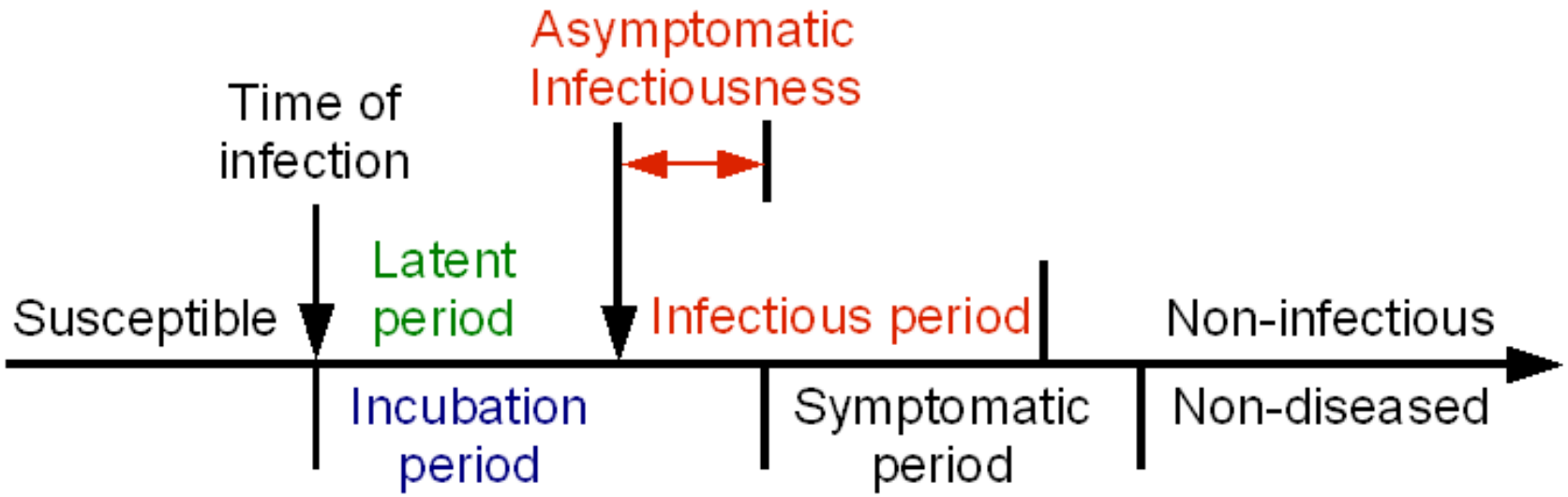
# Natural history of infection: Latent period<Incubation period




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



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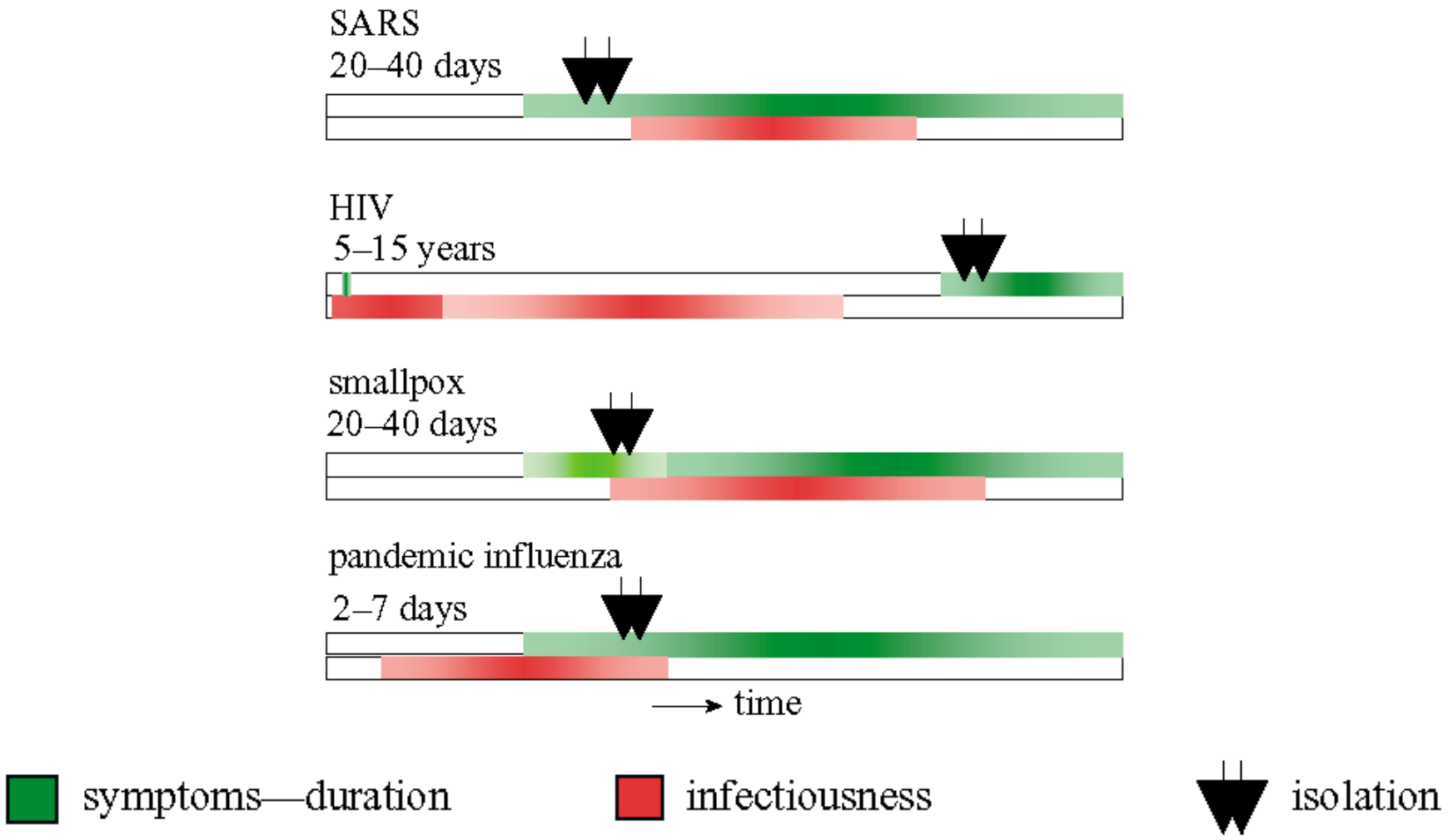
# Distribution of infectiousness of selected infectious diseases




Philos Trans R Soc Lond B Biol Sci. 2004;359:1091



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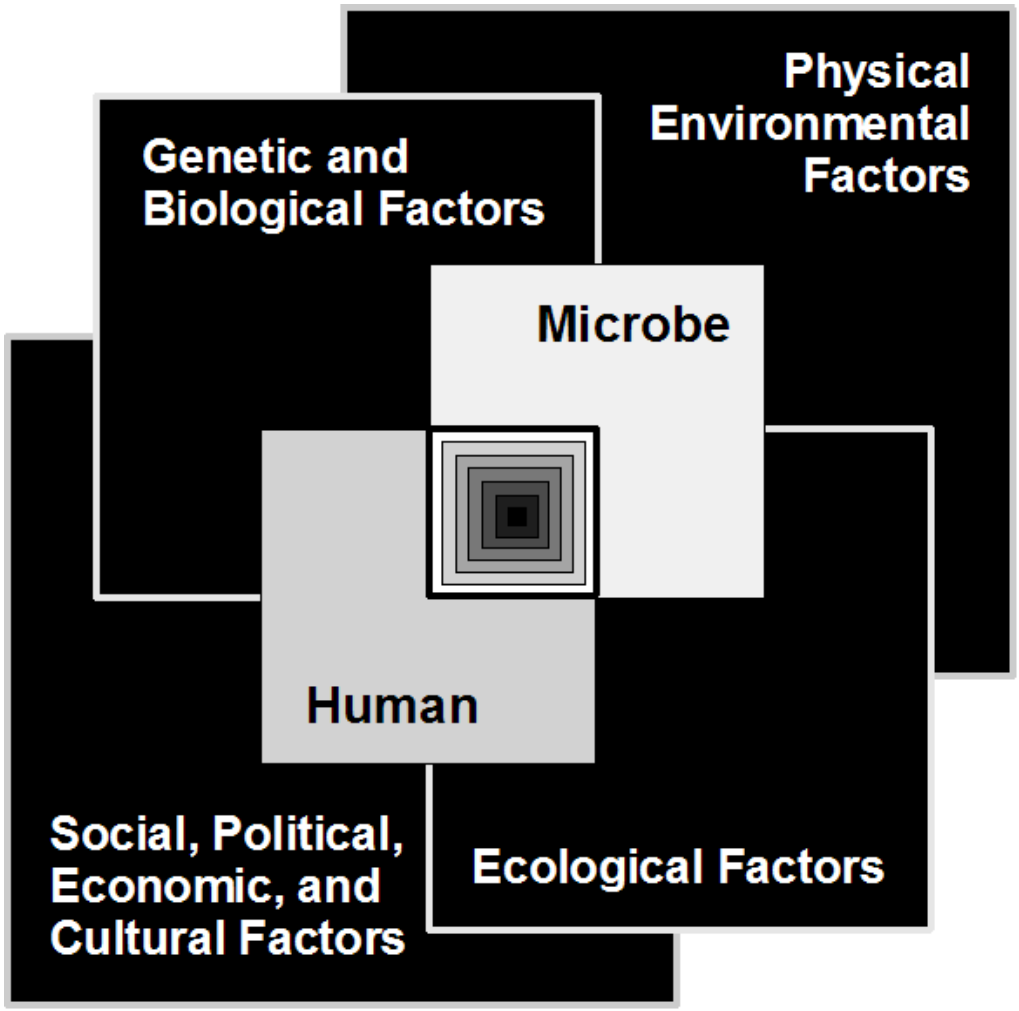
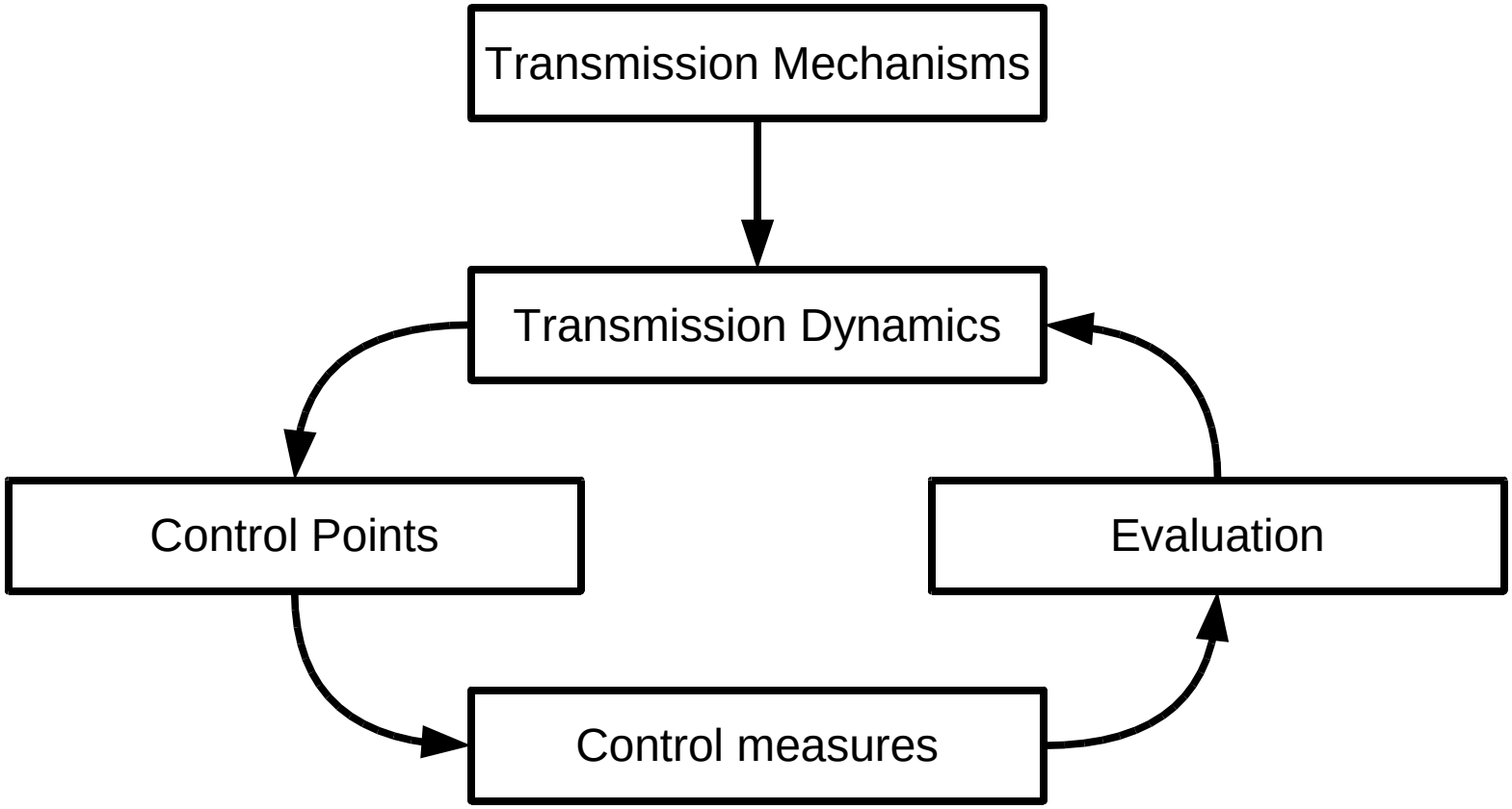
# Convergence model for human-microbe interaction




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

# Epidemiologic concepts for the control of microbial threats



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# Concepts for the prevention and control of microbial threats – 2

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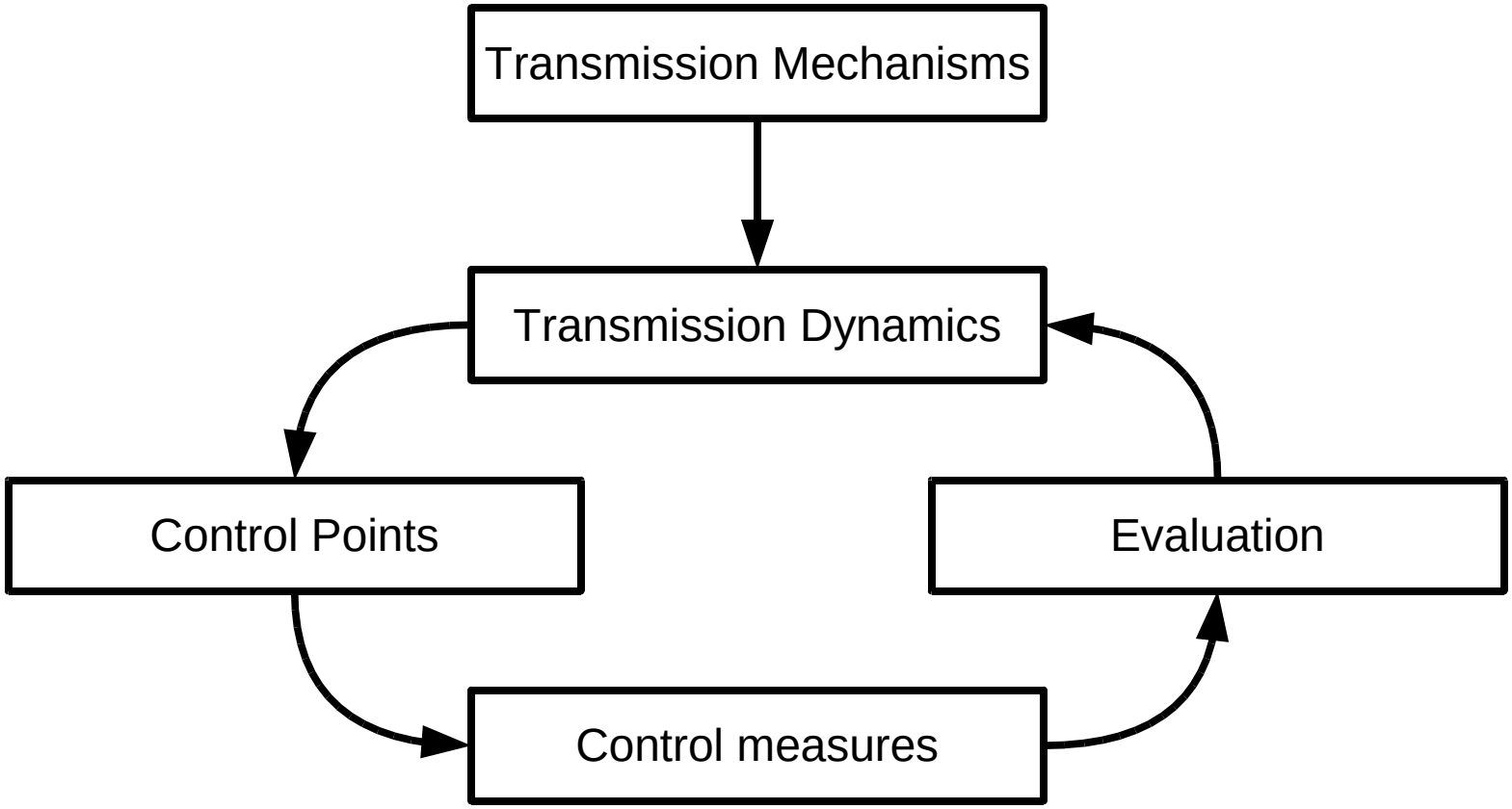




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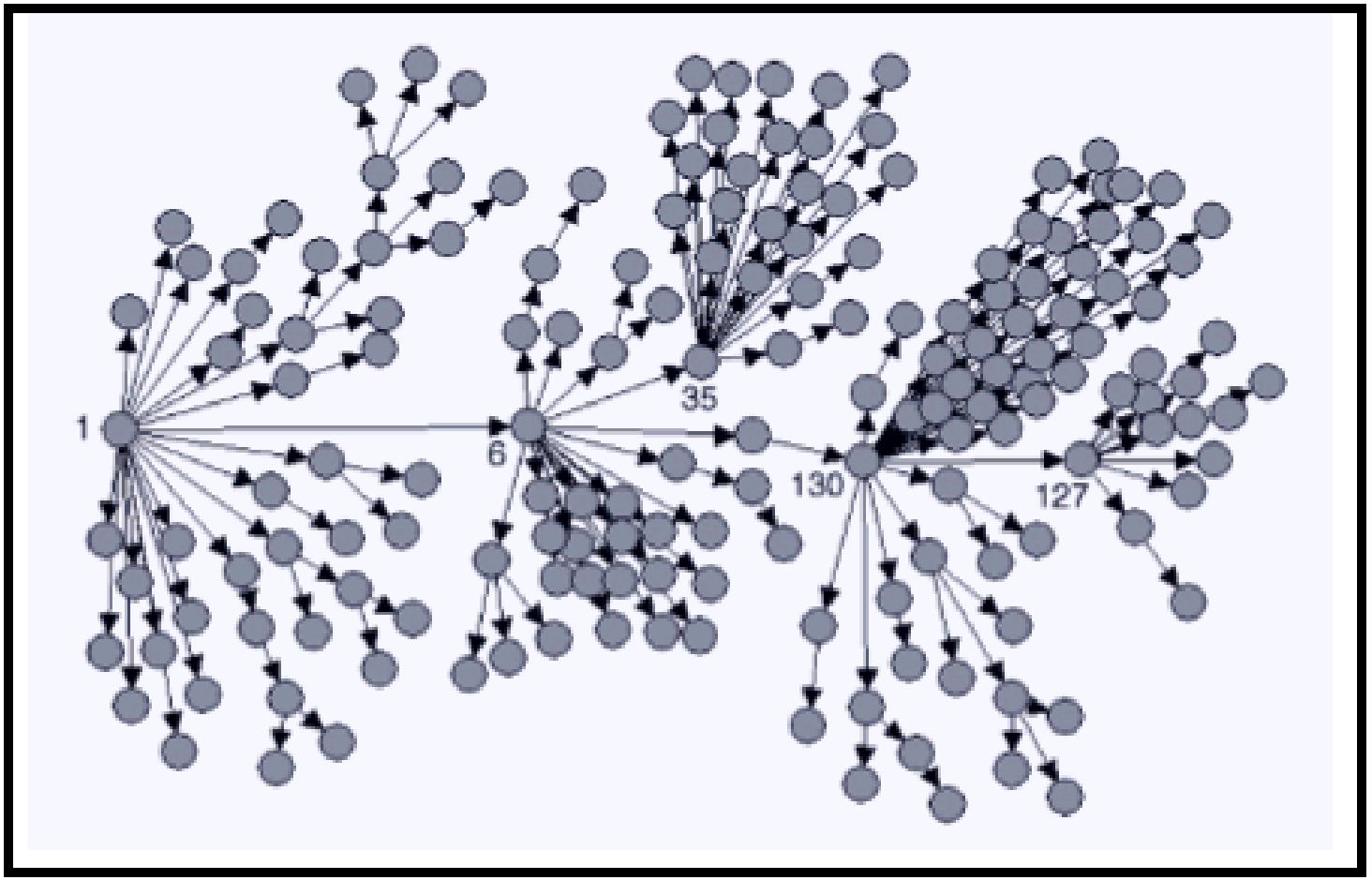
# Reproductive number & conditional infection rate




Probable cases of severe acute respiratory syndrome, by reported source of infection, Singapore, Feb 25-Apr 30, 2003 [CDC. MMWR 2003;52(18):405.]



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# The reproductive number

- 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
- Effective reproductive number ($R$)
  - Average number of secondary infectious cases produced by infectious cases
- Control reproductive number ($R_c$)
  - The effective reproductive number in the presence of control strategies



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# Basic reproductive number ($R_0$) (perspective of infectious case)

DEFINITION

The average number of secondary infectious cases that are produced by a single index case in a completely susceptible population in the absence of control strategies

$$R_0 = c\ p\ d$$

number of contacts per unit time

transmission probability per contact

duration of infectiousness



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# Effective reproductive number

$$R(t) = R_0\, x(t)$$

Fraction of population that is susceptible to infection



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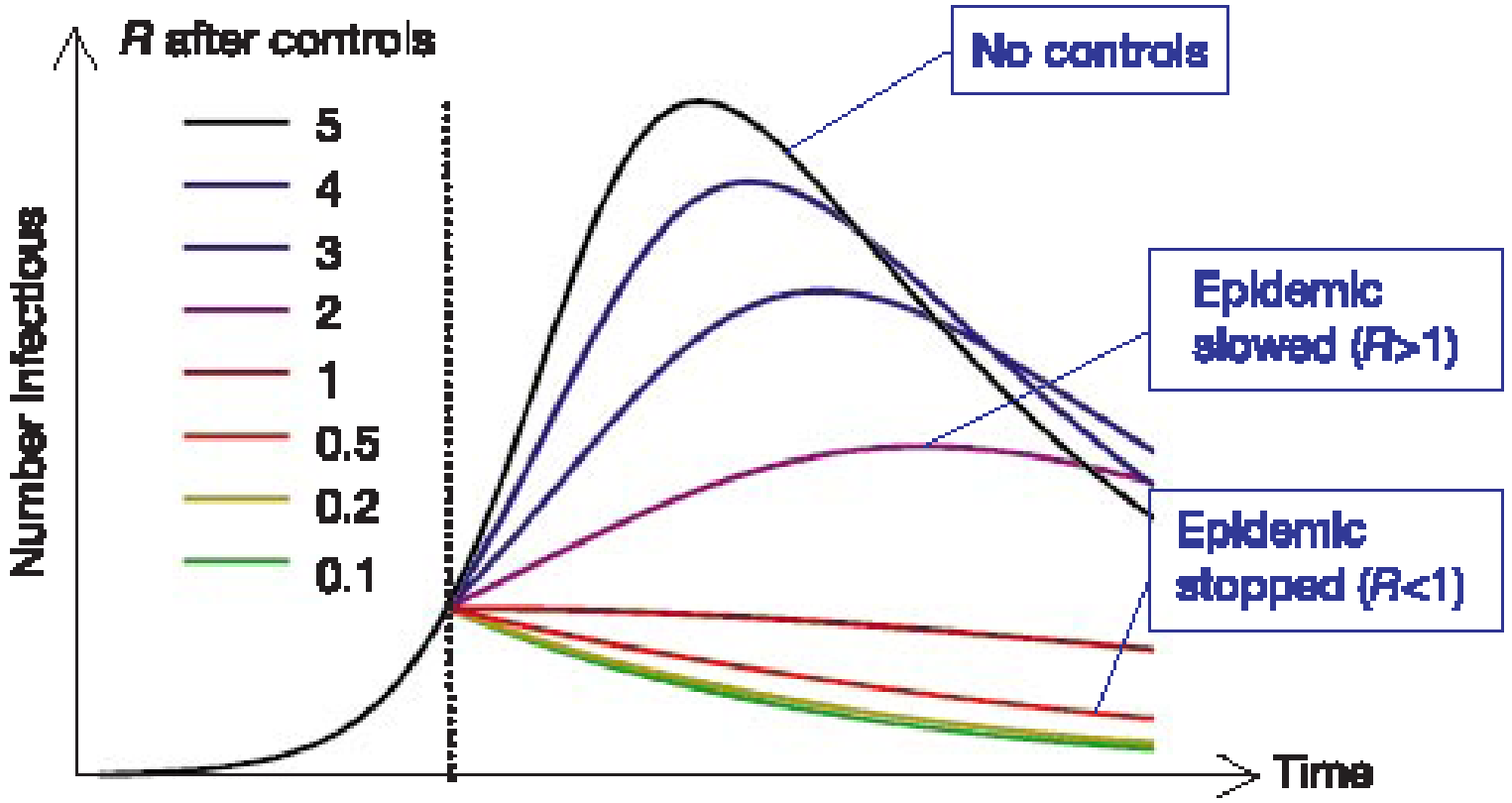
# Planning for smallpox outbreaks




Controls either reduce susceptible numbers (such as vaccination) or limit transmission (for example, through movement controls). Both have the effect of reducing R and slowing the spread of an epidemic; reducing R below 1 means that the chains of transmission cannot be sustained and the epidemic dies out.
Nature 2003 Oct 16;425(6959):681



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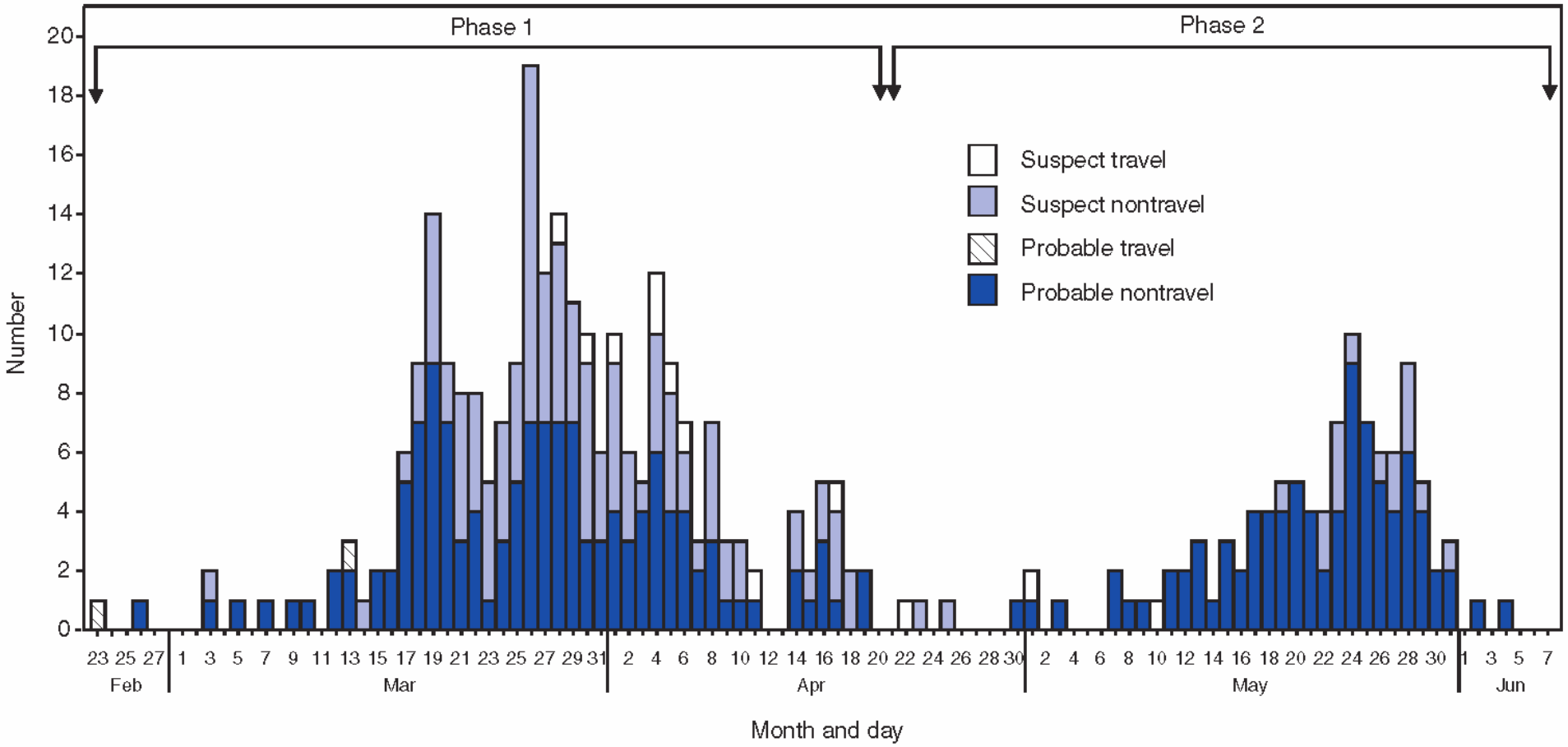
# Number of reported cases of severe acute respiratory syndrome, by classification and date of illness onset — Ontario, 2003




February 23–June 7, 2003 (N = 361)
CDC, MMWR 2003;52:547



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# Control reproductive number: Vaccination example

$$R_c(t) = R_0[1 - hf]$$

Fraction of those vaccinated that have complete protection (vaccine efficacy)

Fraction of population that has been vaccinated (vaccine coverage)



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# Control reproductive number: Vaccination example (cont'd)

Goal: $R_c(t) < 1$

Fraction to vaccinate: $f > \frac{1-(1/R_0)}{h}$



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# Herd Immunity Thresholds for Selected Vaccine-Preventable Diseases

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

| | | | Immunization Levels | |
|---|---|---|---|---|
| **Disease** | **$R_0$** | **Herd Immunity** | **1999 19-35 Months** | **1997-1998 Pre-School** |
| **Diphtheria** | **6-7** | 85%* | 83%* | 97% |
| **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% | __ | __ |

*4 doses

† Modified from Epid Rev 1993;15: 265-302, Am J Prev Med 2001; 20 (4S): 88-153, MMWR 2000; 49 (SS-9); 27-38



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# Per-capita infection rate among susceptible hosts

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

Components

$$I(t) = c\ p\ P(t)$$

Contact rate with a potentially infectious source

Probability of transmission given contact with infectious source

Probability that source is infectious



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# Per capita infection rate: HIV

$$I(t) = c\ p\ P(t)$$

Contact rate with a potentially infectious source

- Unprotected sex
- Homogeneous mixing
- Heterogeneous mixing(sexual sorting, risk factor sorting, agesorting, serosorting)

Probability of transmission given contact with infectious source

- Infectiousness (anti-viral therapy)
- Susceptibility (ulcerative STDs)
- Interrupt transmission (condoms)

Probability that source is infectious

- Reduce Prevalence (Counseling, Testing, and Referral)



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

| Exposure route | Risk per 10,000 exposures |
|---|---|
| Blood transfusion (BT) | 9,000 |
| Needle-sharing injection-drug use (IDU) | 67 |
| Receptive anal intercourse (RAI) | 50 |
| Percutaneous needle stick (PNS) | 30 |
| Receptive penile-vaginal intercourse (RPVI) | 10 |
| Insertive anal intercourse (IAI) | 6.5 |
| Insertive penile-vaginal intercourse (IPVI) | 5 |
| Receptive oral intercourse on penis (ROI) | 1 |
| Insertive oral intercourse with penis (IOI) | 0.5 |

CDC MMWR 2005;54(No. RR-2)



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# Generation or serial time (T)

- Generation or serial time 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 (for example, influenza vs smallpox)





# Transmission dynamics and control points

Effective reproductive number

$$R(t) = c\ p\ d\ x(t)$$

Conditional infection rate

$$I(t) = c\ p\ P(t)$$

| Control points | Prevention and control strategies |
|---|---|
| Contact rate (c) | 1. Reduce contact rate |
| Transmission prob. (p) | 2. Reduce infectiousness<br>3. Reduce susceptibility<br>4. Interrupt transmission |
| Prob. source infectious (P) | 5. Reduce proportion infectious sources |
| Duration infectiousness (d) | (see #2) |
| Fraction susceptible (x) | 6. Increase herd immunity |



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# Control measures (strategies + interventions)

1. Reduce contact rate
   - Behavior change (host and/or source)
   - Case finding for intervention (e.g., isolation)
   - Contact tracing for intervention (e.g., quarantine)
   - Isolation of cases
   - 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, etc.)



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# Control measures [cont'd] (strategies + interventions)

2. Reduce infectiousness
   - Treatment
   - Vaccination
3. Reduce susceptibility
   - Vaccination
   - Immune globulin
   - Treatment (e.g., ulcerative STD)
4. Interrupt transmission
   - Infectious control practices
   - Barrier methods (e.g., masks, condoms)
   - Insect repellent (e.g., reduce feeding time)



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# Control measures [cont'd] (strategies + interventions)

5. Reduce proportion of infectious sources
   - Case finding for intervention (e.g., isolation, treatment)
   - Identify and control infectious sources
   - Environmental measures
6. Increase herd immunity
   - Vaccination, consider the following
     - Naturally acquired immunity
     - Fraction vaccinated
     - Vaccine efficacy



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# Translating control strategies into smallpox control program

Control strategies

1. Reduce contact rate
2. Reduce infectiousness
3. Reduce susceptibility
4. Interrupt transmission
5. Reduce proportion of infectious sources
6. Increase herd immunity

CDC Prevention and control program

- Smallpox pre-event strategies
  - Vaccination program
  - Enhanced surveillance & detection
- Smallpox post-event strategies
  - Epidemiologic investigation
  - Surveillance and case reporting
  - Contact identification, tracing, vaccination, and surveillance
  - Isolation and Quarantine
  - Infection control
  - Personal protective equipment



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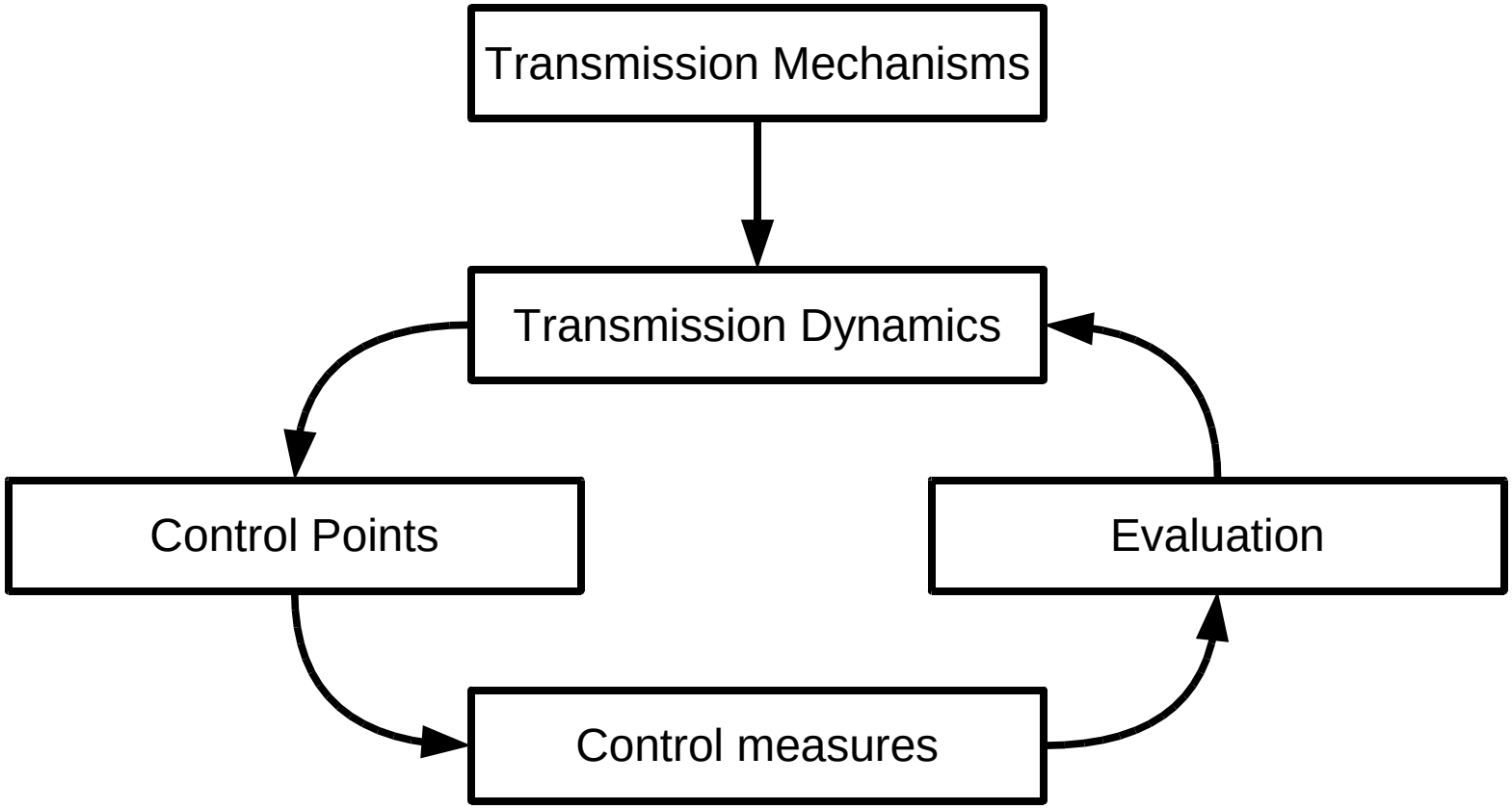




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