Epidemiologic concepts for the prevention and control of microbial threats

CIDER Spring Lecture Series, 2005

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Understanding strategies to prevent and control infectious diseases

1. Reduce contact rate (case finding & isolation, contact tracing & quarantine, behavior change)
2. Reduce infectiousness (treatment, vaccination)
3. Reduce susceptibility (vaccination, immune globulin)
4. Interrupt transmission (infection control)
5. Identify and control reservoir/source (pest/vector control, environmental disinfection)
6. Reduce prevalence of infectious sources (identify and control infectious sources)
7. Reduce duration of infectiousness (treatment, vaccination)
8. Increase herd immunity (vaccination)

Overview

- Traditional epidemiologic approach
- Infectious disease epidemiology concepts
  - Transmission mechanisms
    - Model for human-microbe interaction
    - Chain model of infectious diseases
    - Natural history of infection/infectiousness
  - Transmission dynamics
    - Reproductive number (R)
    - Conditional infection rate (I)
- Application to a smallpox control strategy

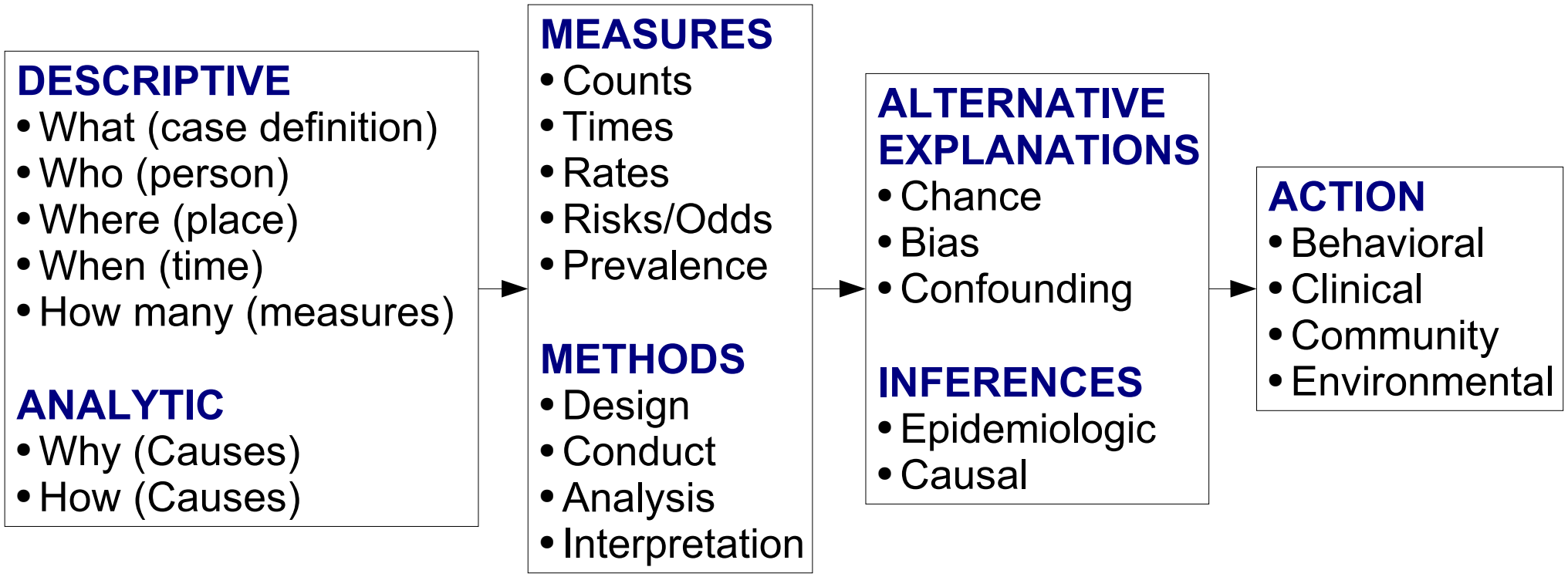
The epidemiologic approach: What is epidemiology?

Epidemiology is the study of the *distribution* and *determinants* of health-related states or events in specified populations, and the application of this study to the control of health problems

The epidemiologic approach: What is epidemiology?

- Study
- Distribution (descriptive epidemiology)
  - The who, what, where, when, and how many?
- Determinants (analytic epidemiology)
  - The how and why?
- Health-related states or events
- Specified populations
- Applications

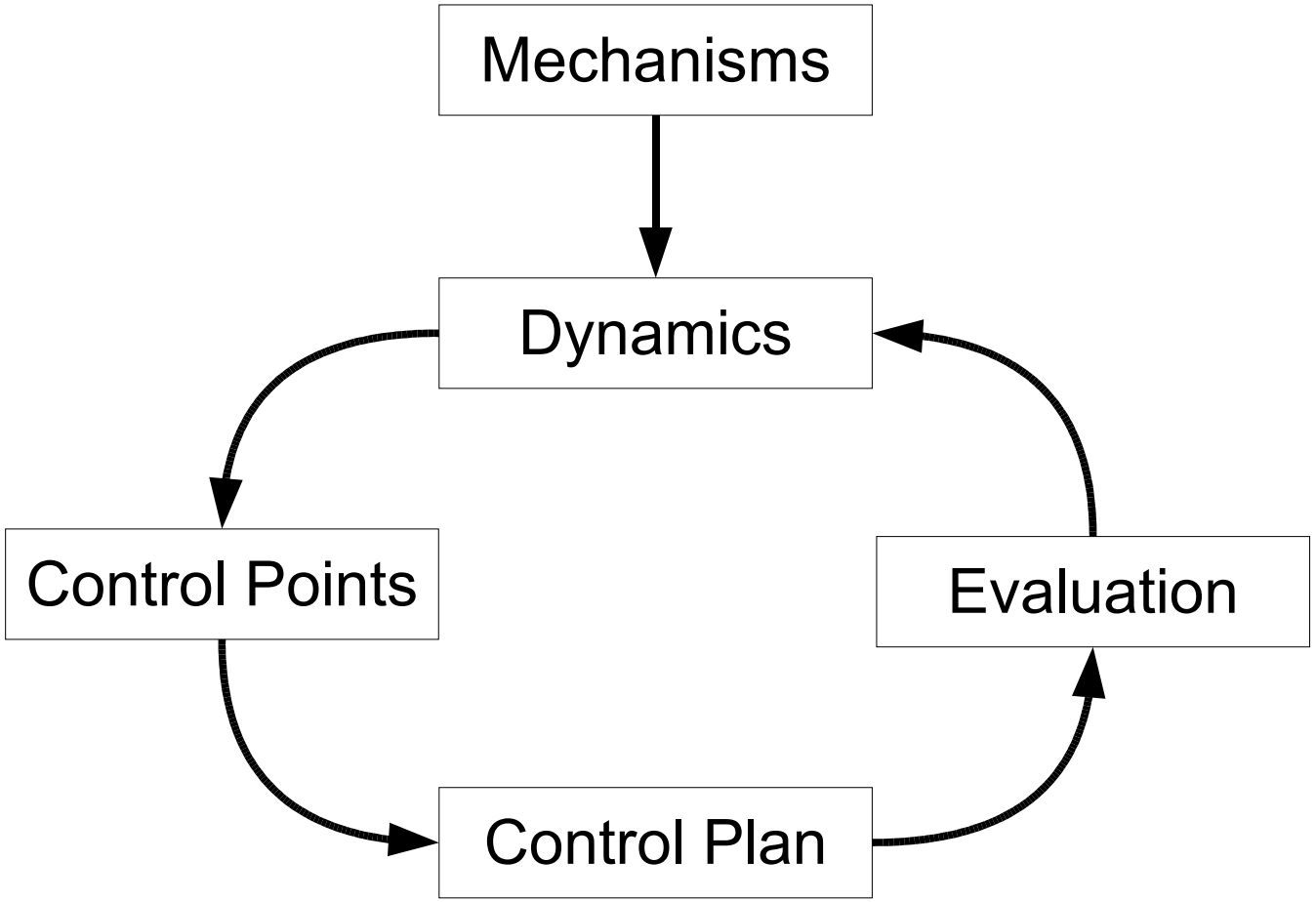
The epidemiologic approach: Steps to public health action



Infectious disease epidemiology concepts

- Mechanisms
  - Model for human-microbe interaction
  - Chain model of infectious diseases
  - Natural history of infection/infectiousness
- Dynamics
  - Reproductive number (R)
  - Conditional infection rate (I)

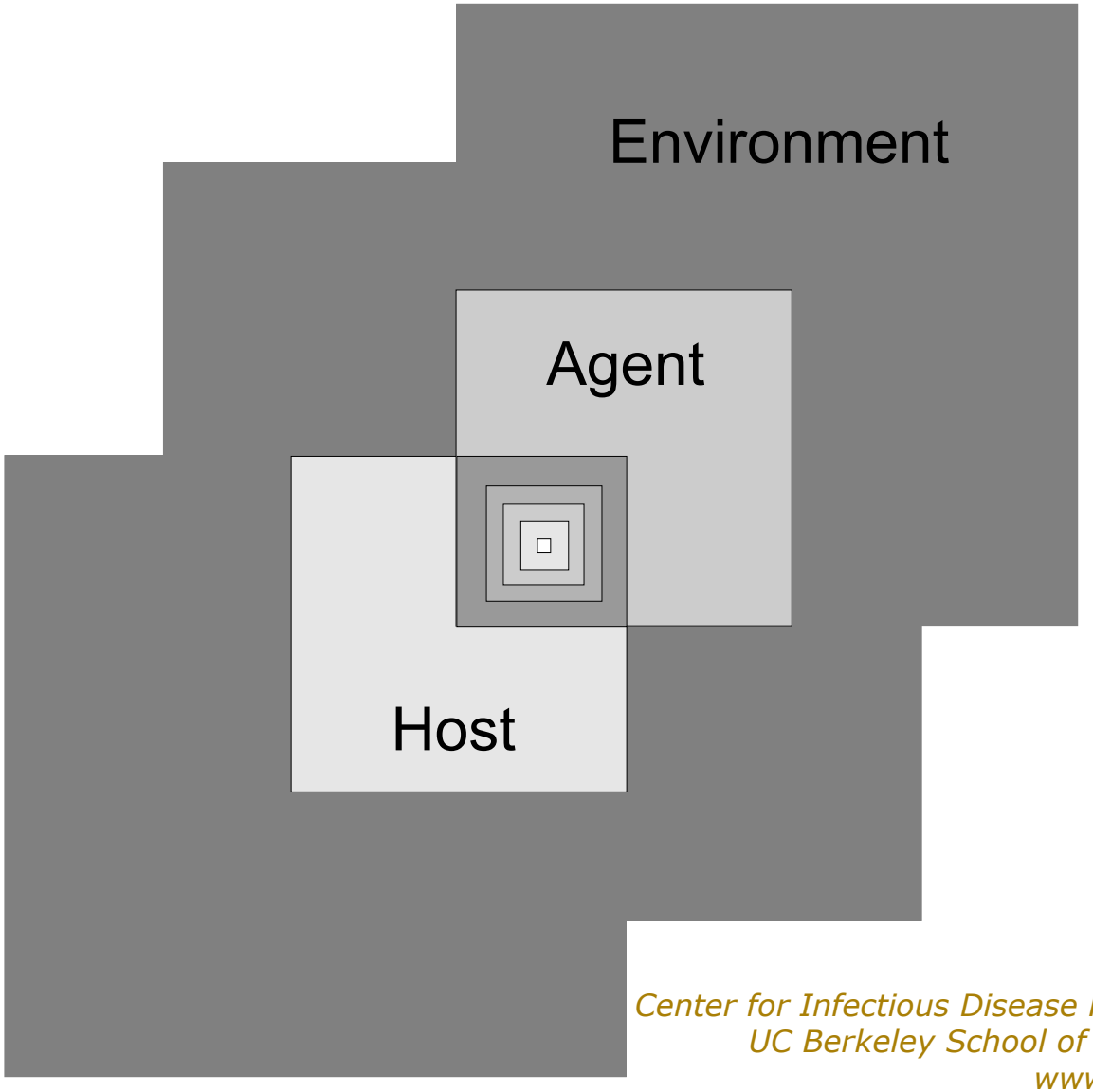
Epidemiologic concepts for the control of microbial threats



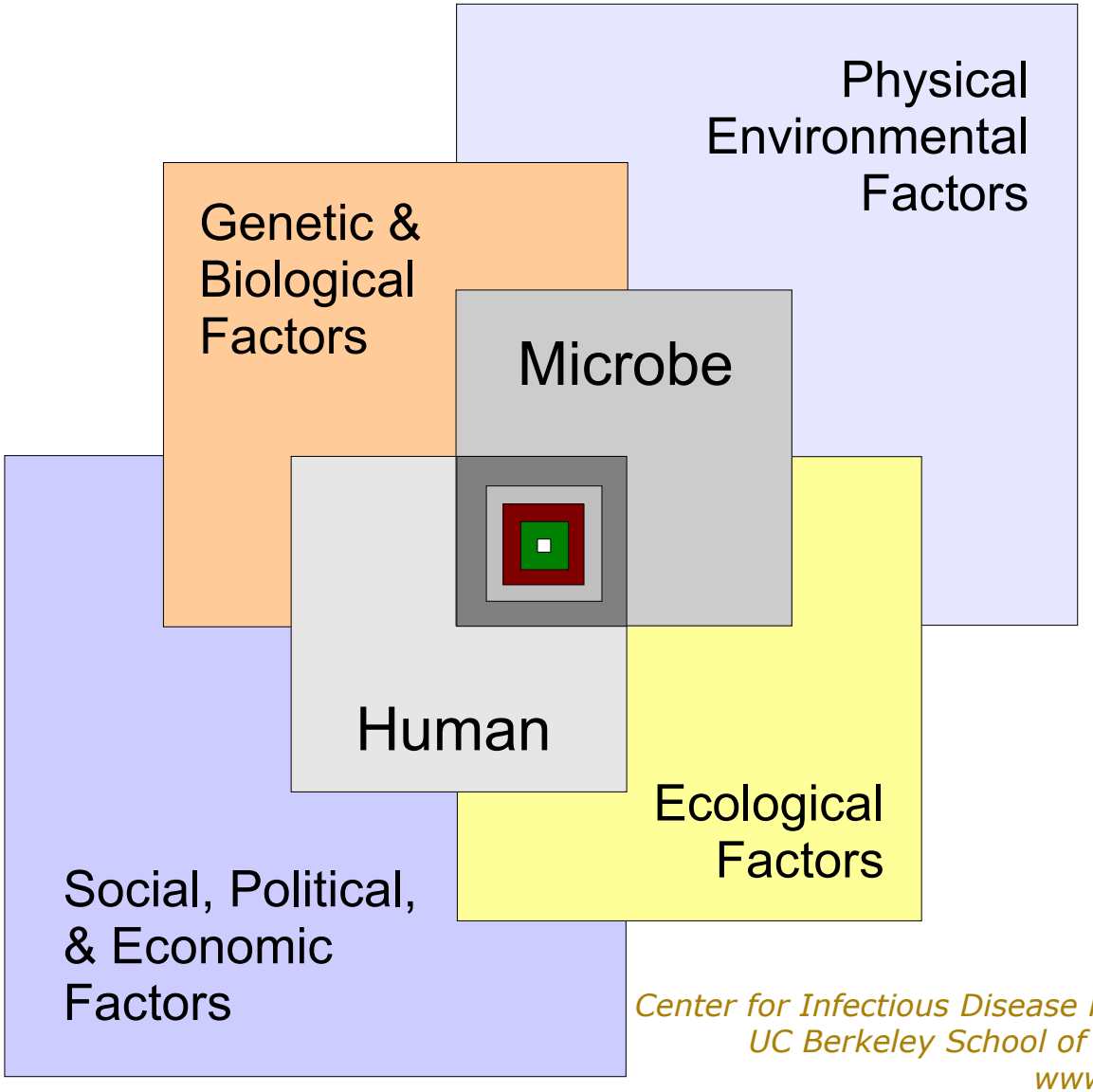
Primary use for these infectious disease epidemiologic concepts

- Research
- Outbreak investigations
- Control of acute microbial threats
- Prevention of endemic infectious diseases
- Bioterrorism preparedness and response planning and operational exercises

Host-Agent-Environment model

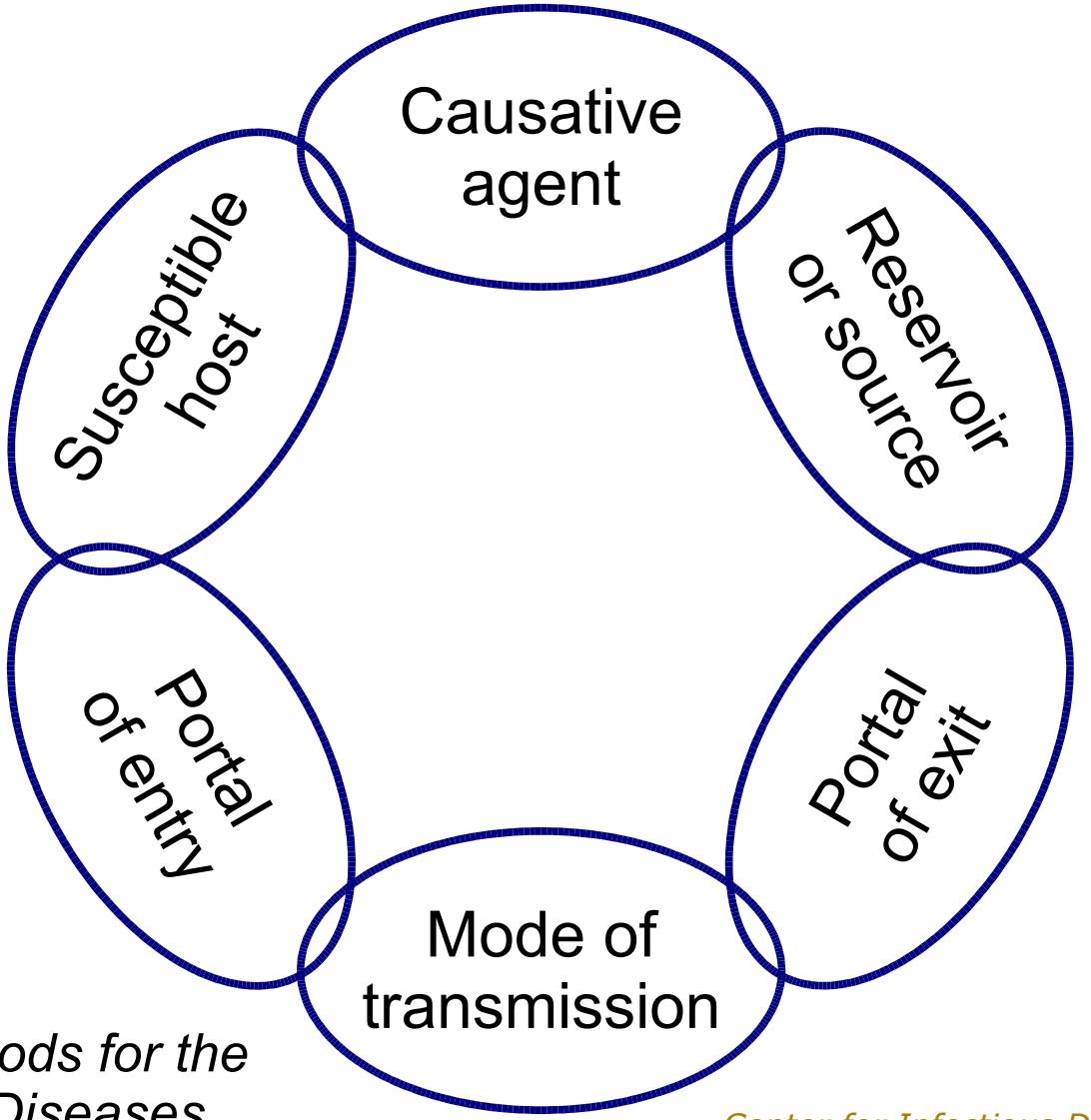


Convergence model for human-microbe interaction



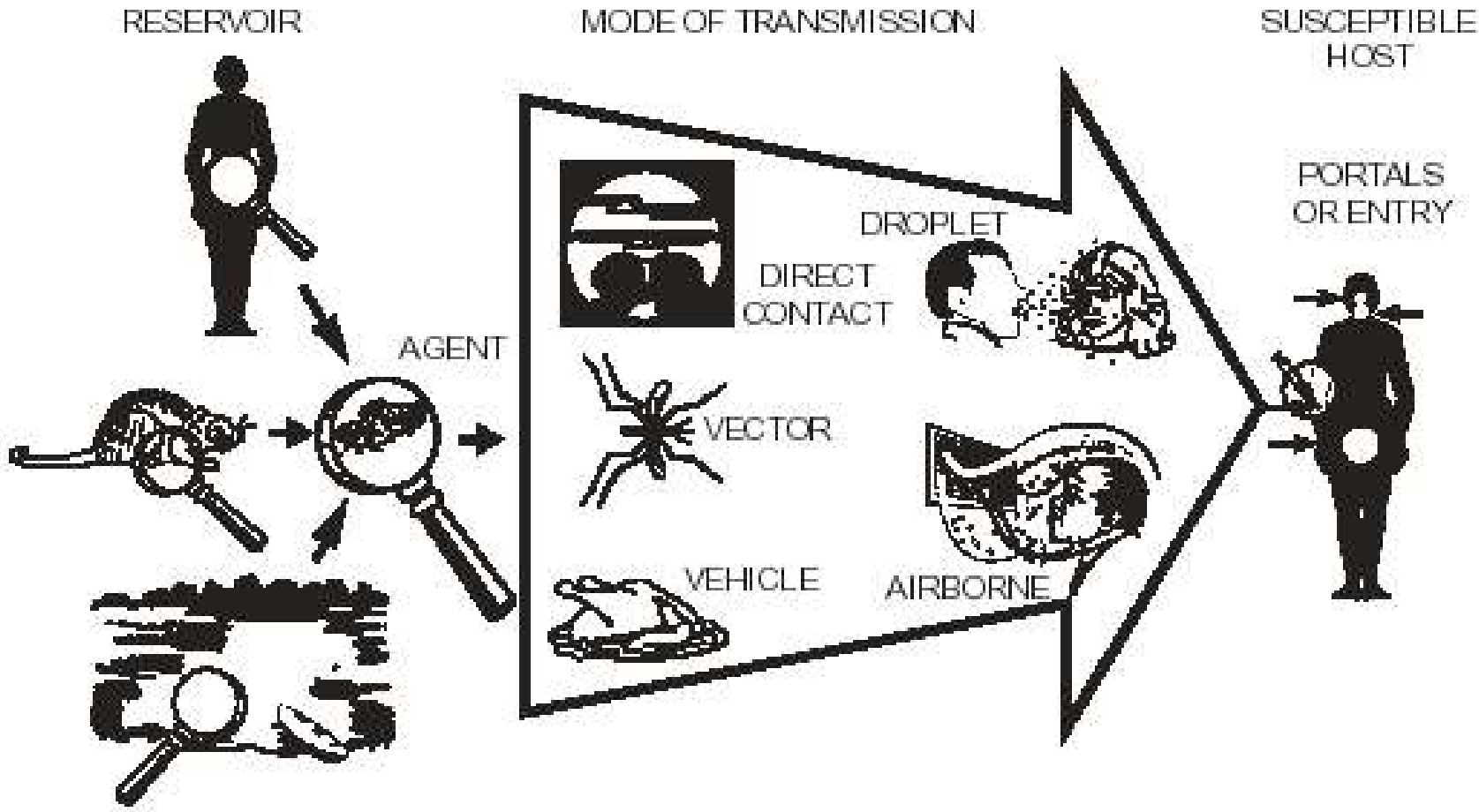
Institute of Medicine. *Microbial threats to health: Emergence, Detection, and Response*. National Academy Press 2003

Chain model of infectious diseases



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

Chain model of infectious diseases



Principles of Epidemiology, 2nd Edition,
Center for Disease Control and Prevention

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 (touch, kissing, sex)
  - Droplet and respiratory secretions
  - Indirect (intermediate object, usually inanimate)
  - Vertical transmission (before, during, & after)
- Airborne (droplet nuclei, dust)
- Vehicle (ingestion, instrumentation, infusion)
- Vector-borne (mechanical, biologic)

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

American Society for Microbiology

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."

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.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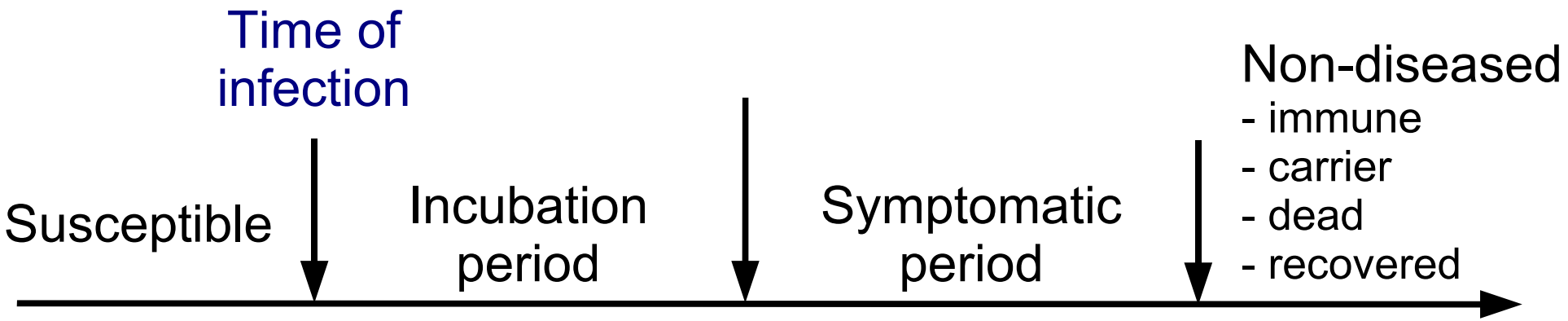
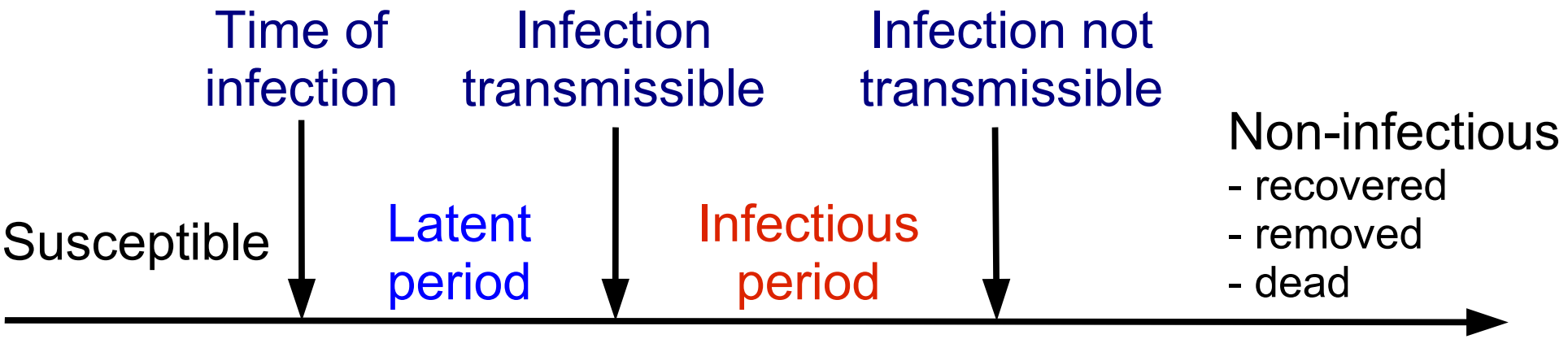
Natural history of infection, infectiousness, and disease

Dynamics of disease

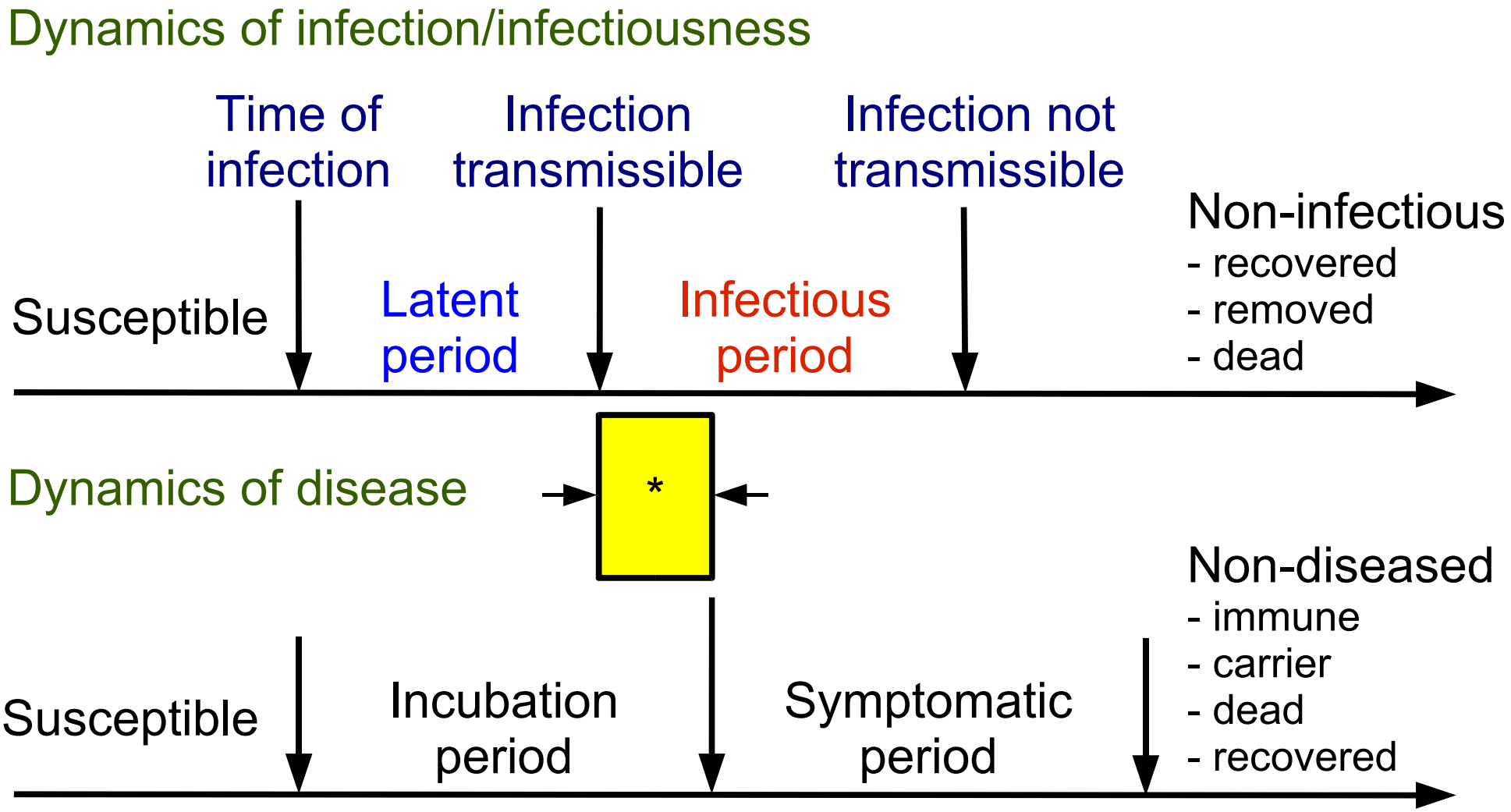


Natural history of infection, infectiousness, and disease

Dynamics of infection/infectiousness

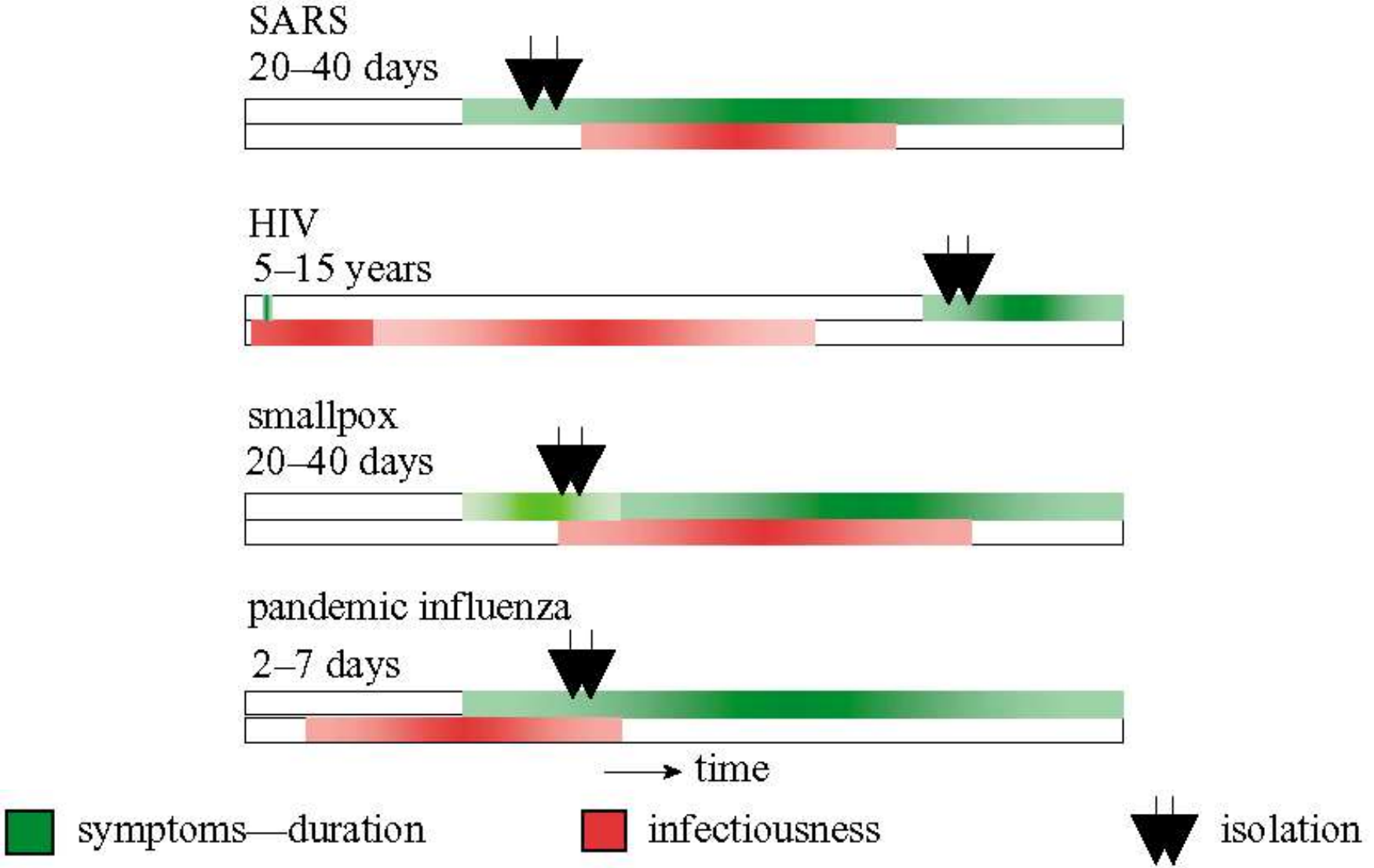


Natural history of infection, infectiousness, and disease



*greatest potential for uninterrupted transmission

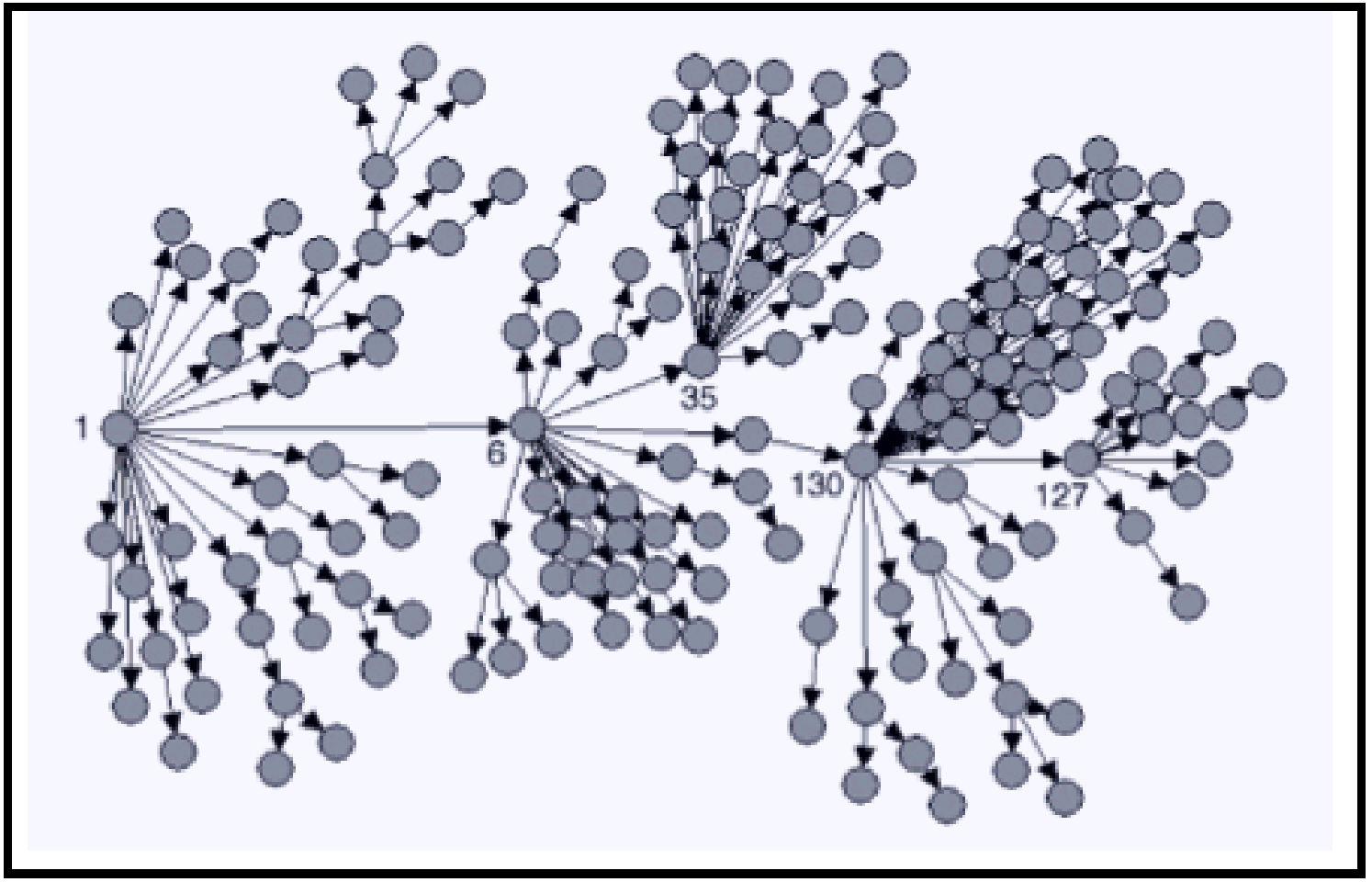
Incubation & infectious distributions of SARS and other infections



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

Center for Infectious Disease Preparedness
UC Berkeley School of Public Health
www.idready.org

Basic reproductive number (R_0)



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

Basic reproductive number (R_0) (perspective of infectious agent)

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

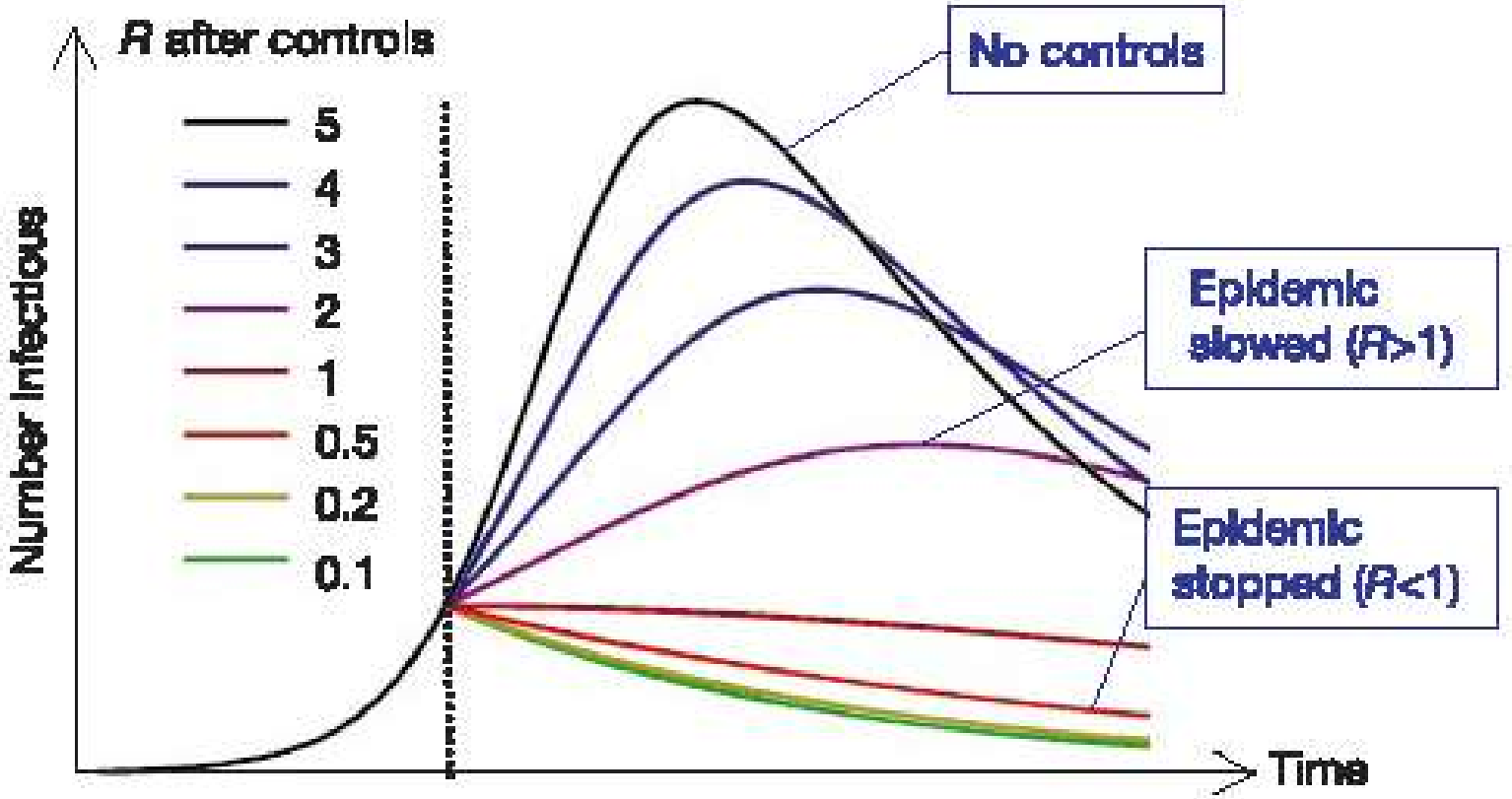
$$R_0 = c\ p\ d$$

number of contacts per unit time

transmission probability per contact

duration of infectiousness

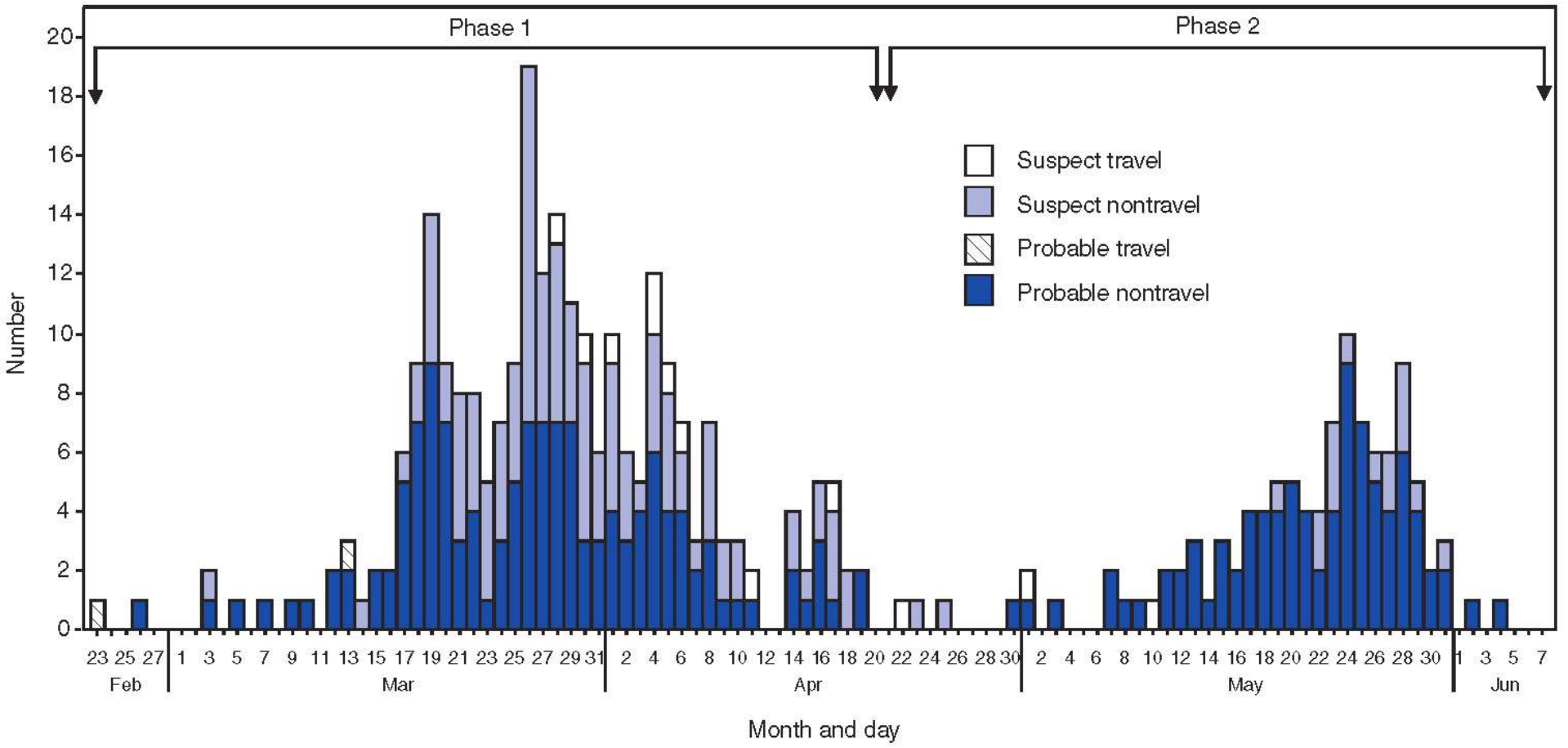
Planning for smallpox outbreaks
Nature 2003 Oct 16;425(6959):681



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.

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

CDC, *MMWR* 2003;52:547



Effective reproductive number (*R*)

DEFINITION
The average number of secondary infectious cases that are produced by infectious cases in the presence of control strategies

$$R = R_0 x$$
$$= R_0 [1 - hf]$$

fraction of population that is susceptible to infection

fraction of those vaccinated that have complete protection

fraction of population that has been vaccinated

Effective reproductive number (R)

Goal: $R < 1$

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

Fraction (f) to vaccinate to eradicate smallpox for different values of R_0 and vaccine efficacy (h)

R_0	Vaccine Efficacy (h)				
	0.94	0.95	0.96	0.97	0.98
3	0.71	0.70	0.69	0.69	0.68
4	0.80	0.79	0.78	0.77	0.77
5	0.85	0.84	0.83	0.82	0.82
6	0.89	0.88	0.87	0.86	0.85
7	0.91	0.90	0.89	0.88	0.87

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

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%*	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%	—	—

*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

Secondary Attack Risk for Smallpox Among Unvaccinated Household Contacts

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

2° Attack Risk (%)	# Studies
36.9 - 47	5
73.3 – 88.4	3
Average	58.4%
Average for vaccinated	3.8% (1.2-26.2)

The secondary attack risk (SAR) among unvaccinated households estimates the transmission probability (p) in the equation $R_0 = c\ p\ d$.

The estimated contact rate per day (c) derived from values of R_0, secondary attack risks among unvaccinated, and average duration of infectiousness (set at 10 days)

R_0	Secondary attack risk				
	0.36	0.49	0.62	0.75	0.88
3	0.83	0.61	0.48	0.40	0.34
4	1.11	0.82	0.65	0.53	0.45
5	1.39	1.02	0.81	0.67	0.57
6	1.67	1.22	0.97	0.80	0.68
7	1.94	1.43	1.13	0.93	0.80

$$c = \frac{R_0}{(SAR)(d)}$$

Conditional infection rate (perspective of susceptible hosts)

Unconditional rate $$I = \frac{\text{Number of new infections}}{\text{Person-time at risk}}$$

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

Contact rate with a potentially infectious source

Probability of transmission given contact with infectious source

Probability that source is infectious

Using *I* and *R* to plan a prevention and control strategy

Effective reproductive number $R = R_0 x = (c\ p\ d)\ x$

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
	3. Reduce susceptibility
	4. Interrupt transmission
Prob. source infectious (*P*)	5. Identify and control reservoir/source
	6. Reduce prevalence of infectious sources
Duration infectiousness (*d*)	7. Reduce duration of infectiousness
Fraction susceptible (*x*)	8. Increase herd immunity

Understanding strategies to prevent and control infectious diseases

1. Reduce contact rate (case finding & isolation, contact tracing & quarantine, behavior change)
2. Reduce infectiousness (treatment, vaccination)
3. Reduce susceptibility (vaccination, immune globulin)
4. Interrupt transmission (infection control)
5. Identify and control reservoir/source (pest/vector control, environmental disinfection)
6. Reduce prevalence of infectious sources (identify and control infectious sources)
7. Reduce duration of infectiousness (treatment, vaccination)
8. Increase herd immunity (vaccination)

Translating effective reproductive number (*R*) and infection rate (*I*) into effective smallpox control strategy

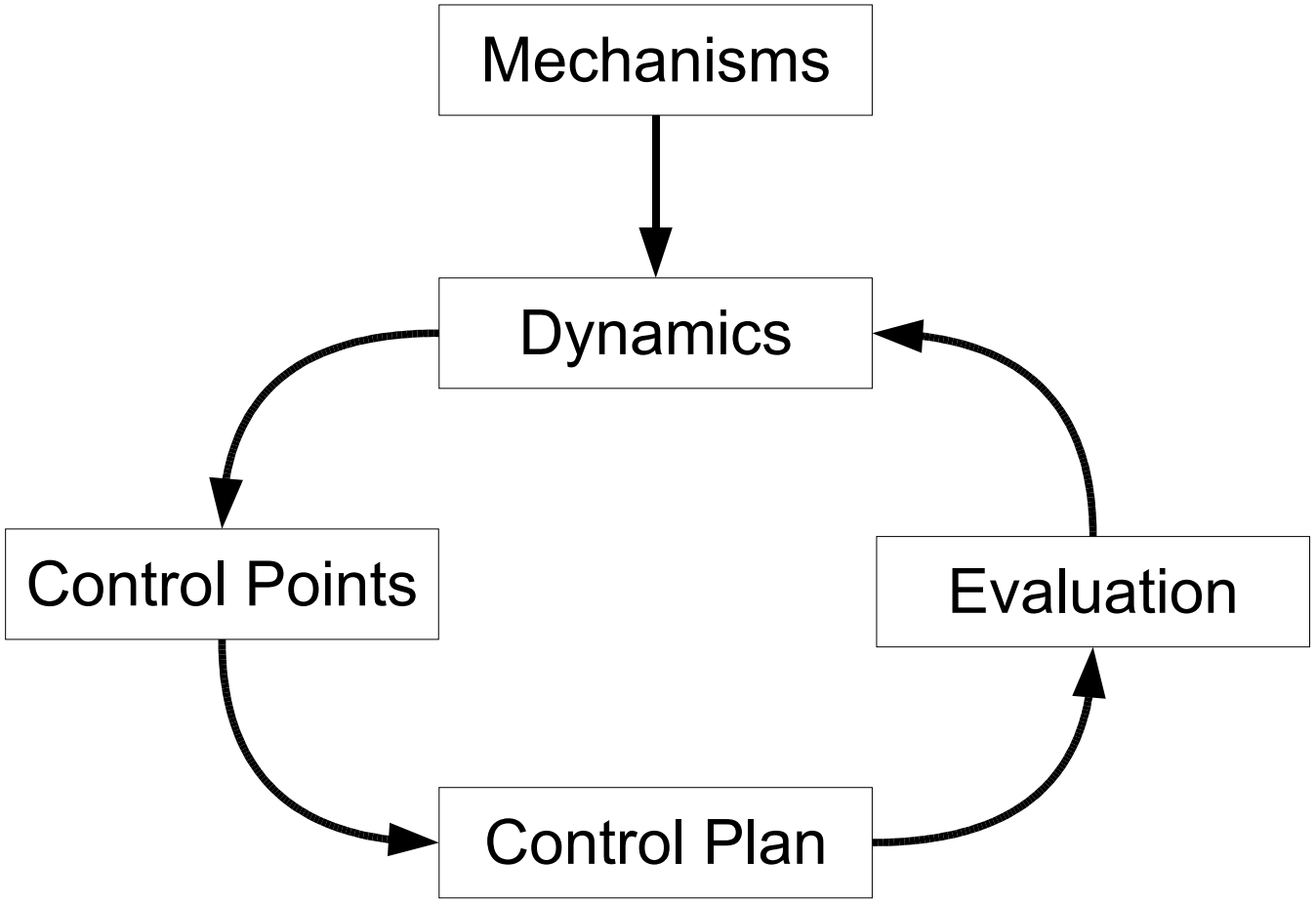
Prevention and control strategy

1. Reduce contact rate
2. Reduce infectiousness
3. Reduce susceptibility
4. Interrupt transmission
5. Identify and control reservoir and source
6. Reduce prevalence of infectious sources
7. Reduce duration of infectiousness
8. Increase herd immunity

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
  - Quarantine
  - Infection control
  - Personal protective equipment

Epidemiologic concepts for the control of microbial threats



Summary

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