Title
Epidemiologic Concepts for the Prevention and Control of Infectious Diseases

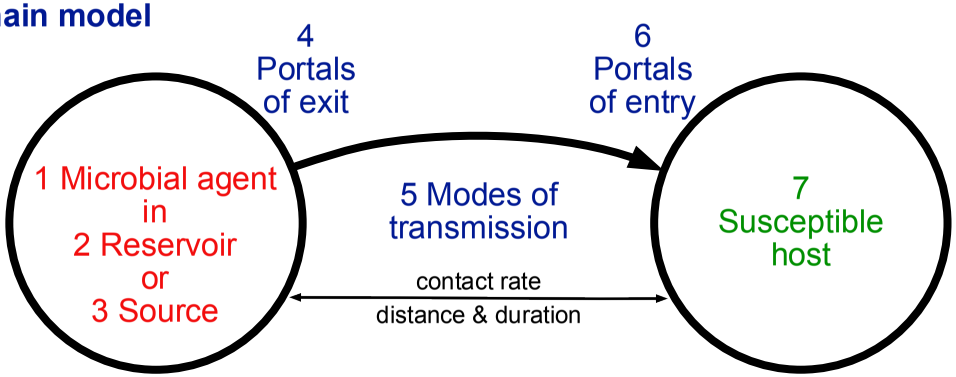
Authors
Aragon, Tomas J
Reingold, Arthur

Publication Date
2011-12-31

Preventing and Controlling Infectious Diseases, COVID-19 Edition

Population Health Division, San Francisco Department of Public Health

Chain model



Reservoir / Source
1 air
2 water
3 food
4 people
5 animals and vectors
6 vehicles
7 soil and debris

Modes of transmission
1 contact - direct
2 contact - indirect (fomites, fecal)
3 droplet
4 airborne
5 vehicle-borne
6 vector-borne
7 vertical (mother to fetus or newborn)

The 7 Habits of Uninfected People
1 physical distancing (6+ feet esp. if susceptible or vulnerable)
2 frequent hand washing; avoid touching eyes, nose, and mouth
3 face covering or mask, respiratory hygiene, and cough etiquette
4 staying home when sick: don't go to school, work, social events
5 keeping vaccinations up-to-date (e.g., flu, hep A)
6 safe consuming of water, food, products (includes harm reduction)
7 understanding infection prevention/control (study this document)

Transmission containment strategies
1 reduce reservoir and / or source (mitigate hazard, disinfection)
2 reduce contact (decrease rate and duration, increase distance)
3 reduce fraction of population that is infectious
4 reduce biological infectiousness (e.g., ART in HIV)
5 reduce biological susceptibility (e.g., PrEP, vaccine)
6 interrupt transmission (infection control, N95s, face masks, etc.)
7 reduce fraction of population that is susceptible

Transmission equations

EQ 1: $R(t) = R_0 \, x(t) \approx c \, p \, d \, [1 - h \, f - r(t)]$

EQ 2: $I(t) = c \, p \, P(t)$

R(t) = effective reproductive number
R_0 = basic reproductive number
x = fraction of population susceptible
c = contact rate between infectious sources and susceptibles
p = transmission probability
d = duration of infectiousness
h = vaccine effectiveness
f = fraction of population vaccinated
r(t) = fraction removed (recovered immune)
I(t) = infection rate among susceptibles
P(t) = probability source is infectious
(t) = at time t

Special transmission drivers
1 asymptomatic infectiousness
2 pre-symptomatic infectiousness
2 short serial (generation) time
3 airborne transmission
4 fomite transmission
5 fecal-oral transmission

Infectious disease control measures / tools
- behavior change of reservoir/source and/or susceptibles
- testing (diagnostic, and targeted and/or mass screening)
- case definition (epidemiological, clinical, and laboratory criteria)
- case finding for isolation, treatment, surveillance
- isolation (separation of infectious person ["case"])
- case management (transport, house, feed, isolate, treat, clear)
- contact tracing for quarantine, PEP, surveillance
- quarantine (separation of exposed individuals)
- social distancing (for individuals or groups)
  * keeping 6 or more feet from others
  * school closures, cancellation of classes
  * cancellation of mass gatherings
  * travel restrictions
- shelter at home ("shelter in place") (avoiding potential exposures)
- vaccination (targeted and/or mass)
- pre- or post-exposure prophylaxis (PrEP, PEP, vaccine, IgG, drug)
- treatment (infectious cases or co-risk factor)
- infection prevention (aka infection control)
- environmental measures (disinfection, ventilation, separators, etc.)
- cordon sanitaire (preventing *exit* from affected region)
- protective sequestration (preventing *entry* into unaffected region)

Updated: 2020-05-02
Tomás J Aragón, MD, DrPH
Health Officer, City & County of San Francisco
Details here: https://escholarship.org/uc/item/7687z08g
Also visit population health blog: https://taragonmd.github.io/

Epidemiologic Concepts for the Prevention and Control of Infectious Diseases

Tomás J. Aragón, MD, DrPH[1,2]
Arthur Reingold, MD[1]

[1] *University of California, Berkeley, School of Public Health, Berkeley, CA*
[2] *San Francisco Department of Public Health, San Francisco, CA*

Abstract

We will review the epidemiologic concepts for the prevention and control of infectious diseases. Public health and medical professionals are familiar with common interventions to prevent or control infectious diseases. However, the underlying epidemiologic concepts that drive and guide these interventions are less familiar. Although we focus on acute infectious diseases, these concepts are broadly applicable to communicable diseases, including chronic or neoplastic diseases caused by exogenous transmissible agents such as human immunodeficiency virus (HIV), hepatitis B and C viruses (HBV and HCV), human papilloma virus (HPV), and prions.

Keywords: Infectious diseases, Communicable diseases, Transmission dynamics, Infectious disease epidemiology

Learning objectives

After completing this review readers will be able to describe…

- The transmission of microbial agents from an infectious source to a susceptible human host;
- The natural history of infection and infectiousness;
- How humans and microbes interact with each other and their environment to produce infectious disease epidemics;
- The haracteristics of infectives that increase transmission;
- The characteristics of susceptibles that increase transmission;
- Six control strategies for interrupting transmission; and
- Control measures based on the six control strategies.

1. Introduction

We will review the epidemiologic concepts for the prevention and control of infectious diseases. Public health and medical professionals are familiar with the interventions to prevent or control infectious diseases (Table 1). However, the underlying epidemiologic concepts that drive and guide these interventions are less familiar. Although we focus on acute infectious diseases, these concepts are broadly applicable to communicable diseases, including chronic or neoplastic diseases caused by exogenous transmissible agents such as human immunodeficiency virus (HIV), hepatitis B and C viruses (HBV and HCV), human papilloma virus (HPV), and prions.

A better understanding of the core epidemiologic concepts will (1) help researchers prioritize and conduct studies to identify and optimize prevention and control interventions; (2) help clinicians understand their role and how it directly and indirectly contributes to containment efforts; (3) help field investigators use a systematic and comprehensive approach to hypotheses generation and testing when conducting outbreak investigations; (4) help responders design, implement, and evaluate interventions to control and prevent acute microbial threats as well as endemic infectious diseases; and (5) help planners design, test, and evaluate infectious disease emergency operations response plans.

Table 1: Common interventions to prevent and control infectious diseases

Control measures
Alter risk factors
Prophylactic immunization
Post-exposure management
Diagnosis and treatment
Infection control practices
Case finding and isolation
Contact tracing and quarantine
Environmental control measures
Identify and control infectious sources

Our primary focus is on infectious disease transmission mechanisms, transmission dynamics, and transmission containment. The design, implementation, and evaluation of strategies to control infectious diseases can be improved by using a systematic, integrated epidemiologic approach, especially for acute or novel microbial threats that require special public health actions (e.g., severe acute respiratory syndrome [SARS], human pandemic influenza, or bioterrorism). Furthermore, we stress the value and importance of understanding the epidemiologic control points that drive infectious disease transmission dynamics.

1.1. Epidemiologic concepts

Epidemiology is "[t]he study of the distribution and determinants of health related states and events in populations, and the application of this study to control health problems" [1].

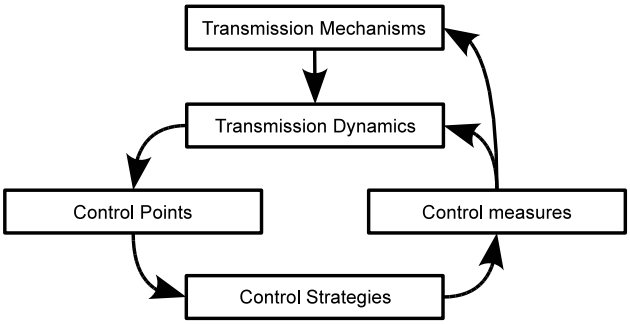


Figure 1: The relationship between infectious disease transmission mechanisms, transmission dynamics, and transmission containment (control points, control measures, and evaluation

By health-related states or events, we mean the occurrence or condition of infection, disease, injury, disability, or death. Epidemiologic studies are designed to answer well-defined investigative questions while minimizing threats to making valid inferences (chance, bias, and confounding). Most medical and public health professionals are familiar with the epidemiologic approach to public health action. Infectious diseases differ in important ways from non-infectious diseases because of the mechanisms by which microbial agents are transmitted and the population dynamics of transmission and disease occurrence. To improve our conceptual understanding, we use a systematic, comprehensive, and integrated approach (Figure 1). Specifically, we cover the following:

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

First, we review infectious disease transmission mechanisms. How are infections transmitted and why? Second, we review infectious disease transmission dynamics. At the population level, what mechanisms explain the transmission of microbial agents and the appearance of infectious cases? How do infectious cases interact with susceptible hosts? Third, we review transmission containment. From our study of transmission dynamics, we identify transmission control points for preventing and controlling infectious diseases. We will use these control points to guide the development of appropriate control measures. This process helps us to evaluate the success or failure of our control measures.

2. Transmission mechanisms

2.1. Chain model of infectious diseases

The Chain Model of infectious diseases contains the key components that must be "linked" in order for an infection to occur. (Figure 2). First, there is a *susceptible host*. Second, there is a *microbial agent* capable of adhering, entering, infecting, and causing disease in the susceptible host. In its natural settings, the microbial agent multiplies and survives in a *reservoir*. The *source* is where the microbial agent is when it is transmitted to the susceptible host. The reservoir can also be a source of infection. The *portal of exit* is how the agent exits the source. The *mode of transmission* is the mechanism by which the agent is transmitted from the source to the host (e.g., contact, droplet, airborne, etc.). And the *portal of entry* is how the agent enters the susceptible host (e.g., respiratory tract, gastrointestinal tract, genitourinary tract, skin). For example, enterohemorrhagic *Escherichia coli* (EHEC), most commonly *E. coli* O157:H7, elaborate Shiga toxins that can result in severe human disease, including hemorrhagic colitis and hemolytic uremic syndrome [2]. Cattle are the major reservoir for EHEC; up to 5% can be asymptomatic excetors of the organism. The source of infection for humans can be ingestion of contaminated foods or water, but also can be direct contact with colonized cattle or their environment. The most commonly recognized mode of transmission is human ingestion of contaminated ground beef.

Susceptible host. Human host susceptibility is a relative attribute and depends on the condition of host defenses. Host defenses consist of innate immunity and acquired immunity. *Innate immunity* consists of nonspecific mechanisms that do not require prior exposure to foreign agents in order to resist or fight invasion of the host by these foreign agents. The first lines of defense are intact skin and mucous membranes, and any breach in these provide a portal of entry. Nonspecific inflammation and phagocytosis[1] provide a second line of innate defense. The other type of host defense is *acquired immunity*, which can be active or passive. Acquired *active* immunity is comprised of

[1] Inflammatory cells (macrophages and granulocytes) fight infection by engulfing microbes.

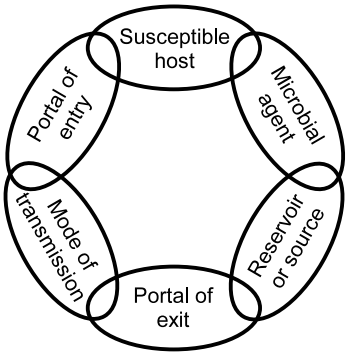


Figure 2: The chain model of infectious diseases

host antibody or cellular immune defense mechanisms that target specific foreign agents based on prior exposure to this or antigenically similar agents. Vaccination is a form of active immunization. Acquired *passive* immunity is when a host receives preformed antibodies that were made in other hosts. Receipt of immune globulin is a form of passive immunization.

Microbial agent. Microbial agents or their toxins can cause human disease. We focus on transmissible agents that are microbes, microbe-like, or their toxins. Microbes are complex, reproducing microorganisms such as viruses, bacteria, parasites, and fungi. Prions are transmissible, self-propagating proteins that can cause disease (usually neurodegenerative diseases called spongiform encephalopathies). With respect to terminology, we refer generically to microbes (or microbial agents), a specific agent (e.g., *Clostridium botulinum*), or a microbial toxin (e.g. botulinum toxin). Although we are focusing on the transmission of microbial agents, diseases can also be caused by transmission of non-microbial agents such as chemical toxicants.

Microbial reproduction can occur outside or inside the host. For example, staphylococcal food poisoning occurs when *S. aureus* grows in food substrate and elaborates enterotoxin. Ingestion of preformed enteroxin in food results in clinical symptoms (nausea, vomiting, watery diarrhea) 1 to 6 hours after ingestion [3]. *S. aureus* can also grow inside a host causing a local abcess or causing systemic shock from the elaboration of the toxic shock syndrome toxin. Host injury can occur directly from the invading microbe, from a inflammatory host immune response, or from organ hypoperfusion (septic shock).

Infection and transmission are two sides of the same coin: infection is from the perspective of a susceptible host and transmission is from the perspective of an infectious source. *Infection* is acquisition of a microbe by a host [4] (see Figure 3). *Infectivity* is the probability of infection given exposure to a microbial agent. *Transmission* is the transfer (infection) of a microbe from an infectious source to a host. Transmission can occur within species (intra-species), between species (inter-species), or between the environment and a species. *Transmissibility* is the probability of microbe transfer to a host given contact (exposure). This is also called the *transmission probability*.

Infection can result in several possible states: elimination, commensalism, colonization, persistence, or disease. Microbe *elimination* from the host occurs from physical factors, host flora interference, immune response, or medical therapy. *Commensalism* occurs when a microbe is acquired early in life and becomes part of the normal microbial flora. Commensals do not cause host damage unless there is impaired immunity or altered microbial flora. Infection can result in *colonization*[2] where a microbe is recovered from a non-sterile site at which host damage is not clinically apparent. Colonization is transient and results in either microbe elimination, persistance, or host disease. Infection can result in microbial *persistence* when the microbe is not eliminated from the host and may or may not continue

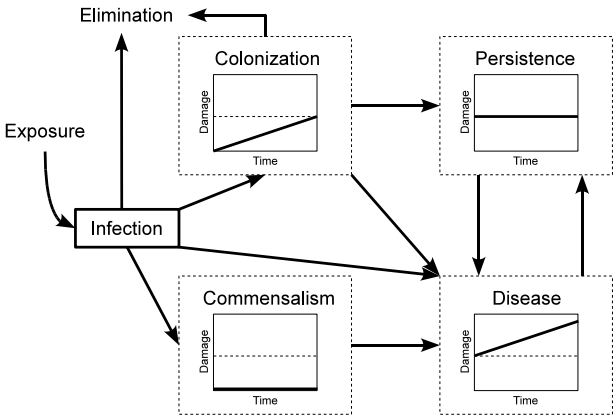


Figure 3: Damage-response framework of microbial pathogenesis: Infection (microbial acquisition by a host) leads to elimination, commensalism, colonization, persistence, or disease. The solid line represents host damage from host-microbe interaction. The dashed line represents the threshold at which the level or quality of host damage leads to persistence or disease. Source: Adapted from [4]

to cause host damage. Chronic hepatitis C infection and latent tuberculosis infection are both examples of persistence.

Disease is a state of infection where the host-microbe interaction results in sufficent host damage to be detectable by diagnostic tests, or to cause clinical symptoms or signs [5]. Disease can occur quickly after infection or can develop from commensalism, colonization, or persistence states. The term *pathogenicity* describes the probability of developing disease given infection. The term *virulence* describes the probability of severe disease, complication, or death given disease. For example, *Neisseria meningitidis* colonizes the human oronasapharynx resulting in a host immune response and eventual elimination. However, pathogenic strains are more likely to invade the bloodstream, causing meningococcemia, and the most virulent strains cause severe meningococcal disease (meningitis or septic shock) and death.

Reservoir. Reservoirs for microbes can be either human, animal, or environmental. Generally, the reservoir contains nutritional substrate to support microbial growth. Bacteria that sporulate are an exception; for example, *Bacillus* and *Clostridium* species can survive extreme conditions as spores, and only germinate into a vegetative form when conditions are favorable. To control an infectious disease, we must know the primary reservoir(s). For some infectious diseases, human are the only reservoir: polio, hepatitis A (B and C), measles, mumps, rubella, varicella, smallpox (before eradication[3]), and malaria. In large part, smallpox was eradicated from the human species because humans were the only reservoir—this is a necessary, but not sufficient, condition for successful eradication [6]. Other necessary conditions for eradication include that the microbial agent is not part of the normal human flora, and that effective prevention measures exist (e.g., vaccination).

[2]Colonization is synonymous with a "carrier" state.

[3]Eradication is defined as the extinction of the causative agent in man as well as in nature, leading to the cessation of all control measure including vaccination [6].

Table 2: Chain Model of Infectious Diseases—Reservoirs

1. Human
   (a) Symptomatic illness
   (b) Carriers
   (c) Asymptomatic (no illness during infection)
   (d) Incubatory (pre-illness)
   (e) Convalescent (post-illness recovery)
   (f) Chronic (persistent infection)
2. Animal (zoonoses)
3. Environment

In contrast, the eradication of human infectious diseases is very unlikely when animals are the primary reservoir for the microbial agent. Examples of human infectious diseases for which animals are the primary reservoir include West Nile virus disease (West Nile virus in migratory birds via mosquito vectors), Lyme disease (*Borrelia burdorferi* in rodents via tick vectors), enterohemorrhagic colitis (bloody diarrhea) and hemolytic-uremic syndrome (*E. coli* O157:H7 in cattle via ingestion), and cryptosporidiosis (*Cryptosporidium parvum* in calves). Human infectious diseases acquired from animals are called zoonoses or zoonotic infections. Several of the potential bioterrorism agents naturally cause zoonotic infections including *Yersinia pestis* (plague), *Bacillus anthracis* (anthrax), *Francisella tularensis* (tularemia), and *Brucella species* (brucellosis). In general, these microbes are well adapted to their animal reservoir, growing inside their hosts, and being efficiently transmitted between animal hosts. When a zoonotic disease occurs in humans, the agent is often not adapted to the human host and sustained human-to-human transmission may not occur. We see this phenomenom with West Nile virus infection, bat and dog-variant rabies, and avian influenza virus—all of which cause human disease, but are then not transmitted efficiently from human to human.

Examples of human infectious diseases for which the environment is the reservoir for the agent include botulism (neurotoxin from *Clostridium botulinum* in soil), tetanus (neurotoxin from *Clostridium tetani* in soil), legionellosis (*Legionella species* in water), Mycobacterium avium complex infections (*Mycobacterium avium complex* in soil and water), coccidioidomycosis (*Coccidioides immitis* in soil and dust), blastomycosis (*Blastomyces dermatitidis* in soil and dust), and aspergillosis (*Aspergillus* fungal species are ubiquitous in the environment). Environmental microbes that are ubiquitous are unavoidable. Many of these microbes are nonpathogenic in the face of a competent host immune system. However, in a severely immunocompromised host, these microbes can be deadly (e.g., *Pneumocystis jirovecii*[4] pneumonia in AIDS patients).

[4]Previously termed *P. carinii* [7]

Source. The source is where the infectious agent survives or reproduces prior to transmission to a host. The source of infection is a primary focus in any investigation of an infectious disease outbreak. However, because the reservoir can serve as the source of infection, understanding microbe reservoirs is necessary to conduct a thorough investigation. Therefore, any reservoir is a potential source (human, animal, environment). A non-reservoir source can be almost anything; the only requirement is that the microbe must survive in or on the source until it is transmitted to the host. In an outbreak investigation, if the known reservoirs or the usual sources are not implicated as the source of the outbreak, then analytic studies may be necessary to identify an unsuspected or new source and redirect the investigation. Only hypotheses that are considered by investigators can be tested in an analytic study. Therefore, if an analytic study does identify a potential source, investigators may need to re-think their current hypotheses or consider new hypotheses (see Case Study 1).

Case Study 1 Postoperative Serratia marcescens wound infections traced to an out-of-hospital source [8]

"From 25 August to 28 September 1994, 7 cardiovascular surgery (CVS) patients at a California hospital acquired postoperative *Serratia marcescens* infections, and 1 died. To identify the outbreak source, a cohort study was done of all 55 adults who underwent CVS at the hospital during the outbreak. Specimens from the hospital environment and from hands of selected staff were cultured. *S. marcescens* isolates were compared using restriction-endonuclease analysis and pulsed-field gel electrophoresis. Several risk factors for *S. marcescens* infection were identified, but hospital and hand cultures were negative. In October, a patient exposed to scrub nurse A (who wore artificial fingernails) and to another nurse—but not to other identified risk factors—became infected with the outbreak strain. Subsequent cultures from nurse A's home identified the strain in a jar of exfoliant cream. Removal of the cream ended the outbreak. *S. marcescens* does not normally colonize human skin, but artificial nails may have facilitated transmission via nurse A's hands."

Portal of exit. When a portal of exit exists, it determines how the infectious agent exits the source/reservoir. The portal of exit for an infectious human or animal is most commonly the respiratory, gastrointestinal or genitourinary tract, or a wound or ulcerative lesion on the skin or mucous membrane. Bloodborne pathogens exit the source through bleeding, phlebotomy, or sometimes genital secretions (e.g., HBV, HIV). When possible, portals of exit should be covered; for example, covering one's mouth and nose when coughing or sneezing, or bandage dressing an oozing skin wound. During the SARS outbreaks, while the respiratory tract was quickly identified as a portal of exit, it was not appreciated that the gastrointestinal tract harbored a large viral load until a single SARS case with diarrhea produced a large outbreak [9].

Table 3: Chain Model of Infectious Diseases—Mode of Transmission

1. Contact
   (a) Direct contact (e.g., touching, kissing, having sex)
   (b) Indirect contact (e.g., intermediate object, fomites)
2. Respiratory droplets (large particles: secrections, cough, sneeze)
3. Airborne (small particles: droplet nuclei, dust)
4. Vehicle-borne (e.g., ingestion, instrumentation, infusion/injection)
5. Vector-borne (e.g., mechanical, biologic)
6. Vertical transmission (e.g., in utero, at birth, breast milk)

Mode of tranmission. The mode of transmission is the mechanism by which the microbial agent gets from the source to the susceptible host (Table 3). Microbes can be transmitted from the source to the host by contact, respiratory droplet, airborne, vehicle-borne, or vector-borne routes.

Contact transmission occurs from direct physical contact with a source (e.g., touching, kissing, having sex), indirect contact with a contaminated intermediate object (e.g., environmental surfaces, fomites), or vertical transmission from mother to child before, during, or after birth. The vehicle-borne category includes ingestion of contaminated food or water, instrumentation (e.g., urinary catheter), injection (including injection drug use), and infusion (e.g., intravenous catheter). Vector-borne transmission can be biologic (vector feeding on the host) or mechanical (contaminated fly appendage contaminating a food item).

Droplet transmission occurs via large droplets ($>$ 10 microns) and secretions generated from the respiratory tract during coughing, sneezing, or talking. These droplets can directly enter the eyes, nose, or mouth, or indirectly by self inoculation by contaminated hands. Large respiratory droplets settle to the ground and environmental surfaces; however, smaller droplets (6–10 microns) may be suspended briefly (for several minutes), and inhaled into the proximal respiratory tract of the host [10].

Airborne transmission occurs when microbes are suspended in air on droplet nuclei ($<$ 5 microns) or dust, and can be transmitted over long distances and time intervals. Suspended droplet nuclei can be inhaled deep into the lungs. Airborne transmission can be obligate, preferential, or opportunistic [11]. *Obligate airborne* transmission occurs with microbes (e.g., *Mycobacterium tuberculosis*) that, under natural conditions, can only infect a host when aerosols are inhaled deep into the lung. *Preferential airborne* transmission occurs with microbes (e.g., measles virus) that predominantly infect a host by deposition of droplet nuclei in distal airways, but can also infect via other modes such as droplet transmission. *Opportunistic airborne* transmission occurs when a microbe infects a host predominantly by non-airborne modes but, under the right host or environmental conditions, can also infect via aerosolization. Opportunistic airborne transmission explained some of the "super spreading" events observed with the SARS outbreaks [12, 13].

Some microbes can be transmitted via multiple modes. Shigellosis, an extremely infectious bacterial gastroenteritis of humans, is an example. *Shigella* is generally described as being transmitted via the "fecal-oral" route. However, this description is insufficient to design control measures because it only summarizes the portals of exit and entry. More specifically, the modes of transmission include direct contact (person-to-person physical contact, including sexual), indirect contact (contaminated fomites), and vehicle-borne (ingestion of contaminated food or water). Therefore, understanding *all* the modes of transmission is necessary to implement preventive measures, to conduct an outbreak investigation, and to implement control measures during an outbreak.

Portal of entry. The portal of entry is where the infectious agent enters the host. Possible portals of entry include the following:

- Mucous membrane surfaces
  - Nose, mouth, oropharynx
  - Gastrointestinal tract
  - Genitourinary tract
  - Respiratory tract
  - Anorectum
- Cutaneous (or percutaneous)[5]

Practical application. Understanding the chain model of infectious diseases is essential for implementing common sense infection control and worker safety measures. For example, agents transmitted primarily by large repiratory droplets and secretions include influenza virus, *Neisseria meningitidis* (meningococcal disease), *Yersinia pestis* (pneumonic plague), and *Variola virus* (smallpox).[6] Large respiratory droplets fall out of the air, settling close to the source (usually within 3 feet). Therefore, common sense transmission control measures for these communicable agents include: having the infectious case cover the portal of exit ("respiratory hygiene" and "cough etiquette"); having the susceptible host use barrier methods to cover portals of entry (face mask, goggles); having the infectious case and susceptible host disinfect their hands ("hand hygiene"); and having the susceptible host increase their awareness of touching their face, mouth, nose and eyes with their hands ("hand awareness"). Hand awareness may reduce self inoculation from hands that have had contact with infectious patients or contaminated environmental surfaces.

Respiratory airborne agents transmitted by droplet nuclei include measles and varicella viruses, and *Mycobacterium tuberculosis*. Droplet nuclei remain suspended in the air for longer periods of time and can travel over distances. Reducing the risk of airborne transmission requires diluting and/or filtering air. Air can be diluted by increasing ventilation (opening the

[5] Skin or skin penetration

[6] Historically, small proportion of patients aerosolized the virus.

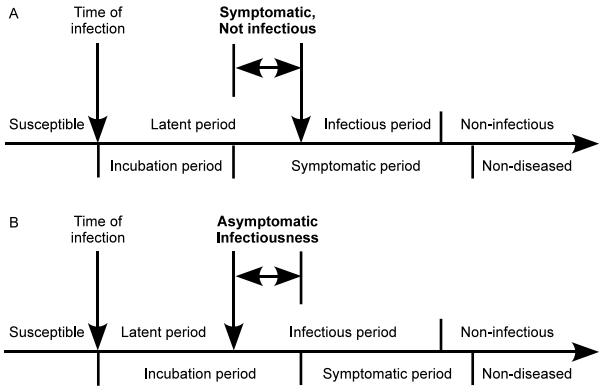


Figure 4: The Natural History of Infection and Infectiousness: A: When the latent period is longer than the incubation period, an infected person develops symptoms before becoming infectious. B: when the latent period is shorter than the incubation period, the infected person becomes infectious before developing symptoms (asymptomatic infectiousness).

windows), and it can be filtered by wearing a personal respirator. The common N-95 respirator is a snug-fitting face mask that filters air by the negative pressure generated by normal inspiration. To work properly, these respirators must be fitted and tested with the intended user. A higher level of protective, but much more expensive, alternative is wearing a powered air-purifying respirator (PAPR) hood. Preventing the spread of droplet nuclei to distant areas in a given facility can be achieved by implementing engineering controls that might include a negative pressure room for the infectious patient and assuring that any potentially recirculated air undergoes high efficiency particulate air (HEPA) filtration. Hospital and community infection control practices are derived from these basic concepts. We now understand the conceptual basis for contact, droplet, and airborne precautions in infection control practices [14].

2.2. *Natural history of infection and infectiousness*

To effectively interrupt transmission we also need to understand the natural history of infection, infectiousness, and disease and how they relate to each other. While clinicians focus on curing diseases and relieving symptoms, in public health we focus on understanding the dynamics of infection and infectiousness in order to prevent transmission (Figure 4). From the time a susceptible person is infected until he or she develops symptoms is called the *incubation period*. Clinicians are familiar with the incubation period because it helps them narrow their differential diagnosis when the causative agent is unknown. From the time a susceptible person becomes infected until he or she becomes infectious is called the *latent period*. The latent period is followed by the infectious period. The infectious period ends because the patient has cleared the infection or has died. When the latent period is longer than the incubation period, an infected person develops symptoms before becoming infectious. However, when the latent period is shorter than the incubation period, the infected person becomes infectious before developing symptoms (asymptomatic infectiousness).

Asymptomatic infectiousness. Asymptomatic infectiousness is the important driver of several infectious diseases with a large public health impact. For example, HIV infection is transmitted by direct person to person contact via blood or genital fluids. In the absence of any treatment, HIV-infected persons are infectious for a median of 10 years before developing symptoms of AIDS [15]. Hence, HIV-infected persons are potentially infecting many people (by sex or sharing injection drug use paraphenelia) for years before knowing they are infected. Likewise, many hepatitis C virus (HCV) infected persons can be infectious decades before developing symptoms that lead to a diagnosis of chronic HCV infection [16]. Persons with hepatitis A, measles, and influenza infection are infectious about 1 week, 3–4 days, and 1–2 days before developing symptoms, respectively [17]. Identifying exposed contacts can be more difficult when the exposure occurred before the infectious source developed symptoms, especially if the exposure occurred years before.

In contrast, with smallpox (when it existed), the latent period was longer than the incubation period, therefore patients developed symptoms (e.g., high fevers, muscle aches) before becoming infectious. In fact, patients with smallpox were most infectious after the rash onset. This made detection and isolation of cases and contact tracing and vaccination an effective disease control strategy. Likewise, patients infected with the human SARS coronavirus were infectious after developing respiratory symptoms and were progressively more infectious as their disease worsened. Hence, most secondary infections occurred among health care workers and close household contacts caring for very ill persons. This also helped to explain why transmission of SARS in the community was not sustained [18].

2.3. *Convergence model of microbe-human interaction*

In March, 2003, the "Convergence model of human-microbe interaction" was published by the Institute of Medicine (IOM), Committee on Emerging Microbial Threats to Health in the 21st Century [19]:

> The convergence of any number of factors can create an environment in which infectious diseases can emerge and become rooted in society. A model was developed to illustrate how the convergence of factors in four domains impacts the human-microbe interaction and results in infectious disease (Figure 5). . . . The emergence and spread of microbial threats are driven by a complex set of factors, the convergence of which can lead to consequences of disease much greater than any single factor might suggest. Genetic and biological factors allow microbes to adapt and change, and can make humans more or less susceptible to infections. Changes in the physical environment can impact on the ecology of vectors and animal reservoirs, the transmissibility of microbes, and the activities of humans that expose them to certain threats. Human behavior, both individual and collective, is perhaps the

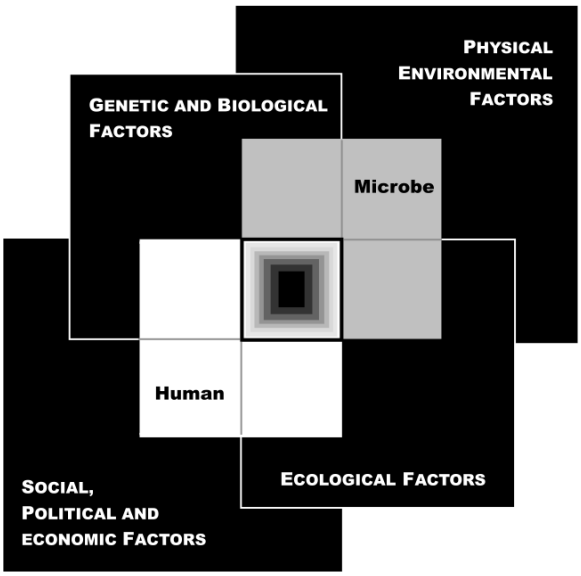


Figure 5: Convergence model of human-microbe interaction. At the center of the model is a box representing the convergence of factors leading to the emergence of an infectious disease. The interior of the box is a gradient flowing from white to black; the white outer edges represent what is known about the factors in emergence, and the black center represents the unknown. Interlocking with the center box are the two focal players in a microbial threat to health—the human and the microbe. The microbe-host interaction is influenced by the interlocking four domains of the determinants of the emergence of infection [19].

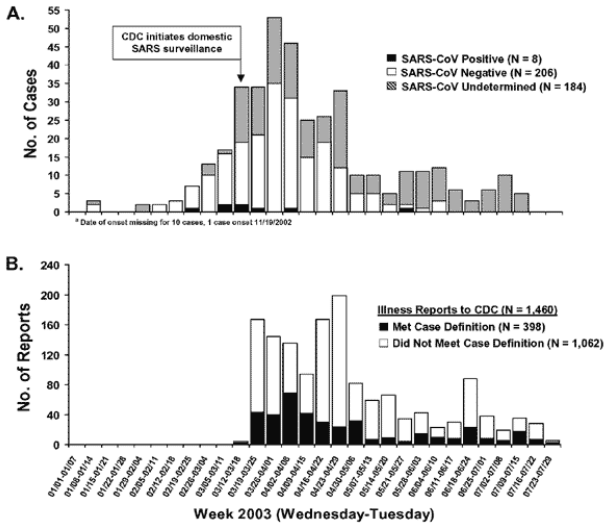


Figure 6: Probable cases of severe acute respiratory syndrome, by reported source of infection—Singapore, February 25–April 30, 2003. Source: CDC [22]

> most complex factor in the emergence of disease. Emergence is especially complicated by social, political, and economic factors—including the development of megacities, the disruption of global ecosystems, the expansion of international travel and commerce, and poverty—which ensure that infectious diseases will continue to plague us. Today we also face the threats of intentionally introduced biological agents.

Epidemiologists can think of this model as an updated version of the agent-host-environment model of infectious disease causation, also referred to as the "epidemiologic triad" [20]. However, the Convergence model provides important detail. More specifically, the IOM Committee considered the following individual factors as major contributors to the emergence and re-emergence of microbial threats to health:

- 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.

Through this integrated approach, we are reminded that causes can be complex, interrelated, and interdependent. The success or failure of our infectious disease prevention and control programs may depend on these factors, and how they interact. The current epidemic of highly pathogenic H5N1 avian influenza and the imminent threat of human pandemic influenza highlight the Convergence model [19, 21].

3. Transmission dynamics

Transmission dynamics is the population-level view of transmission of microbial agents with the occurrence of infectious disease cases. We cover the reproductive number, the infection rate among susceptibles, and the generation time.

3.1. The reproductive number

To understand the reproductive number it helps to adopt the perspective of a microbial agent that has infected and produced an infectious human case. In order for a communicable microbial agent to survive among humans, it must produce (directly or indirectly), on average, at least one other infectious human case. This is the only way microbes can survive in a host population. The reproductive number is the average number of secondary infectious cases produced by cases during their infectious periods. If $R < 1$, the number of new cases will decline and eventually go to zero. If $R \approx 1$, the production of new cases will assume a steady state. If $R > 1$, the number of new cases will increase (growing epidemic). The SARS outbreak in Singapore, 2003, illustrates this general process (Figure 6).

Under different host population conditions, the reproductive number gives us different insights. We will consider the reproductive number under two primary scenarios: when an infection is introduced into a population (at time $t = 0$) and as

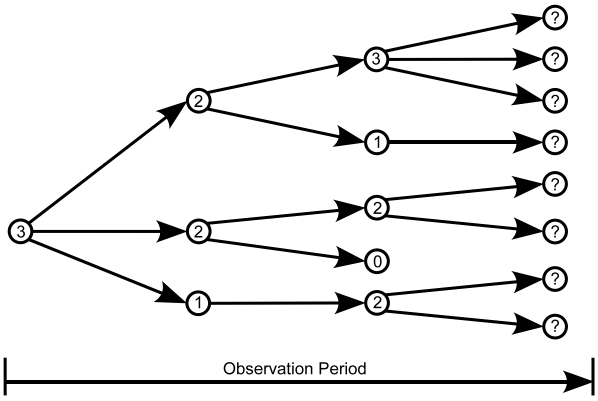


Figure 7: The reproductive number is the average number of secondary cases produced by infectious cases during their infectious periods. Each circle represents an infectious case, and the circle contains the number of secondary cases he or she produced. For example, the first case (at the far left) produced 3 secondary infectious cases, and so forth. Therefore, to calculate the average reproductive number, calculate the arithmetic average of the number of secondary cases: $(3+2+2+1+3+1+2+0+2)/9 = 1.8$.

an epidemic evolves ($t > 0$). Two key factors affect how an epidemic (and R) evolves: the fraction of the population that is susceptible, and the presence and level of control measures. Under different scenarios, we will cover the basic reproductive number (R_0), the effective reproductive number (R), and the control reproductive number (R_C). Figure 7 illustrates how the reproductive number is calculated.

3.1.1. Basic reproductive number (R_0)

If an infectious case were introduced into a population ($t = 0$), we would like to know the inherent potential for this case to cause an epidemic. To do this, we pose the following question: If a single infectious case[7] was introduced into a completely susceptible population with no control measures, how many secondary infectious cases would be produced, on average? This is called the basic reproductive number (R_0).[8] The basic reproductive number allows us to compare different microbial agents for their potential to cause epidemics in a population. More importantly, understanding the components that determine R_0 is necessary to designing and implementing control strategies.

$$R_0 = dcp \tag{1}$$

In Equation 1 (from the perspective of an infectious case), d is the duration of infectiousness, c is the contact rate with susceptible hosts, and p is the transmission probability—the probability of infecting a susceptible host when contact occurs. By "source," we are usually thinking of an infectious human case; however, it could be an infectious mosquito or a contaminated blood product used for transfusion. For each microbial agent and infectious disease, "contact" and "transmission" need

[7] Also called "infective."

[8] R_0 is pronounced "R naught" or "R zero"

Table 4: Estimated per-act risk (Transmission probability) for acquisition of HIV, by exposure route to an infected source. Source: CDC [25]

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

to be defined carefully. Contact is an exposure episode. For example, for an HIV-infected man, contact might be defined as unprotected, insertive intercourse with another person. For a microbial agent, we generally define transmission to mean sufficient transfer of the agent to lead to an infection (pathological persistence in host, subclinical injury to host, or evidence of a host immune response). For example, transmission of hepatitis C virus can result in HCV infection (pathological persistence in blood), subclinical injury (liver inflammation with or without scarring), or presence of anti-HCV antibodies (evidence of a host immune response). Therefore, the operational definition of transmission probability will vary depending on the microbial agent and the outcomes under consideration.

Understanding the transmission probability can be less intuitive. Consider sexual transmission of HIV infection. Before the era of anti-retroviral therapy, the median time from infection to the development of AIDS was 10 years [23]. Therefore, the median duration of infectiousness was well over 10 years because even patients with advanced HIV disease could remain sexually active. The contact rate of HIV-infected patients with potentially susceptible hosts was measured through confidential surveys [24]. The transmission probability—the per act risk of an HIV-infected patient transmitting HIV to a susceptible sexual partner—has been studied extensively and the results are summarized in Table 4. In general, the per sexual act HIV transmission risk is very low. For example, the average risk of a woman contracting HIV infection from an infected man after having a single episode of unprotected penile-vaginal intercourse would be 10 in 10,000 (1 in 1,000). Therefore, R_0 for HIV transmission would be determined primarily from the duration of infectiousness and the contact rate.

Another familiar example of transmission probability is the secondary attack "rate" (really a risk) among susceptible household contacts who are exposed to an infectious index case. Secondary attack risks are usually estimated for infections that can be transmitted through household contact, such as tuberculosis, measles, chickenpox, influenza, and viral gastroenteritis.

In spite of the importance of R_0, it is difficult to measure empirically. This is because the necessary conditions—an index infectious case being introduced into a completely suscepti-

ble population without control measures—rarely occurs except when a novel microbial agent is introduced and spreads before it has been identified. For example, when HIV infection was introduced into San Francisco's gay male community in the late 1970s and early 1980s, these conditions were met. Similarly, the uncontrolled transmission of HCV among injections drug users before the availability of anti-HCV antibody testing is another of these rare occurrences in which R_0 can be measured. Another situation in which the necessary conditions for measuring R_0 were met occurred when the human SARS-coronavirus was introduced into several countries (China, Canada, Singapore, Taiwan, Viet Nam, etc.) causing outbreaks before the agent of SARS was identified.

3.1.2. Effective reproductive number (R)

The R_0 represents the inherent potential for an agent to cause an epidemic after the introduction of an infectous case into a population. However, the actual or effective reproductive number (R) after the introduction of an infectious cases into a population (still without control measures) would be a function of the basic reproductive number (R_0) and the fraction of the population (x) that is susceptible upon the introduction ($t = 0$) of the infectious case (Equation 2). If $x = 1$ (completely susceptible population), then $R = R_0$.

$$R = R_0 x \tag{2}$$

3.1.3. Control reproductive number (R_C)

From Equation 2, it is apparent that we could prevent an epidemic ($R < 1$) by sufficiently reducing x by some control measure. In this case, the effective reproductive number in the presence of control measures is called the control reproductive number (R_C) [26]. If the fraction susceptible, x, gets small enough, eventually R_C becomes less than 1. Therefore, decreasing the fraction of susceptibles is a proven strategy to get $R_C < 1$: we usually achieve this by vaccination.

The effect of vaccination:. If vaccination is our control measure, then $x = 1 - hf$, where f is the fraction of the population that has been vaccinated (*vaccine coverage*), and h is the fraction of those vaccinated that have complete protection (*vaccine efficacy*[9]). For a well-studied, vaccine-preventable disease, the basic reproductive number and vaccine efficacy are known. Armed with these data, and using simple algebra, we can estimate what fraction of the population would need to be vaccinated to bring $R_C < 1$. In other words, $R_C = R_0(1 - hf) < 1$ becomes

$$f > \frac{1 - (1/R_0)}{h}, \tag{3}$$

where f is the minimum vaccine coverage necessary to get $R_C < 1$.

For example, R_0 was between 3 and 5 for smallpox. The smallpox vaccine had a pre-exposure vaccine efficacy of about 98%. Therefore, if smallpox were re-introduced into the human population and spread naturally, then we would need to vaccinate at least 68% of the population if $R_0 \approx 3$, and at least 82% of the population if $R_0 \approx 5$, to get $R_C < 1$.

Table 5: Basic reproductive number for selected vaccine-preventable diseases

Disease	R_0
Measles	12–18
Pertussis	12–17
Diphtheria	6–7
Smallpox	5–7
Polio	5–7
Rubella	5–7
Mumps	4–7
HIV/AIDS	2–5
SARS	2–5
Influenza A (1918 H1N1)	2–3

Displayed in Table 5 are various R_0 values and vaccine coverage thresholds (f) for selected vaccine-preventable diseases [28]. This information is useful in several ways. First, we can use R_0 to compare the communicability of these infectious diseases. Notice that the R_0 for smallpox is much smaller than the R_0 for, say, measles. The differences in R_0 are primarily explained by the transmission mechanisms (p. 2). Smallpox was primarily transmitted by large respiratory droplets, and patients were not infectious until they developed a rash (that is, there was little to no asymptomatic infectiousness). In contrast, measles is spread by the airborne mode, and an infected person is infectious before the onset of the rash. As a result, measles is much more infectious than smallpox. Second, notice that an effective control measure (in this case, vaccination) does not need to be applied to the whole susceptible population to be successful; it only needs to be implemented sufficiently to make $R_C < 1$, although in public health practice we strive to protect as many people as is feasible and affordable.

Figure 9 displays a real-world example of these concepts—both R_0 and R_C [29]. On February 23, 2003, SARS was introduced into Toronto, Canada, and followed by two epidemic curves representing hospital outbreaks. In March, the early part of the first curve 1 rises rapidly and its slope approximates R_0: the average number of secondary cases when an index case was introduced into a completely susceptible population and without control measures. Once the outbreak was recognized and control measures were implemented, the epidemic curve peaked and returned to baseline approximately mid-to-late April. However, lulled by the disappearance of cases, infection control practices were relaxed and SARS was re-introduced in early May. Infection control measures were immediately re-instituted and we can see the subsequent "blunting of the curve" in late May. In this second curve, the initial slope was less steep and it approximates R_C. Therefore, in this completely susceptible population, the initial slope in the first curve measures R_0, the average number of secondary cases in the absence of control measures, and the initial slope in the second curve measures R_C, the average number of secondary cases in the presence of

[9] This is a simplification but serves our purposes. For a complete discussion, see Halloran [27].

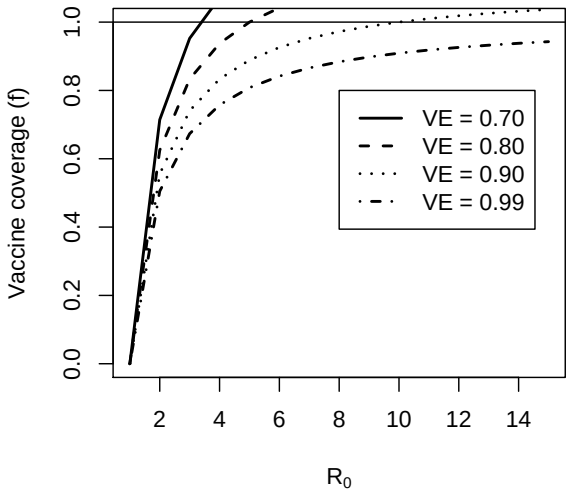


Figure 8: The vaccine coverage (f) required to get the control reproductive number ($R_C < 1$) given the basic reproductive number (R_0) and vaccine effectiveness (h). For a high effective vaccine or low R_0, only a proportion of the population needs to gets vaccinated to get $R_C < 1$. This is a general property of interventions: they need to reach a sufficient proportion of the population to get $R_C < 1$

control measures.

3.1.4. Reproductive number changes with time ($t > 0$)

So far, we have considered the reproductive number upon the introduction of an infectious case into a population. However, as an epidemic evolves over time ($t > 0$), the average number of secondary cases changes. As a function of time (t), the effective reproductive number is denoted by $R(t)$, and the control reproductive number is denoted by $R_C(t)$.

For illustration, we simulated a smallpox outbreak where an infectious case of smallpox was introduced into a closed population of 10,000 susceptible people under four different scenarios (Figure 10). Curve A1 is the epidemic curve of prevalent smallpox cases in the absence of control measures. Curve B1 is the corresponding curve for the effective reproductive number,

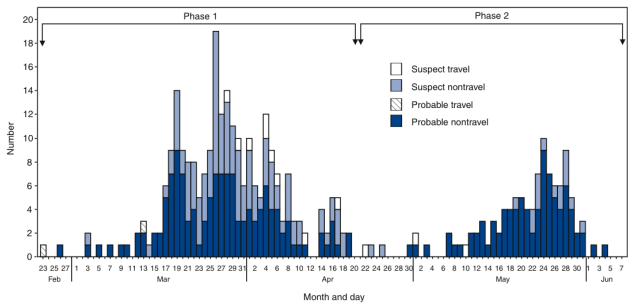


Figure 9: Number of reported cases of severe acute respiratory syndrome ($N = 361$), by classification and date of illness onset—Ontario, February 23–June 7, 2003. Source: CDC [29]

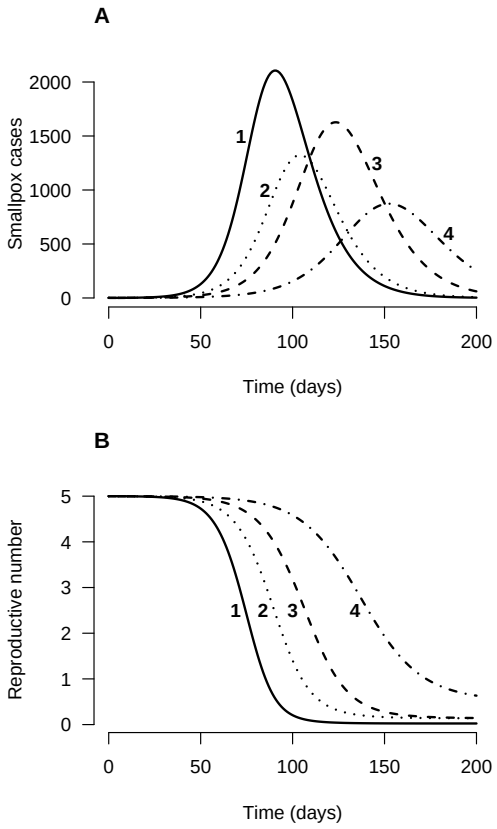


Figure 10: Simulated smallpox outbreak after introducing a single infectious case into a susceptible population of 10,000. Incubation period was 12 days, duration of infectiousness was 10 days, and $R_0 = 5$. Top curve (A) displays the prevalent cases, and bottom curve (B) displays the effective reproductive numbers. Curves A1 and B1 are without control measures. Curves A2 and B2 display the effect of vaccinating 70% of susceptibles. Curves A3 and B3 display the effect of case isolation, reducing the effective duration of infectiousness from 10 days to 7 days. Curves A4 and B4 display the effect of both control measures. Curves B2, B3, and B4 display the control reproductive number (R_C).

calculated from $R(t) = R_0 x(t)$. R_0 drives the initial exponential increase in Curve A1. Even in the absence of control measures, the epidemic curve peaks and the number of prevalent cases declines. In a closed population, this happens because the supply of susceptible hosts is depleted (and $x(t)$ decreases). This also happens with infections, such as influenza, that move rapidly through open communities. Notice that the effective reproductive number changes with time (Curve B1). The effective reproductive number is a dynamic number and, in this case, eventually drops below 1, and the epidemic burns out. Even in the absence of control measures, the natural transmission dynamics of an epidemic may lead to extinction of the disease ($R(t) < 1$); particularly in a closed (or approximately closed) population.

In Figure 10, Curves A2, A3, and A4 are the epidemic smallpox curves in the presence of control interventions. Curves B2, B3, and B4 are the corresponding $R_C(t)$s. Notice that the effect of control measures is to shift and blunt the epidemic curve. Our goal in communicable disease control is to blunt the epidemic curve (representing occurrence of fewer cases) *and* get $R_C(t) < 1$ so that the epidemic burns out. The effects of early control measures on an outbreak curve can also be seen in Figure 9.

As an epidemic spreads, susceptibles are infected and become infectious (known as "infectives"). Eventually, infectives are "removed" from the infectious state; they

- become noninfectious and immune;
- become noninfectious and not immune (susceptible again); or
- die.

For a closed population (no migration in or out) where infectives either die or become noninfectious with immunity, the number of susceptibles declines even in the absence of control measures. For an epidemic that moves rapidly through the population, the number of susceptibles also declines, even if the population is open. When the number of susceptibles declines, even in the absence of control measures, the average number of secondary cases produced by infectious cases also declines with time. In other words, the effective reproductive number ($R(t)$) actually changes over time:

- If $R(t)$ persists above 1, the epidemic continues to grow.
- If $R(t)$ persists around 1, the infection becomes endemic.
- If $R(t)$ persists below 1, the infection becomes extinct.

In summary, when an infectious case is introduced into a population ($t = 0$), the basic reproductive number (R_0) represents the inherent epidemic potential when the population is completely susceptible and there are no control measures. When a fraction x of the population is susceptible, the effective reproductive number (R) represents the actual epidemic potential where $R = R_0 x$. In the presence of control measures, R becomes R_C. If $R > 1$ at $t = 0$, an epidemic occurs; however, both $R(t)$ and $R_C(t)$ will change as the epidemic evolves over time ($t > 0$). The difference between $R(t)$ and $R_C(t)$ represents the impact of control measures. We see this in Figure 10. Consequently, using this approach, a logical goal of control measures is to (1) delay the outbreak peak, (2) decrease the magnitude of the outbreak peak, and (3) reduce the total number of infectious disease cases [30].

3.2. *Infection rate among susceptibles*

Understanding the components of the reproductive number focused our attention on key transmission control points, including duration of infectiousness, contact rate, transmission probability, and fraction of the population that is susceptible. However, to complete the picture we must consider the transmission process from the perspective of a susceptible host.

In epidemiology, the infection rate among susceptibles is the number of new infections divided by the person-time at risk. However, it's more instructive to consider the components of infection (Equation 4) with the following questions: First, what is the contact rate (c) with a potentially infectious source? Second, what is the probability that the potential source is infectious ($P(t)$)? And third, what is the transmission probability (p) given contact with an infectious source?

$$I(t) = cpP(t) \tag{4}$$

This perspective introduces an important new parameter to consider—the probability the potential source is infectious, $P(t)$. The contact rate is driven by behavior, the probability a potential source is an infectious case is driven by the prevalence of infectious cases, and the transmission probability is driven by biology and behavior.

3.2.1. *Contact rate*

The infection rate among susceptibles, $I(t)$, is a common and important epidemiologic measure of occurrence. Understanding the underlying components not only gives insights into the population level processes, but also helps us to develop and refine research questions, and to incorporate new research findings. Consider, for example, sexual contact rates among men who have sex with men (MSM). HIV researchers have hypothesized that selection of sexual partners (sexual mixing) in the MSM community is not random. In fact, sexual mixing is heterogeneous, with selection being influenced by age and HIV serological status. Older men (who are more likely to be infected) tend to select younger men (who are less likely to be infected). Known HIV-positive men tend to select known HIV-positive partners, and known HIV-negative men tend to select known HIV-negative partners. This has been called "serological sorting." At a population level, for a given contact rate, age sorting can result in more new infections, and serological sorting can result in fewer new infections. We can appreciate that these new research findings must act through the contact rate parameter.

3.2.2. *Probability a source is infectious*

A first approximation of $P(t)$ is the prevalence of infectious cases circulating in the target community. For example, in San Francisco in the mid-1980s, an MSM who randomly selected a

sexual partner from the MSM community had an approximate 50% chance of selecting an HIV-infected sexual partner [31]. That is, P was approximately 0.5. These components (contact rate (c), transmission probability (p), and prevalence (P)) act together to cause an increase or decrease in the infection rate, $I(t)$. Knowing individual parameters is not sufficient to predict infection rates. For example, if the contact rate was very high (e.g., high rates of unprotected anal intercourse), but the prevalence of HIV-infection was zero, the infection rate would still be zero. HIV transmission prevention efforts have focused on affecting the contact rate and the transmission probability.

Blood banks prevent the transmission of bloodborne pathogens, such as HIV, HBV, and HCV, by donor deferral and screening blood to reduce the prevalence of contaminated blood units, P. The transmission probability (p)—the risk of infection after receiving a contaminated unit—is close to 1, and not amenable to post-exposure interventions to reduce the risk. Reducing the contact rate (i.e., blood transfusions) has limited effectiveness because, for many patients, blood transfusions are medically indicated and life-saving. Hence, an effective prevention strategy targets lowering the prevalence of contaminated units. The prevalence largely determines the per blood unit risk, and this risk has continued to decline as better methods for blood screening are developed and implemented [32].

3.2.3. Transmission probability

The transmission probability (p) is the risk of infection given contact to an infectious case. The transmission probability is determined by

- Susceptibility of the uninfected host;
- Infectiousness of the source; and
- Interruption of transmission (by physical, chemical, engineering, or environmental methods).

For an HIV-uninfected person, an ulcerative sexually transmitted disease increases their susceptibility to HIV infection. For an HIV-infected person, anti-viral therapy may reduce their infectiousness by reducing the blood and seminal/vaginal fluid viral load. Finally, condoms can interrupt HIV transmission.

3.3. Generation time

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, the generation time of influenza cases is about 3 days [33]. During human pandemic influenza, this leaves little time to effectively identify, contact, and quarantine exposed persons. In contrast, the generation time of hepatitis A cases is measured in weeks, leaving more time to identify exposed persons and administer post-exposure immune globulin.

Table 6: Transmission control points and control strategies

Control points	Control strategies
Contact rate (c)	1. Reduce contact rate
Probability potential source is infectious (P)	2. Reduce probability potential source is infectious
Duration of infectiousness (d)	See #3
Transmission probability (p)	3. Reduce infectiousness
	4. Interrupt transmission
	5. Reduce susceptibility
Fraction susceptible in population (x)	6. Reduce fraction susceptible

4. Transmission containment

Designing and implementing transmission containment interventions involves three steps:

1. Identify control points;
2. Derive control strategies; and
3. Design and implementing control measures.

4.1. Control points

From Equations 1 (p. 8), 2 (p. 9), and 4 (p. 11), we have identified five transmission control points. All infectious diseases act through these control points. Therefore, the success or failure of our disease control interventions is ultimately explained by their impact on these five control points:

1. Contact rate (c);
2. Probability potential source is infectious (P);
3. Duration of infectiousness (d);
4. Transmission probability (p); and
5. Fraction of population that is susceptible (x)

4.2. Control strategies

Now we can develop a comprehensive prevention and control strategy that always makes sense. Using this approach, we derive six control strategies (Table 6). These six strategies map back onto the five control points. Here are the six essential contral strategies in more detail:

1. Reduce contact between susceptibles and potential infectives
2. Reduce probability potential sources are infectious
3. Reduce biological susceptibility of susceptibles
4. Reduce biological infectiousness of infectives
5. Interrupt transmission between infectious source and susceptible host

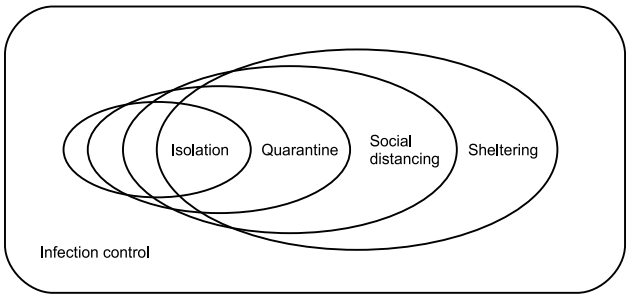


Figure 11: Summary of community mitigation measures. Isolation measures are applied to infectious cases. Quarantine measures are applied to exposed persons who may be in their incubation period yet infectious (i.e., past their latent period). Sheltering measures apply to persons or communities who have not been exposed. Social distancing measures apply to persons who are mixing or potentially mixing and whose exposure and infectious status may be unknown. All these measures require different levels of competence in infection control practices. Source: Adapted from [35].

6. Reduce fraction susceptible

It is important to consider the six strategies together. Failure to do so can result in unintended adverse effects. For example, suppose we introduce an HIV vaccine with a low efficacy. Although this will decrease the fraction of susceptibles, if the vaccination provides vaccinees with a false sense of protection and they increase their high risk behavior (i.e., increase the contact rate), then we may actually worsen the epidemic with this intervention [34].

4.3. Control measures

To design infectious disease control measures, we select control measures based on these six strategies (Table 7). Using these control strategies assures that our control measures are comprehensive and make epidemiologic sense. For example, consider the public health and medical response measures for human pandemic influenza (Table 8). Our epidemiologic concepts provide the rationale for these measures, and they provide guidance in the development of specific containment activities. To develop infection control guidelines, we apply concepts from the Chain Model of Infectious Diseases (reservoir, mode of transmission, etc.). Community mitigation measures are designed to reduce the contact rate between potential infectives and susceptibles (Figure 11 and Table 9) at home, school, workplace, and community [30]. Notice that some of these measures can act at multiple levels: finding cases ("case finding") provides data for surveillance, results in case isolation, and can lead to treatment. In turn, case isolation reduces the contact rate, and treatment reduces the magnitude and the duration of infectiousness. Finally, these concepts help us evalute the success or failure of our control measures.

5. Summary

In this review, we covered the epidemiologic concepts for preventing and controlling infectious diseases. We described transmission mechanisms, transmission dynamics, and transmission containment. Under transmission mechanisms, we reviewed the Chain Model of Infectious Diseases, the Natural History of Infection and Infectiousness, and the Convergence Model of Human-Microbe Interaction. Under transmission dynamics, we reviewed the reproductive number, the infection rate among suseceptibles, and the generation time. And under transmission containment, we reviewed control points, control strategies, and control measures.

Understanding of these core concepts helps us prioritize and conduct studies to identify and optimize prevention and control interventions. Clinicians can be informed about their role and how it directly and indirectly contributes to overall containment efforts. Field investigators can be guided to conduct an outbreak investigations using a systematic and comprehensive approach to hypothesis generation and testing. Communicable disease controllers can improve their design, implementation, and evaluation of interventions to control and prevent acute microbial threats as well as endemic infectious diseases. Finally, public health planners can improve the design, testing, and evaluation of their infectious disease emergency operations response plans.

References

[1] Last JM, editor. A Dictionary of Epidemiology. 4th ed. Oxford University Press, USA; 2000. Available from: http://amazon.com/o/ASIN/0195141695/.

[2] Caprioli A, Morabito S, Brugère H, Oswald E. Enterohaemorrhagic Escherichia coli: Emerging issues on virulence and modes of transmission. Vet Res. 2005;36(3):289–311. Available from: http://dx.doi.org/10.1051/vetres:2005002.

[3] Centers for Disease Control & Prevention. Diagnosis and management of foodborne illnesses: a primer for physicians and other health care professionals. MMWR Recomm Rep. 2004 Apr;53(RR-4):1–33. Available from: http://www.cdc.gov/mmwr/PDF/rr/rr5304.pdf.

[4] Pirofski L, Casadevall A. The meaning of microbial exposure, infection, colonisation, and disease in clinical practice. Lancet Infect Dis. 2002 Oct;2(10):628–635.

[5] Casadevall A, Pirofski L. The damage-response framework of microbial pathogenesis. Nat Rev Microbiol. 2003 Oct;1(1):17–24.

[6] Arita I, Wickett J, Nakane M. Eradication of infectious diseases: Its concept, then and now. Jpn J Infect Dis. 2004 Feb;57(1):1–6.

[7] Redhead SA, Cushion MT, Frenkel JK, Stringer JR. Pneumocystis and Trypanosoma cruzi: nomenclature and typifications. J Eukaryot Microbiol. 2006;53(1):2–11. Available from: http://dx.doi.org/10.1111/j.1550-7408.2005.00072.x.

[8] Passaro DJ, Waring L, Armstrong R, Bolding F, Bouvier B, Rosenberg J, et al. Postoperative Serratia marcescens wound infections traced to an out-of-hospital source. J Infect Dis. 1997 Apr;175(4):992–995.

[9] McKinney KR, Gong YY, Lewis TG. Environmental transmission of SARS at Amoy Gardens. J Environ Health. 2006 May;68(9):26–30; quiz 51–2.

[10] Tellier R. Review of aerosol transmission of influenza A virus. Emerg Infect Dis. 2006 Nov;12(11):1657–1662.

[11] Roy CJ, Milton DK. Airborne transmission of communicable infection–the elusive pathway. N Engl J Med. 2004 Apr;350(17):1710–1712. Available from: http://dx.doi.org/10.1056/NEJMp048051.

[12] Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med. 2003 May;348(20):1986–1994. Available from: http://dx.doi.org/10.1056/NEJMoa030685.

[13] Yu ITS, Li Y, Wong TW, Tam W, Chan AT, Lee JHW, et al. Evidence of airborne transmission of the severe acute respiratory syndrome virus.

N Engl J Med. 2004 Apr;350(17):1731–1739. Available from: http://dx.doi.org/10.1056/NEJMoa032867.

[14] Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings; 2007.

[15] Collaborative Group on AIDS Incubation and HIV Survival. Time from HIV-1 seroconversion to AIDS and death before widespread use of highly-active antiretroviral therapy: a collaborative re-analysis. Collaborative Group on AIDS Incubation and HIV Survival including the CASCADE EU Concerted Action. Concerted Action on SeroConversion to AIDS and Death in Europe. Lancet. 2000 Apr;355(9210):1131–1137.

[16] Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. Lancet Infect Dis. 2005 Sep;5(9):558–567. Available from: http://dx.doi.org/10.1016/S1473-3099(05)70216-4.

[17] Heymann DL, editor. Control of Communicable Diseases Manual. American Public Health Association; 2004.

[18] Svoboda T, Henry B, Shulman L, Kennedy E, Rea E, Ng W, et al. Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. N Engl J Med. 2004 Jun;350(23):2352–2361. Available from: http://dx.doi.org/10.1056/NEJMoa032111.

[19] Smolinski MS, Hamburg MA, Lederberg J, editors. Microbial Threats to Health Emergence, Detection, and Response: Emergence, Detection, and Response. National Academies Press; 2003. ISBN: 030908864X.

[20] Centers for Disease Control and Prevention. Principles of Epidemiology in Public Health Practice: An Introduction to Applied Epidemiology and Biostatistics. 3rd ed. Centers for Disease Control and Prevention; 2006. Available from: http://www.cdc.gov/training/products/ss1000/ss1000-ol.pdf.

[21] Knobler SL, Mack A, Mahmoud A, editors. Threat of Pandemic Influenza: Are We Ready? National Academies Press; 2005. ISBN: 0309095042.

[22] Centers for Disease Control and Prevention. Severe acute respiratory syndrome—Singapore, 2003. MMWR Morb Mortal Wkly Rep. 2003 May;52(18):405–411. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5218a1.htm.

[23] Blattner WA. HIV epidemiology: past, present, and future. FASEB J. 1991 Jul;5(10):2340–2348.

[24] Boerma JT, Weir SS. Integrating demographic and epidemiological approaches to research on HIV/AIDS: the proximate-determinants framework. J Infect Dis. 2005 Feb;191 Suppl 1:S61–S67. Available from: http://dx.doi.org/10.1086/425282.

[25] Centers for Disease Control and Prevention. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep. 2005 Jan;54(RR-2):1–20. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5402a1.htm.

[26] Bauch CT, Lloyd-Smith JO, Coffee MP, Galvani AP. Dynamically modeling SARS and other newly emerging respiratory illnesses: past, present, and future. Epidemiology. 2005 Nov;16(6):791–801.

[27] Halloran ME, Longini IM, Struchiner CJ. Design and interpretation of vaccine field studies. Epidemiol Rev. 1999;21(1):73–88.

[28] Centers for Disease Control and Prevention. History and Epidemiology of Global Smallpox Eradication; 2003. World Wide Web. Available from: http://www.bt.cdc.gov/agent/smallpox/training/overview/pdf/eradicationhistory.pdf.

[29] Centers for Disease Control and Prevention. Update: severe acute respiratory syndrome—Toronto, Canada, 2003. MMWR Morb Mortal Wkly Rep. 2003 Jun;52(23):547–550. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5223a4.htm.

[30] CDC. Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States—Early, Targeted, Layered Use of Nonpharmaceutical Interventions. Centers for Disease Control and Prevention; 2007. Available from: http://www.pandemicflu.gov/plan/community/mitigation.html.

[31] Catania JA, Osmond D, Stall RD, Pollack L, Paul JP, Blower S, et al. The continuing HIV epidemic among men who have sex with men. Am J Public Health. 2001 Jun;91(6):907–914.

[32] Goodnough LT, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. First of two parts—blood transfusion. N Engl J Med. 1999 Feb;340(6):438–447.

[33] Germann TC, Kadau K, Longini IM, Macken CA. Mitigation strategies for pandemic influenza in the United States. Proc Natl Acad Sci U S A. 2006 Apr;Available from: http://dx.doi.org/10.1073/pnas.0601266103.

[34] Blower SM, McLean AR. Prophylactic vaccines, risk behavior change, and the probability of eradicating HIV in San Francisco. Science. 1994 Sep;265(5177):1451–1454.

[35] Heyman D. Model Operational Guidelines for Disease Exposure Control. Center for Strategic & International Studies; 2005. Available from: http://www.csis.org/component/option,com_csis_pubs/task,view/id,2504/type,1/.

Table 7: Transmission control strategies and control measures

1. Reduce contact between susceptibles and potential infectives
   (a) Behavior change (host and/or source)
   (b) Case isolation
   (c) Case finding for intervention (e.g., isolation)
   (d) Contact tracing for intervention (e.g., quarantine)
   (e) Quarantine of exposed (individual, community, geographic boundary [Cordon sanitaire])
   (f) Sheltering (e.g., isolation of nonexposed)
   (g) Reduction in the number of infectious sources
   (h) Social distancing (school closures, travel restrictions)
2. Reduce probability potential sources are infectious
   (a) Case finding for intervention (isolation, treatment, etc.)
   (b) Identification and control of infectious sources
   (c) Vaccination
3. Reduce biological susceptibility of susceptibles
   (a) Vaccination (Pre- and post-exposure)
   (b) Immune globulin (Pre- and post-exposure)
   (c) Antimicrobial drug (Pre- and post-exposure)
   (d) Treatment of co-factor (e.g., ulcerative STD)
4. Reduce biological infectiousness of infectives
   (a) Treatment of cases
   (b) Vaccination (Pre- and post-exposure)
5. Interrupt transmission between infectious source and susceptible host, given contact
   (a) Physical and chemical methods (e.g., barriers: masks, goggles, condoms; respirators; hand sanitizers, etc.)
   (b) Engineering controls (e.g., HEPA filters, negative pressure rooms)
   (c) Environmental controls (e.g., disinfection)
6. Increase herd immunity (population-level effects)
   (a) Vaccination, consider the following:
      i. Naturally-acquired immunity
      ii. Fraction vaccinated (vaccine coverage)
      iii. Vaccine efficacy (fraction fully protected)

Table 8: Public health and medical response to pandemic influenza

1. Surveillance and epidemiology
2. Laboratory diagnostics
3. Transmission containment
   (a) Community mitigation measures
      i. Isolation of cases (infectious)
      ii. Quarantine of exposed (potentially infectious)
      iii. Social distancing measures
         A. School closures or suspension of classes
         B. Cancellation of large public gatherings, events, etc.
         C. Travel restrictions (to and from affected areas)
      iv. Sheltering (isolation of non-exposed)
   (b) Vaccine distribution and use
   (c) Antiviral drug distribution and use
4. Environmental and occupational health services
5. Infection control and clinical guidelines
6. Health care services, including mental health, and surge capacity
7. Health communications (media, public, clinicians, health care facilities)

Table 9: Community mitigation strategies for pandemic influenza

Home interventions

- Voluntary isolation of ill at home (adults and children); combine with use of antiviral treatment as available and indicated;
- Voluntary quarantine of household members in homes with ill persons (adults and children); consider combining with antiviral prophylaxis if effective, feasible, and quantities sufficient.

School interventions (child social distancing)

- Dismissal of students from schools and school based activities, and closure of child care programs;
- Reduce out-of-school social contacts and community mixing.

Workplace/Community interventions (adult social distancing)

- Decrease number of social contacts (e.g., encourage teleconferences, alternatives to face-to-face meetings);
- Increase distance between persons (e.g., reduce density in public transit, workplace);
- Modify, postpone, or cancel selected public gatherings to promote social distance (e.g., postpone indoor stadium events, theatre performances);
- Modify workplace schedules and practices (e.g., telework, staggered shifts).