Infectious Disease Epidemiology: Basic Principles for Mathematical Modelling

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Learning Objectives

- Understand basic concepts necessary for the study and control of infectious diseases
- Become familiar with some commonly used epidemiologic terms and study designs
- Describe how these epidemiologic concepts relate to mathematical modelling
Outline

* Part I - Basics of Infectious Disease Epidemiology
  * Epidemiological triangle
  * Classification of infectious diseases
  * Transmission

* Part II - Sources of Epidemiological Data
  * Basic terms
  * Study designs

* Part III - Public Health Interventions
  * Examples of interventions aimed at preventing spread of infectious diseases
Part I: Basics
Goals of Infectious Disease Epidemiology

1. Identify and describe causative agent

2. Understand relationship between the host, the agent, and the environment

3. Interrupt disease transmission to prevent spread

Part I: Basics
Goals of Infectious Disease Modelling

* Better understanding of disease transmission
* Predict future course of epidemics
  * Number of cases
  * Medical costs
  * Impact of outbreaks
* How to control the spread of epidemics
  * Education?
  * Immunization?
  * Isolation?
Epidemiological Triangle

HOST

Age, gender, genetics
Behaviour (smoking, sex, work)
Immune suppression, vaccination

AGENT

Pathogenicity
Infectivity
Immunogenicity

ENVIRONMENT

Social
crowding
“networks”
public health status

Physical
urban/rural
climate

Part I: Basics
Classification schemes for infectious diseases

- Microbiological
- Clinical
- Mode of transmission
- Reservoir
Microbiological classification

* Bacteria
  * e.g. Tuberculosis, gonorrhea, syphilis
* Viruses
  * e.g. HIV, influenza, measles
* Fungi
  * e.g. Cryptococcus
* Parasites
  * e.g. Malaria, giardia, helminths (worms)
* Prions
  * e.g. Bovine Spongiform Encephalopathy (BSE) (mad cow disease)

Part I: Basics
Clinical classification

Respiratory
Liver
Skin, Soft Tissue
Central Nervous System
Cardiovascular
Gastrointestinal
STIs, Genitourinary
Bones, Joints

Part I: Basics

Classification by reservoir in nature

* Human
  * E.g. HIV, gonorrhea, syphilis

* Environmental
  * Plants, soil, water
  * E.g. cholera – water,
    botulism – soil

* Animal (zoonoses)
  * E.g. rabies, hantavirus,
    * Yersinia pestis (plague)
Classification by mode of transmission

- **Contact:**
  - Direct – Skin/Sexual
  - Indirect - E.g. Infected blood
- **Airborne:**
  - Breathing in contaminated air
  - E.g. TB
- **Vectorborne**
  - E.g. Anopheles mosquitoes -> malaria
- **Foodborne, waterborne**
  - E.g. Cholera
- **Vertical**
  - Perinatal, post-partum (E.g. breastfeeding)
Stages of infection

- Susceptible
- Exposed
- Infectious
- Recovered/Immune
- Dead

Level of agent in host

Minimum level for transmission

Latent

Incubation

Symptomatic

Generation time

Time

Part I: Basics

Infection

(Adapted from Nelson, Masters Williams, 2007 pg 183)
Incubation period

- Time from exposure to development of disease
  - Expressed as a range (e.g. influenza: 1-3 days)
  - Varies by, e.g. organism, individual host, dose
  - Represents time needed for agent to reach a critical level to create clinical signs and symptoms
  - Can be infectious during incubation period, resulting in difficulty controlling spread of, e.g.
    - Measles, hepatitis A, chickenpox, etc.

Part I: Basics
Examples of incubation periods:
Viral diseases

Figure 2-2 Incubation periods of common bacterial diseases (top panel) and viral diseases (bottom panel). Source: Reprinted with permission from Viral Infections of Humans, 4th Edition, A.S. Evans and R.A. Kaslow, eds., p. 20, Copyright © 1997, Plenum Publishing Corporation.

(Nelson & Masters Williams, 2007; pg 38)
Examples of incubation periods:
Bacterial diseases

(Nelson & Masters Williams, 2007; pg 38)
Outcomes of exposure

- Depend on 3 biological characteristics of organism:
  - Infectivity
  - Pathogenicity
  - Virulence
- Terms often confused with each other
Outcomes of Exposure

Progression depends on exposed person and agent

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf
Infectivity

Secondary attack rate = \( \frac{\text{Number infected}}{\text{Number exposed}} \)

* Related to dose of agent transmitted – i.e. number of infectious particles transmitted
* Related to beta (\( \beta \)) in models
* E.g.
  * High infectivity: Smallpox
  * Low infectivity: Tuberculosis
Pathogenicity

\[ \text{Illness rate} = \frac{\text{Number with symptoms}}{\text{Number infected}} \]

* E.g.
  * High pathogenicity: Measles
  * Low pathogenicity: Polio

Part I: Basics
Virulence

Number of severe/fatal cases
---------------
Total number cases

* E.g.
  * High virulence: Rabies
  * Low virulence: Chicken pox
## E.g. Outcomes of Exposure

<table>
<thead>
<tr>
<th>Disease</th>
<th>Infectivity</th>
<th>Pathogenicity</th>
<th>Virulence</th>
</tr>
</thead>
<tbody>
<tr>
<td>chickenpox</td>
<td>high</td>
<td>high</td>
<td>very low</td>
</tr>
<tr>
<td>common cold</td>
<td>intermediate</td>
<td>intermediate</td>
<td>very low</td>
</tr>
<tr>
<td>leprosy</td>
<td>very low</td>
<td>very low</td>
<td>high</td>
</tr>
<tr>
<td>measles</td>
<td>high</td>
<td>high</td>
<td>low</td>
</tr>
<tr>
<td>smallpox</td>
<td>high</td>
<td>high</td>
<td>high</td>
</tr>
<tr>
<td>tuberculosis</td>
<td>low</td>
<td>low</td>
<td>high</td>
</tr>
</tbody>
</table>

http://www.nwcphp.org/docs/infectious/attachments/transcript.pdf

Part I: Basics
Inapparent infections

- Person is infected, but asymptomatic
- Measure of pathogenicity
- Varies by organism
- Carrier state
  - E.g. “Typhoid Mary”
Factors affecting risk of contracting infection
* May be biological, behavioural, sociodemographic
* Examples
  * Age (young/old)
  * Immunity
  * Genetic susceptibility
  * Socioeconomic status
  * Nutritional status
  * High-risk behaviours
    * E.g. Condom use, high number of sex partners
Example: Age

- Young
  - Immature immune system
  - New exposures
- Older Adults
  - Waning immune system
    - E.g. decreased antibody production
  - Malnutrition – increased infection risk
  - Comorbid illnesses
    - E.g. Lung disease – pneumonia
    - E.g. Incontinence – urinary tract infections
Example: Immunity

- Host’s ability to resist infection
- Variable length of time
- By Infection
  - E.g. Measles, mumps, rubella, chickenpox, etc.
    - (vs. infections that do not generate long-lasting immunity, e.g. chlamydia)
- By Vaccination
  - Variable Protection – may need multiple doses or boosters
Lifetime vs. Short Immunity

- **Susceptible**
  - **Infected**
  - **Recovered/Immune**

  **E.g. Measles**

- **Susceptible**
  - **Infected**
  - **Susceptible**

  **E.g. Chlamydia**

**Part I: Basics**
SIR model and Immunization

Part I: Basics

Susceptible

Immunization

Infected

Immune
Vaccinations

* 1798 Smallpox
* 1882 Rabies
* 1890’s (Cholera)
* 1890’s Typhoid
* 1920’s BCG
* 1920’s Diphtheria
* 1920’s-90’s Pertussis
* 1930’s Yellow Fever
* 1940’s Influenza
* 1950’s/60’s Polio
* 1960’s Measles, Mumps, Rubella

* 1970’s Meningocococcus
* 1980’s Hemophilus B
* 1970’s Varicella
* 1980’s Hepatitis B
* 1920’s-90’s Pneumococcus
* 1980’s Hepatitis A
* 1990’s Rotavirus
* 1990’s Lyme
* 2002 Papillomavirus

Part I: Basics
**Impact of Immunization**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Baseline 20th Century Annual Morbidity</th>
<th>1998 Provisional Morbidity</th>
<th>% Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallpox</td>
<td>48,164*</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>175,885†</td>
<td>1</td>
<td>100%‡</td>
</tr>
<tr>
<td>Pertussis</td>
<td>147,271§</td>
<td>6279</td>
<td>95.7%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1314</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis (paralytic)</td>
<td>16,316¶</td>
<td>0**</td>
<td>100%</td>
</tr>
<tr>
<td>Measles</td>
<td>503,282‡‡</td>
<td>89</td>
<td>100%‡</td>
</tr>
<tr>
<td>Mumps</td>
<td>152,209‡‡</td>
<td>606</td>
<td>99.6%</td>
</tr>
<tr>
<td>Rubella</td>
<td>47,745§§</td>
<td>345</td>
<td>99.3%</td>
</tr>
<tr>
<td>Congenital rubella syndrome</td>
<td>823</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> type B</td>
<td>20,000¶¶</td>
<td>54***</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

*Table 3.12-1: Baseline 20th Century Annual Morbidity and 1998 Provisional Morbidity from Nine Diseases with Vaccines Recommended before 1990 for Universal Use in Children—United States*
Herd immunity

- Number of people immune in the population decreases risk of infection among susceptible because of decreased probability of exposure
- Related to the proportion of individuals with complete immunity in order to prevent transmission/epidemics (e.g. measles & other vaccine-preventable infections)
- More infectious => higher levels of population immunity required
Herd Immunity

Low immunity

High immunity

Susceptible

Infected

Immune
Basic Reproductive Number ($R_0$)

- The number of secondary cases generated by a single infective case entering an entirely susceptible population

- If $R_0 > 1$ →

- If $R_0 = 1$ →

- If $R_0 < 1$ →

Part I: Basics

[Imperial College course notes, 2007]
Basic formula for $R_0$

$$R_0 = D \, c \, p$$

- $D = \text{Mean duration of infectivity}$
- $c = \text{Average number of contacts per unit time}$
- $p = \text{Probability of transmission per contact}$

[Imperial College course notes, 2007]
Factors influencing $R_0$

- $p$ (risk of transmission)
  - Differs by disease, type of contact
- $c$ (# contacts/unit time)
  - Depends on transmission route, population density
- $D$ (duration of infectivity)
  - Biological constant for a disease, can sometimes be altered with antibiotics

Part I: Basics
Environment

* Allows exposure to occur
* Physical: Geology, climate, habitat
* Biological: Human populations, flora, fauna
  * Sources of food, influence on habitat, vectors
* Socioeconomic: Occupations, crowding, urbanization
* Disasters: Earthquakes, floods, wars
Example: Conflict and HIV

- Social environment
- Sexual abuse/rape of female civilians
- Large proportion of military infected
  - 2-5X higher than general population
  - 2000: HIV prevalence rates among some South African military units of between 60% and 90%
  - Uganda: 27% of military personnel have tested HIV positive.
- Food insecurity – sex for food or money
- Forced migration
- Loss of Infrastructure

Part I: Basics
E.g. Cholera outbreak in Haiti

- Earthquake January 2010
  - 200,000+ people killed, 1 million+ displaced
- Cholera outbreak announced October 2010
  - 470,000+ cases, 6,631 deaths associated
- Evidence that cholera accidentally imported into Haiti, possibly by relief workers from Nepal (Piarroux et al, EID 2011;17:1161-7)
  - Controversial

http://www.cdc.gov/haiticholera/haiti_cholera.htm
Part II: Surveillance & Epidemiologic Study Designs
Part II: Surveillance & Epidemiologic Study Designs

* Epidemiologic terms
  * Incidence, prevalence
* Surveillance
  * Definition, functions, notifiable diseases
* Overview of epidemiologic study designs

Part II: Data
Incidence and prevalence

- Incidence =
  \[
  \frac{\text{Number of new cases of disease in a given time period}}{\text{Total number at risk during that time period}}
  \]

- Prevalence =
  \[
  \frac{\text{Number of existing cases of disease at a specific time}}{\text{Total number at risk at that specific time}}
  \]

\[
\text{Prevalence} = \text{Incidence} \times \text{Duration}
\]
Global summary of the AIDS epidemic  |  2009

Number of people living with HIV

<table>
<thead>
<tr>
<th>Total</th>
<th>33.3 million [31.4 million–35.3 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>30.8 million [29.2 million–32.6 million]</td>
</tr>
<tr>
<td>Women</td>
<td>15.9 million [14.8 million–17.2 million]</td>
</tr>
<tr>
<td>Children (&lt;15 years)</td>
<td>2.5 million [1.6 million–3.4 million]</td>
</tr>
</tbody>
</table>

Prevalence

People newly infected with HIV in 2009

<table>
<thead>
<tr>
<th>Total</th>
<th>2.6 million [2.3 million–2.8 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>2.2 million [2.0 million–2.4 million]</td>
</tr>
<tr>
<td>Children (&lt;15 years)</td>
<td>370 000 [230 000–510 000]</td>
</tr>
</tbody>
</table>

Incidence
Public Health Surveillance

“Public health surveillance is the ongoing, systematic collection, analysis, interpretation and dissemination of data regarding a health-related event for use in public health action to reduce morbidity and mortality and to improve health.” [German et al MMWR 2001;50(RR13):1-35]

Performed through network of labs, physicians and public health departments

Part II: Data
Functions of Surveillance

1. Estimate the magnitude of a health problem
2. Determine the distribution of illness
3. Detect an epidemic or outbreak
4. Evaluate control measures (eg. vaccines)
5. Monitor changes in infectious agent (eg. drug resistant strains)
6. Facilitate planning and setting priorities
7. Respond to emerging health threats

Part II: Data
Notifiable Diseases

- Mandatory reporting of these infections by physicians and/or laboratories
- Choice of diseases based on factors such as:
  - Incidence
  - Severity
  - Transmissibility
  - Preventability
<table>
<thead>
<tr>
<th></th>
<th>Blood Borne Pathogens</th>
<th>Communicable Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>* Blood Borne Pathogens</td>
<td>* Communicable Diseases</td>
</tr>
<tr>
<td></td>
<td>* HIV/AIDS</td>
<td>* Congenital CMV</td>
</tr>
<tr>
<td></td>
<td>* Hepatitis B</td>
<td>* Congenital Rubella</td>
</tr>
<tr>
<td></td>
<td>* Hepatitis C</td>
<td>* Diphtheria</td>
</tr>
<tr>
<td></td>
<td>* STIs</td>
<td>* Leprosy</td>
</tr>
<tr>
<td></td>
<td>* Chlamydia</td>
<td>* Malaria</td>
</tr>
<tr>
<td></td>
<td>* Chancroid</td>
<td>* Measles</td>
</tr>
<tr>
<td></td>
<td>* Gonorrhea</td>
<td>* Mumps</td>
</tr>
<tr>
<td></td>
<td>* Lymphogranuloma Venereum</td>
<td>* Pertussis</td>
</tr>
<tr>
<td></td>
<td>* Syphilis</td>
<td>* Poliomyelitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* Rubella</td>
</tr>
<tr>
<td></td>
<td></td>
<td>* Tuberculosis</td>
</tr>
</tbody>
</table>

Part II: Data
E.g. HIV reporting process

Detected by lab

Physician

Treats Patient

Public Health

Public Health Nurse Assigned to a case and collects information (eg. sex, age, exposure risks)

Province Compiles Data

Provincial Data sent to Federal Public Health

National Statistics Compiled
E.g. HIV surveillance in Canada

**FIGURE 2A**

Proportion of positive HIV test reports among women, by year of test and exposure category, 2000-2009

Proportion de rapports de tests positifs pour le VIH chez les femmes, selon l’année du test et la catégorie d'exposition, 2000-2009

<table>
<thead>
<tr>
<th>Year of diagnosis</th>
<th>Année du diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>2001</td>
</tr>
<tr>
<td>2002</td>
<td>2003</td>
</tr>
<tr>
<td>2004</td>
<td>2005</td>
</tr>
<tr>
<td>2006</td>
<td>2007</td>
</tr>
<tr>
<td>2008</td>
<td>2009</td>
</tr>
</tbody>
</table>

- IDU
- UDI
- Recipient of blood/Blood Products
- Receveur de sang/Produit sanguins
- Heterosexual Contact
- Contacts hétérosexuels
- Other
- Autres

Surveillance data: Tip of the Iceberg

Reported disease

Unreported disease

Part II: Data

Which cases are not reported?

* Patient with mild illness doesn’t seek medical care
* Disease not accurately diagnosed by health care provider
* Lab test not ordered
* Lab errors (false-negative)
* Public health officials not notified of disease

Part II: Data
Epidemiologic Study Designs

- Descriptive studies
  - Case reports
  - Case series
  - Ecological studies
- Analytic studies
  - Cross-Sectional Studies
  - Case-Control Studies
  - Cohort Studies
  - Randomized Clinical Trials

Part II: Data
Cross-Sectional Study

- Point in time “snapshot”
- Infection status and exposure measured at same time
  - Cannot determine which occurred first
- Measures of association:
  - Prevalence
  - Odds ratio

Defined Population

Gather Data on Exposure and Disease

- Exposed Have Disease
- Exposed Do Not Have Disease
- Not Exposed Have Disease
- Not Exposed Do Not Have Disease
E.g. Risk factors & HIV prevalence in Thailand

* 21 year old army recruits
* “Snapshot” of HIV prevalence & associated risk factors
* HIV prevalence:
  * 10.4% in 1991
  * 12.3% in 1993
  * 6.7% in 1995
* Prevalence of HIV & risky sexual activity decreased

Case-Control Studies

- Compare past exposures of people with disease (cases) to people without disease (controls)
- Can identify exposures associated with an outcome
- Measure of association: Odds ratio

<table>
<thead>
<tr>
<th></th>
<th>Exposed</th>
<th>Unexposed</th>
<th>Exposed</th>
<th>Unexposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Have disease)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(No disease)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Part II: Data
E.g. Risk factors for HIV after needle stick

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Stuck &amp; infected (Cases) (n=33)</th>
<th>Stuck &amp; not infected (Controls) (n=665)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep injury</td>
<td>52%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Visible blood</td>
<td>84%</td>
<td>35%</td>
</tr>
<tr>
<td>Needle in vein/artery</td>
<td>73%</td>
<td>31%</td>
</tr>
<tr>
<td>Postexposure zidvudine</td>
<td>27%</td>
<td>36%</td>
</tr>
<tr>
<td>Used gloves</td>
<td>78%</td>
<td>78%</td>
</tr>
</tbody>
</table>

Part II: Data

Cohort Study

* Follow subjects over time and compare disease status of those with and without exposure
* Measures of association:
  * Incidence, relative risk, odds ratio

Part II: Data
E.g. Cohort study: HIV and Human Papillomavirus (HPV) infection

* Certain high-risk types of HPV cause cervical cancer

HIV-Positive (n=871) → HPV: 8.1 per year

HIV-Negative (n=439) → HPV: 4.4 per year

Followed over time

RR = 1.8 (95% CI 1.3–2.7)

* Therefore, being HIV positive was associated with higher incidence of high-risk oncogenic HPV infections

Randomized Clinical Trial (RCT)

- Study subjects randomly allocated to two or more treatments, e.g., new and current (or placebo)
- Follow subjects forward in time and determine outcomes
- Measures of association: Incidence, relative risk, odds ratio

Part II: Data
E.g. RCT: Male Circumcision and HIV

2,784 HIV Negative Men in Kenya 18-24 years old

- 1393 Circumcised
  - 22 HIV + (2.1% / 2 years)
  - 1371 HIV -

- 1391 Not Circumcised
  - 47 HIV + (4.2% / 2 years)
  - 1344 HIV -

* 53% reduction in HIV incidence in circumcised group
* Examining adverse events and implementation strategies

Public Health Interventions
Public Health Interventions

- Improved water supply
  - Access, quality
- Sanitation
  - Sewer systems
- Hygiene
  - E.g. Handwashing
- Vaccination
- Vector control
- Treatment of infectious cases
- Sexual behaviour change
  - E.g. condoms, # partners
- Regulatory measures
  - E.g. quarantine, food standards
- Other
  - E.g. Antimicrobial prophylaxis, screening of blood supply

Part III: Interventions
Why use modelling?

An epidemiological perspective

- Understand spread of disease
- Predict future course of epidemics
- Evaluate possible impact of interventions
  - Vaccination
  - Isolation
  - Treatment
- Conduct conceptual experiments that would otherwise be difficult/impossible
- Relatively inexpensive
Question

* Using chlamydia (a sexually transmitted infection) as an example, for each of the 3 variables making up $R_0$, can you think of an intervention that would reduce its value, thereby reducing the reproductive number of this infection in the community?

$$R_0 = D c p$$
Basic concepts in infectious disease epidemiology include: epidemiological triangle, stages of infection, characteristics of the agent, different classification schemes.

Some key epidemiologic terms include incidence, prevalence, incubation period, infectivity, pathogenicity, virulence.

Surveillance is critical in epidemiology and a valuable data source.

Analytic epidemiologic study designs include: cross-sectional, case-control, cohort, and RCTs.

Knowledge of ID epidemiology helps to understand and develop effective mathematical models.
Acknowledgements

* Drs. Sabrina Plitt and Stan Houston for slides
* References:
  * Giesecke. Modern Infectious Disease Epidemiology.
  * Nelson KE, Masters Williams CF. Infectious Disease Epidemiology Theory and Practice, 2\textsuperscript{nd} ed. Mississauga, ON: Jones and Bartlett; 2007.
  * Gordis. Epidemiology.
  * Northwest Centre for Public Health Practice –Basic Infectious Disease Concepts in Epidemiology.
  * Course notes from Epidemiology & Control of Infectious Diseases. Imperial College London. 3-14 September 2007.
Resources

* Infectious disease epidemiology:

* Infectious diseases:

* Basic epidemiology:
Thank you!

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