Introduction

This week in Epiville, you will continue with the remaining steps of the outbreak investigation and begin to learn how to frame a hypothesis, design a study, and draw conclusions from your investigation.

Good luck and have fun!

Learning Objectives

A. Identify new concepts and terms:

1. What are the modes of disease transmission?
2. Distinguish among epidemic, endemic, and pandemic.
3. Define an incubation period.
   - Describe the use of epidemic curves to distinguish among different types of epidemic (point source, continuous source, propagated epidemic).
4. Define an epidemic curve and its properties:
5. Understand the different types of attack rate and calculate primary and secondary attack rates.
6. Explain the meaning of case-fatality ratio and ways how it can be calculated
7. Calculate the reproductive rate ($R_0$).
   - Describe the different components of the reproductive rate ($\beta$, $c$, and $D$).
Demonstrate the effects that varying these parameters have on R0.

Describe how an epidemic can be controlled by altering these parameters

B. Gather the information you need to formulate study aims, and hypotheses:

1. Who is at risk of becoming ill?
2. What is the disease?
3. What is the source of the epidemic?
4. What type of epidemic is this?
5. What is the route of transmission?
6. What measures to control the outbreak should be implemented?

C. Use your study findings to help you expand and refine the SARS outbreak control measures you developed in SARS I.

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SARS Outbreak Study 2

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Student Role

Since the initial outbreak in 2003, SARS (Severe Acute Respiratory Syndrome) has been reported in Asia, North America, and Europe, and has now made its way to Epiville. The Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), and local Department of Health (DOH) have all played essential roles in preventing a full-blown pandemic. A great deal of groundwork has been completed in our understanding of SARS in terms of its biology as well as the populations who are most at risk. The causal agent of SARS has been identified as a coronavirus, the genome of which has now been sequenced in its entirety. Subsequently, a diagnostic test has been developed which enables clinicians to distinguish patients with SARS from those with a similar set of respiratory symptoms. Such a test is essential in performing active surveillance to monitor the progression of the outbreak.

Intellectually curious?

Learn more about the diagnostic test developed for SARS

You are now responsible for designing the optimal outbreak management plan. You are required to conduct a formal study of the Epiville outbreak by analyzing the case data which have been collected. All individuals suspected of having contact with SARS cases have been quarantined, and those having been diagnosed with the disease, isolated. Everyone in Epiville and the surrounding communities is on high alert.

Before proceeding to the study design, review the available information collected about SARS at the Epiville Department of Health website.

**Intellectually curious?**

Visit these websites for the latest SARS situation update, as well as guidelines, recommendations, and other resources.

- World Health Organization's (WHO)
- U.S. Centers for Disease Control and Prevention's (CDC)

Now you are ready to move forward with designing a study. One of the first and most important steps in any study is developing specific aims and hypotheses.

Who is at risk of becoming ill?

What is the disease?

Where is the source of the epidemic?

What type of epidemic is this?

What is the route of transmission?

What measures to control the outbreak should be implemented?

1. Based on the facts as presented, select the answer below that represents the best hypothesis for the agent and transmission of SARS as well as the optimal control policy for the Amory Apartment Complex.
The possible agent of infection is coronavirus. The most likely spread of SARS is person-to-person.

b. The possible agent of infection is coronavirus. The most likely spread of SARS is person-to-person. The best approach for control of future SARS outbreaks is isolation of cases and quarantine of exposed.

c. The most likely mode of transmission of SARS is vector-borne, a mosquito. The best approach for control of the future SARS outbreaks is to stop traveling by airplane.

d. The possible agent of infection is a West Nile Virus. The most likely mode of spread of SARS is through sexual contact.

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SARS Outbreak Study 2

Data Analysis

Types of Epidemic Curves (Please see Giesecke, ch.12)

An epidemic curve is defined as a plot of the number of cases against the time of onset of disease, with time on the horizontal x-axis and the number of new cases on the vertical y-axis. It is a method of visualizing the progression of a disease over time which helps epidemiologists answer several important questions:

- What was the mode of transmission?
- When were the cases first exposed?
- What was the incubation period?
- Is this a point source epidemic or a propagated epidemic?
- What is the nature of observed cases?
  - Primary cases (persons initially infected from a point source), and
  - Secondary cases (person-to-person transmission from primary cases to others)?

In fact, our plot of the number of cases against the date of onset would be an example of a histogram (a row of columns). If we fit a line to it to show a trend, we will obtain an epidemic curve. This curve has some very specific and useful properties described below. The shape of the epidemic curve is determined by the epidemic pattern (point source vs. person-to-person spread), the period of time over which susceptible persons are exposed, and the minimum, average, and maximum incubation periods for the disease.
Point source epidemic:

In a point source epidemic, all members of the population at risk are exposed to the causal agent over a short period of time. The incubation period may vary among exposed individuals, reflecting differences in the intensity of exposures and/or differing immune responses among the exposed. The epidemic curve in a point source exposure commonly follows a log-normal distribution, in which the number of cases increases rapidly, reaches a peak, and then gradually tapers off, creating a right-skewed curve, or a curve in which the mode (or highest point of the curve) is shifted to the left of center.

In a point source epidemic, the shape of the epidemic curve, or the distribution of the cases over time, can reveal important clues about the type of exposure and the incubation period, and may offer hints as to the causal agent at work. Three elements of the point source epidemic curve are of particular importance: agent, incubation period, and date of exposure. It is noteworthy that given any two of these elements, we will be able to make inferences about the third element. This is typically known as "two out of three" rule.

The following example shows a plot of the distribution of cases over the outbreak period.

Assuming that a new point source outbreak will follow a similar lognormal distribution allows us to predict the projected severity of the epidemic in near real-time. For example, if in the above graph we only had information on the number of new cases through 11/15, we could fit a lognormal curve to the data we have accumulated and use it to predict the expected duration of the outbreak. Assuming a lognormal distribution also enables us to calculate the median incubation period by plotting the graph on a lognormal scale and establishing the peak.

Continuous Source Epidemic

Other types of epidemics lead to different epidemic curves. For example, in a situation where drinking water is being polluted, or some food source is being continuously contaminated, we may see a characteristic Continuous source epidemic curve (see below) in which the number of cases rises, and plateaus rather than tapering off (as in common-source above) when exposure ceases. In this situation no information on average incubation periods can be obtained, since the time of exposure is continuous and is therefore not known for each new case.
**Person-to-Person Transmission** (Propagated epidemic)

In a situation involving person-to-person mode of transmission, the epidemic curve will appear to have multiple peaks as wave after wave of infection spreads through a population, as shown below. In this example, cases in one peak may be sources for cases in a subsequent peak. If the incubation period and the infectious period are similar, peaks may, on average, be separated by one incubation period.

![Epiville Epidemic Curve](http://epiville.ccnmtl.columbia.edu/sars_outbreak_study_2/)

The Epiville Epidemic Curve

See the complete list of cases which appeared in the Amoy Apartment Complex and at the Star Hospital.

By plotting the number of cases which occurred on each day of the Epiville SARS outbreak, we can generate the following plot.

Now try to label the cases so that you can distinguish between cases which were identified at Amoy Apartment Complex and those from Star Hospital. Also, try fitting a line to the histogram to obtain an epidemic curve.

2. Based on histograms 1 and 2 and the following assumptions, estimate the incubation period range for the entire Epiville SARS epidemic.

   - The first SARS exposure took place at the Amoy Apartment Complex Luau party on 8/1
   - The first SARS exposure took place at the Star Hospital on August 3rd with the admission of an elderly patient from the Amoy Apartment
a. 5 days  
b. 5 to 12 days  
c. 2 to 20 days

3. Should we combine cases from the Amoy Apartment Complex and Star Hospital? Why or why not?  
   a. Yes  
   b. No

<table>
<thead>
<tr>
<th></th>
<th>Amoy Apartment Complex Outbreak</th>
<th>Star Hospital Outbreak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of people at risk</td>
<td>600</td>
<td>110</td>
</tr>
<tr>
<td>Number of SARS cases from 08/03-08/23</td>
<td>66</td>
<td>22</td>
</tr>
<tr>
<td>Number of deaths</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Number alive / ill</td>
<td>54</td>
<td>19</td>
</tr>
</tbody>
</table>

4. Calculate the primary attack rate for the outbreak in the Amoy Apartment Complex (hint: 65 residents of the Amoy Apartment Complex were hospitalized at the Epiville General Hospital and 1 resident was hospitalized at the Star Hospital).  
   a. See answer

5. Use the following equation to calculate the secondary attack rate using the data for the Star Hospital.  
   a. See answer

\[
\text{Secondary Attack Rate (\%)} = \frac{\text{Number of new cases in group} \cdot \text{[initial case(s)]}}{\text{Number of susceptible persons in the group} \cdot \text{[initial case(s)]}}
\]

Another useful measure is the **Case-Fatality ratio**. The case-fatality ratio tells you what percent of people diagnosed as having a certain disease die within a certain time after diagnosis. Case-fatality (usually expressed as a percentage) is the proportion of cases ending in death compared to the total number of cases of the disease within a population. The higher the case-fatality the more deadly the infection. (See Giesecke, p.11)

6. Perform the following calculations using the data in the tables provided above:  
   a. Calculate the case-fatality ratio for the Amoy Apartment Complex assuming the only fatalities from the disease are those who have already died; all currently infected subjects will recover.  
   b. Calculate the case-fatality ratio for the Amoy Apartment Complex assuming the following:  
      * Outcome of all infections is unknown  
      * Out of the 66 people WHO got sick, 12 died
c. Calculate the case-fatality ratio for the Star Hospital assuming the following:
   - We know the outcome of all infections.
   - All infected subjects recover

d. Calculate the case-fatality ratio for the Star Hospital assuming the following:
   - Outcome of all infections is unknown
   - Out of the 22 people working at the Star Hospital who got sick, 3 died
   - Out of the remaining 19 sick personnel 5 are still ill and the outcome of their illness is unknown.

7. Based on what you now know about SARS, which is the most ‘conservative’ way of determining the case-fatality ratio? Should we calculate case-fatality assuming that those who are still ill will recover?
   a. A and C (in question 6) - assume all patients will recover
   b. B and D (in question 6) - exclude those with the unknown outcome from the denominator

Intellectually curious?

Learn about other ways to calculate case-fatality.

At this point in the outbreak investigation, your primary concern is to contain the spread of SARS. Looking at the very different experiences of the two Epiville hospitals, you see the importance of public health measures which were instituted at the Epiville General Hospital, where no secondary transmission occurred.

Reproductive rate \( R_0 \), is the number of secondary infections per 1 infected case. This measure is useful in determining the outbreak control measures. It is defined by the following equation:
\[ R_0 = \beta \cdot c \cdot D \]

where:

- \( \beta \) = average probability a contact will be infected over duration of a relationship (depends on the biology and behavior of infection)
- \( c \) = average rate of getting into contact (isolation and quarantine minimize this parameter because infectious persons and those who are suspected to be infected are in minimal contact with healthy individuals)
- \( D \) = average duration of infectiousness (this parameter represents length of symptomatic disease; we can modify D by shortening duration of infectiousness. This could be achieved by proper treatment of cases, as well as improving the general health of the at risk population.)

8. There are a number of important policy implications derived from this formula. Which parameter of \( R_0 \) would you expect each of these to alter?

a. Wearing masks
b. Closing schools
c. Public advisory on attending public gatherings (cinemas were closed in Hong Kong during the SARS epidemic)
d. Precautionary measures at the hospitals (negative pressure wards and properly clothed personnel)
e. Travel advisories
f. Early identification and treatment of symptoms

Exercise:

The objective of this exercise is to understand how \( R_0 \) changes with varying of its parameters: \( \beta \), \( c \), and \( D \)

Directions for this exercise:

- This interactive map reflects the epidemic outbreak given 66 cases that occurred in Amoy Apartment Complex and 22 cases of secondary transmission in the Star Hospital.
- Use the dropdown boxes to demonstrate the effect that changing each of the parameters has on the magnitude of the outbreak
Discussion Questions

Carefully consider the following questions. Write down your answers (1 - 2 paragraphs) for question # 1 within a word document and submit your answers to your seminar leader. Be prepared to discuss all questions during the seminar section.

- What are the most cost effective and easily implementable ways of manipulating the parameters of reproductive rate to slow the spread of the SARS epidemic? Which of the parameters do you expect would be the most difficult to alter? What if the disease in question was not SARS but HIV/AIDS?

- Measures such as the attack rate and the case-fatality ratio give us a crude idea of the virulence and mortality of the infectious disease. During an active outbreak, when would the case-fatality ratio be most useful for public health planning and hypothesis testing: at the beginning, middle, or end of the outbreak?

- Consider the scenario in question 2. When would the attack rate be most useful for stopping the spread of the epidemic? How do changes in the definition of who is at risk affect the calculation of the attack rate, and how might these changes impact public health planning?