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Introduction

One of the most important tools of Infectious Disease Epidemiology is [outbreak](#) investigation. The following exercise will show you how epidemiological methods were applied to an outbreak of SARS in the fictitious city of EpiVille.

Good luck and have fun!

Faculty Highlight: Dr. Ian Lipkin

Dr. Ian Lipkin, head of the Center for Infection and Immunity, is a pre-eminent figure in the area of Emerging Infectious Diseases Epidemiology. In the fall of 1999, Dr. Lipkin and his team first identified West Nile Virus in New York State encephalitis victims. He is currently the head of the Jerome L. and Dawn Greene Infectious Disease Laboratory at the Mailman School of Public Health.



Dr. Lipkin is among the researchers from around the world who collaborated on the investigation of the SARS outbreak in the spring of 2003. Through a collaboration with other Columbia researchers, he recently received a \$3 million NIH grant supporting the development of technology to both detect and discriminate among multiple infectious diseases- including the SARS-associated coronavirus.

Read more about Dr. Lipkin's work

1. [Severe acute respiratory syndrome coronavirus persistence in Vero cells.](#)
2. [Real-Time Polymerase Chain Reaction for Detecting SARS Coronavirus, Beijing, 2003.](#)

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Learning Objectives

- A. Describe the principles of an outbreak investigation.
1. Define an [outbreak](#).
 2. Describe an epidemic in terms of person, place and time.
 - Describe key factors to consider when developing a [case definition](#).
 - Describe how the choice of case definition can influence an outbreak investigation.
 - List different [surveillance](#) methods used to ascertain cases
 3. List the six steps in an outbreak investigation.
 4. Describe the role of an epidemiologist during an outbreak investigation.
- B. Describe the principles of outbreak management
1. Describe different methods of outbreak management as they pertain to the epidemiological triad (i.e., host, agent and environment).
- C. Explain the importance of unrestricted flow of information among different public health agencies during an outbreak investigation and the timely communication of this information to the public.

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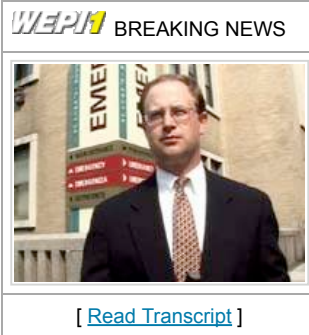
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Student Role

The EpiVillage Department of Health -- the site of your internship -- has been abuzz with activity concerning an outbreak of unusual cases of pneumonia deaths among patients in the EpiVillage General Hospital. Your supervisor, Dr. Zapp, gives you an assignment: acquaint yourself with the Department's surveillance and reporting systems and collect all available information about this outbreak.

Upon poring through the heavy folios in the Department's library, you learn a lot of information about disease surveillance. In EpiVillage, all hospitals, physicians and laboratories are required to report any suspicious symptoms that could pose a potential health risk to the general public. These reports provide the valuable clinical and demographic data the Department needs for monitoring disease trends and public health intervention. Your new colleagues also clue you in to WEPI1 TV, which is the best place to

hear the latest information about what's happening in Epiville. As it so happens, Stew O'Neil did a piece on the new outbreak in last night's news. You turn to the WEPI1 channel website to read the text file of his report.



Based on your own research and the newscast, you decide to look for the following background information on the internet:

- [Information about SARS on the Epiville Department of Health Website](#)
- [Epiville Map from the Epiville Chamber of Commerce Website](#)
- [SARS case definition from the World Health Organization \(WHO\) Website](#)

Getting information from books and the net is fine, but Dr. Zapp tells you that nothing beats the fieldwork. She directs you to visit the Epiville General Hospital to do the preliminary work for the outbreak investigation.

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Data Collection

Infectious Ward of the Epiville General Hospital

You begin your detective work with the infectious disease ward of the Epiville General Hospital. You start by reviewing the charts of patients who died from the mysterious disease. The administrator at the Admissions Office tells you that they suspect that this is severe acute respiratory syndrome (SARS), but the hospital has not yet received the materials to conduct diagnostic tests that could confirm these suspicions.

You decide to create a list with the names of the patients who have died from the mysterious disease, their symptoms upon admission to the hospital, symptom duration and if any patient family members became sick as well. You end up reviewing 12 charts of the patients who seem to have died from the same disease. Six persons were 60 and older, 4 persons were in the age range of 25 to 50, and 2 were children (3 and 11 years old). As you review the charts, you suddenly realize that all of the patients who died from the disease also happened to have the same street address and lived in the Amoy Apartment Complex. You decide to proceed by going over to their place of residence.

Amoy Apartment Complex

You arrive at the Amoy Apartment Complex and speak to Mr. Jones, one of the complex managers. Mr. Jones tells you that one tragedy after another has struck this set of buildings and people of all ages, young and old, are coming down with a severe flu and are dying. People are panicking and hardly anybody has left the building over the last three days. He has received 100 phone calls from tenants about breaking rent contracts. (The complex contains 200 apartments and serves a total of 600 residents.) Aside from those persons who have already passed away, there are 70 other people who have come down with similar respiratory flu-like symptoms. Most of these individuals were hospitalized at the nearby Epiville General Hospital. You take down the names of these people who reported being affected with flu-like symptoms and race back to the Department of Health.

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Data Analysis

Back at the DOH:

You suspect that what you have on your hands is an outbreak of SARS. Before going any further with your investigation you need to get guidance from your supervisor. Dr. Zapp compliments you on the job

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well done and outlines the following steps of the outbreak investigation to aid your work:

1. Define the epidemic
 - a. Define the "numerator" (cases)
 - b. Define the "denominator" (population at risk for developing disease)
 - c. Calculate attack rates
2. Examine the distribution of cases by person, place, and time (PPT)
3. Look for combinations (interactions) of relevant variables
4. Develop hypotheses based on the following:
 - a. Existing knowledge (if any) of the disease
 - b. Analogy to diseases of known etiology
5. Test hypotheses
 - a. Further analyze existing data utilizing an appropriate study design
 - b. Collect additional data
6. Recommend control measures

You return to your modest cubicle at the DOH and eagerly embark upon the first steps of an outbreak investigation: [descriptive analysis](#).

The epidemic should be characterized using the criteria in the [case definition](#).

NOTE: Despite your hard work, no case definitions are perfect because of possible case misclassification. For instance, a diagnostic test may show that a person has the disease when in fact they do not (false positives), or conversely, that a person is free of disease when in fact he or she is truly infected (false negatives). It is very important to have reliable and valid diagnostic tools to decrease the number of false positives and false negatives. The costs of misdiagnosing a case and delaying the appropriate treatment, especially in the case of such a deadly infection as SARS, can be significant. (For more information on this topic, please see Aschengrau & Seage pp. 418-422)

1. Based on what you just have learned, how would you go about preparing a case definition for this outbreak in EpiVillage?

- a. Compile a table of symptoms from all suspected SARS cases and from patients with other diagnosed respiratory illnesses, then provide information in terms of PPT.
- b. Compile a table of symptoms of all patients who were admitted to the hospital during the same time that the first patients were admitted to the EpiVillage General Hospital.
- c. Compile a table of symptoms of all patients who were admitted to the EpiVillage General Hospital over the last year and who lived in the Amoy Apartment Complex.

With your case definition at hand, you go back to the EpiVillage General Hospital to review the charts of the 70 persons who reside at the Amoy Apartment Complex. Based on your review of the charts, you confirm that 53 out of the 70 suspected cases in the apartment complex are most likely to be SARS cases. Out of the 17 patients who did not meet the case definition, 5 had similar symptoms as SARS cases but their chest X-rays were clear, others (6) recovered within a week (this was an indication that they just had flu), and the rest (6) had pneumonia of known etiology. All of these 53 individuals are alive and battling the disease. The case definition you came up with is remarkably similar to the case definition of SARS developed by the World Health Organization (WHO) in 2003.

You remember from your reading at the beginning of the day that surveillance is an essential feature of epidemiologic practice and is often divided into two "types": passive and active. Most of the surveillance done on a routine basis is called passive surveillance. In [passive surveillance](#), physicians, laboratories, and hospitals are required to report diseases from the list of reportable diseases (usually a list of 70-80 diseases) and are given the appropriate mailing forms and instructions, with the expectation that they will report all of the cases of reportable disease that come to their attention. [Active surveillance](#) requires

periodic telephone calls or personal visits to the reporting individuals/hospitals/laboratories to obtain required data.

2. Would you categorize each of the following activities as passive or active surveillance?

- a. Hospitals reporting SARS cases to the Department of Health
- b. Your visit to the Amoy Apartment Complex
- c. Your review of case records

3. What type of surveillance do you think is more difficult to carry out and why?

- a. Passive surveillance
- b. Active surveillance

The next morning, you are eager to show your case definition and report on your visit to the Amoy Apartment Complex to your supervisor. Dr. Morissa Zapp compliments you on your good work and recommends that you contact two other hospitals in the city to see if they have similar cases that were not reported through passive surveillance. Your advisor's suspicions are confirmed. There have been 3 suspicious deaths at the Star hospital. You set out to do your detective work immediately.

The hospital administrator tells you that they had a 70 year old man admitted two weeks ago with respiratory symptoms, and that a doctor and nurse who were taking care of him got sick within a week of his admission. When the administration realized how contagious the disease was, the patient, doctor and nurse were put into isolation. Unfortunately, by the time extraordinary precaution measures were instituted, 20 additional staff members had become infected, including 5 medical residents. All of them had visited the patient's room while attending the weekly rounds and may have had close physical contact with the patient. The hospital administration notified the DOH by a phone call about the situation, but failed to follow up with proper documents.

Employing your understanding of PPT, you decide to review the chart of the elderly man who was admitted to the hospital. His chart reveals that he lives in the Amoy Apartment Complex. Several days before he got ill, on August 1, 2003, he had attended an annual luau party held in the garden of the Amoy Apartment Complex. Approximately 300 other tenants also attended.

Now that you have gathered information on all the suspected SARS cases, you are ready to create a [spot map](#) (For more information on mapping, please see Giesecke pp. 23-24).

4. Given the place of residence of each "SARS affected-case" map the distribution of cases.

[[Open map](#)]

Do you see any clustering?

- a. Clustering around the hospital
- b. Clustering around the Amoy Apartment Complex
- c. No clustering

Now that you have mapped out all the cases according to the place of residence, you are ready to do some data analysis. The best measure to use in describing an epidemic is [cumulative incidence](#). Cumulative incidence is calculated as the number of new cases over a defined study period, divided by population at risk over that period. Cumulative incidence is usually expressed per 100, per 1,000, per 10,000, or per 100,000 (For more information, please see Aschengrau & Seage pp. 42-44).

Let's calculate the cumulative incidence for 5 residential areas of EpiVillage

Area ^a	Population Size	SARS Cases From the Outbreak at the Amoy Apartment Complex	SARS Cases From the Outbreak at the Star Hospital ^c	Total SARS Cases Reported from 08/03 to 08/24
A	14,000	0	3	3
B	53,000	66 ^b	4	70
C	13,000	0	5	5
D	12,000	0	8	8
E	8,000	0	2	2

^a The Amoy Apartment Complex is located in Area B, the Star Hospital is located in Area C, the staff of 110 persons who works at the Star Hospital resides all over EpiVillage and EpiVillage suburbs.

^b 65 cases were hospitalized at the EpiVillage General Hospital and 1 case was hospitalized at the Star Hospital.

^c 22 cases from the Star hospital include only staff members. Hospital staff reside in different areas of EpiVillage.

5. In the table above, EpiVillage is divided into five residential areas: A, B, C, D, and E. Calculate the cumulative incidence of SARS (per 1,000) in each area. Cumulative incidence is calculated as follows: [# of new cases of disease / # in candidate population] over a specified period of time (Please see Aschengrau pp. 42-44).

- What is the cumulative incidence of SARS (per 1,000) in Area A?
- What is the cumulative incidence of SARS (per 1,000) in Area B?
- What is the cumulative incidence of SARS (per 1,000) in Area C?
- What is the cumulative incidence of SARS (per 1,000) in Area D?
- What is the cumulative incidence of SARS (per 1,000) in Area E?

6. In which area do you observe the highest cumulative incidence of SARS? Why?

- Area D because the largest number of Star hospital employees resides there
- Area B because it has the largest population
- Area B because this is where the Amoy Apartment Complex is located and where the largest number of new cases live.

Disease transmission refers to any mechanism by which an infectious agent is spread from a source or reservoir to another person. The mechanisms, or [modes of transmission](#), are divided into two categories: direct and indirect. For instance, a disease can be transmitted from person to person by means of direct contact (e.g., influenza). Indirect transmission usually occurs through a common vehicle (e.g., contaminated air or a contaminated water supply) or through a vector such as a mosquito]. (For more information, please see Giesecke pp. 16-17 and the EpiVillage glossary).

7. Based on the cases from the Amoy Apartment Complex, which mode of transmission is most probable?

- Indirect: food or water.
- Direct: Person-to-Person

- c. Indirect: vector-borne (cockroaches)

8. Based on the cases from the Star Hospital, which mode of transmission is most probable?

- a. Direct: Only through bodily fluids
- b. Indirect: Air-borne through the hospital ventilation system
- c. Direct: Person-to-Person

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Outbreak Control

Just as you are going over your descriptive analysis, Dr. Zapp calls you in your office to let you know that the SARS diagnosis has been confirmed for all 12 dead cases from the Amoy Apartment Complex. Your primary goal now is to plan an effective [outbreak management](#).

During the outbreak management it may be necessary to take the following measures: quarantine (isolate a person until he or she is no longer infectious), isolate contacts, and conduct additional surveillance (passive and active).

9. What do you think would be an appropriate measure to control the outbreaks given what we know about SARS?

- a. Isolation and quarantine
- b. Educate the public on how to avoid infection

Intellectually curious?

[Learn more about the laboratory methods used in the outbreak investigation.](#)

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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.

- Based on what you know about HIV and SARS, how is SARS different from HIV? [Hint: consider the following points to compare these two epidemics: (1) Strategies for prevention, (2) Modes of transmission, (3) Time from disease emergence to its identification, (4) Resources, (5) Involvement of global community]
- 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?

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