SARS Outbreak Study 2

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!

Step 1: Learning Objectives

1. Identify new concepts and terms:
    1. What are the <u>modes of disease transmission</u> ?
    2. Distinguish among <u>epidemic</u> , <u>endemic</u> , and <u>pandemic</u> .
    3. Define an <u>incubation period</u> .
    4. Define an epidemic curve and its properties:
        - Describe the relationship between the <u>lognormal curve</u> and the incubation period in the point source epidemic
        - Describe the use of epidemic curves to distinguish among different types of epidemic (point source, continuous source, propagated epidemic)
    5. Understand the different types of attack rate and calculate primary and secondary attack rates.
    6. Explain the meaning of <u>case-fatality ratio</u> and ways how it can be calculated
    7. Calculate the <u>reproductive rate (R0)</u> .
        - Describe the different components of the reproductive rate (ß, c, and D).
        - Demonstrate the effects that varying these parameters have on R0.
        - Describe how an epidemic can be controlled by altering these parameters
2. 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?
3. Use your study findings to help you expand and refine the your SARS outbreak control measures you developed in SARS I.

Step 2: Student Role - Your Plan of Action

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

- Link to Real-time polymerase chain reaction for detecting SARS coronavirus, Beijing, 2003.
- Zhai J, et al. Institute of Microbiology and Epidemiology, Academy of Military Sciences, Beijing, China. Emerg Infect Dis. 2004 Feb;10(2):300-3.

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)

Step 3: Study Design

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.**

   a. The possible agent of infection is coronavirus. The most likely spread of SARS is person-to-person.
   Incorrect. While it is correct that the causing agent of the SARS epidemic is coronavirus and the most likely mode of spread of infection is person-to-person, this answer does not provide information on the control measures which will stop the outbreak.
   Correct. Based on what we know about SARS so far, the best formulated hypothesis is one that includes coronavirus as the most likely agent of infection, spread of SARS via person-to-person and isolation of cases and quarantine of exposed as measures of control of the spread of epidemic.

   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.
   Incorrect. From the previous SARS epidemic we have no data regarding its mode of transmission via mosquitoes. While it is certainly true that airplane travel has played a role in the spread of the SARS epidemic around the globe, it is unlikely that banning air travel to effected areas will completely stop the epidemic as the epidemic can spread by many other ways, e.g. local travel by buses and on foot

   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.
   Incorrect. Symptoms which are characteristic of West Nile virus infection differ from those of SARS infection, and therefore, the case definition of SARS cannot be met. In addition, the CDC has established that SARS is caused by a virus from the corona family, not by a West Nile virus. It has also been established that the most likely way of spread of SARS is person-to-person (which could be an artifact of sexual contact but sexual contact is not necessary to get the disease).

   d. The possible agent of infection is a West Nile Virus. The most likely mode of spread of SARS is through sexual contact.
   Incorrect. Symptoms which are characteristic of West Nile virus infection differ from those of SARS infection, and therefore, the case definition of SARS cannot be met. In addition, the CDC has established that SARS is caused by a virus from the corona family, not by a West Nile virus. It has also been established that the most likely way of spread of SARS is person-to-person (which could be an artifact of sexual contact but sexual contact is not necessary to get the disease).

Step 4: 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)?

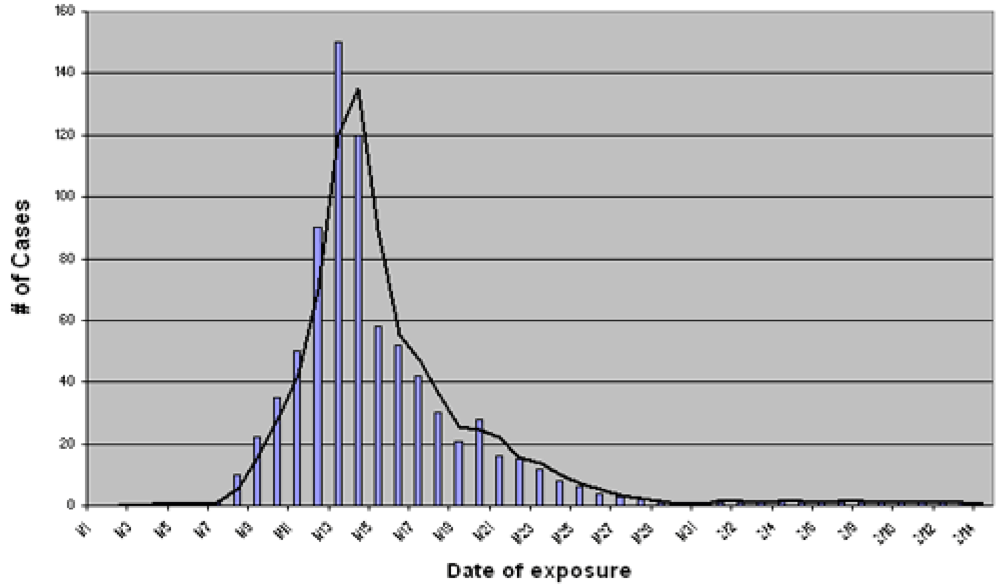
In fact, our plot of the number of cases against the date of onset would be an example of a histogram (a row of columns). If we fit a line to it to show a trend, we will obtain an epidemic curve. This curve has some very specific and useful properties described below. The shape of the epidemic curve 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:

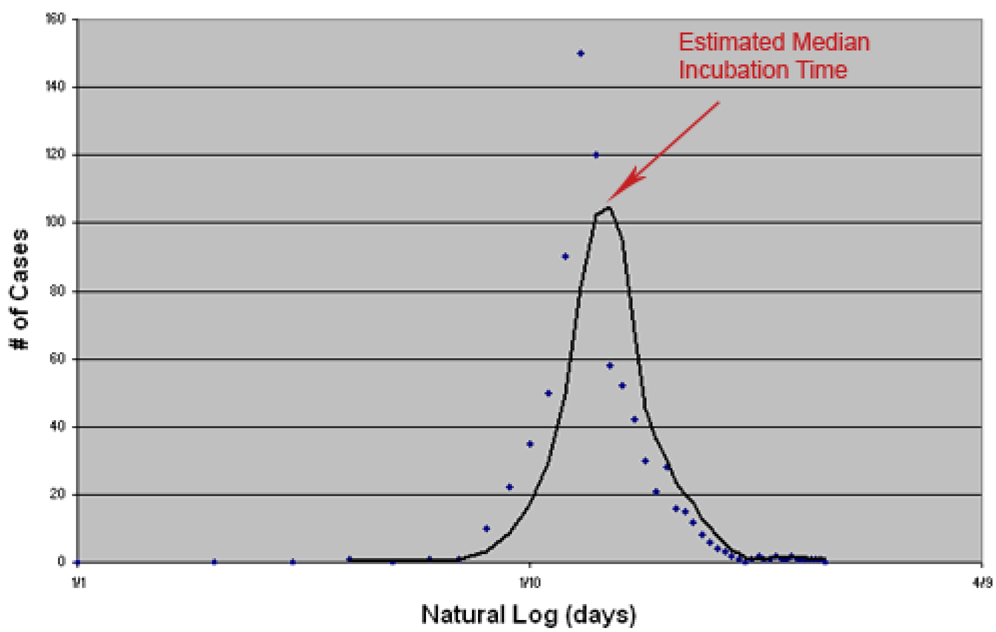
In a point source epidemic, all members of the population at risk are exposed to the causal agent over a short period of time. The incubation period may vary among exposed individuals, reflecting differences in the intensity of exposures and/or differing immune responses among the exposed. The epidemic 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.

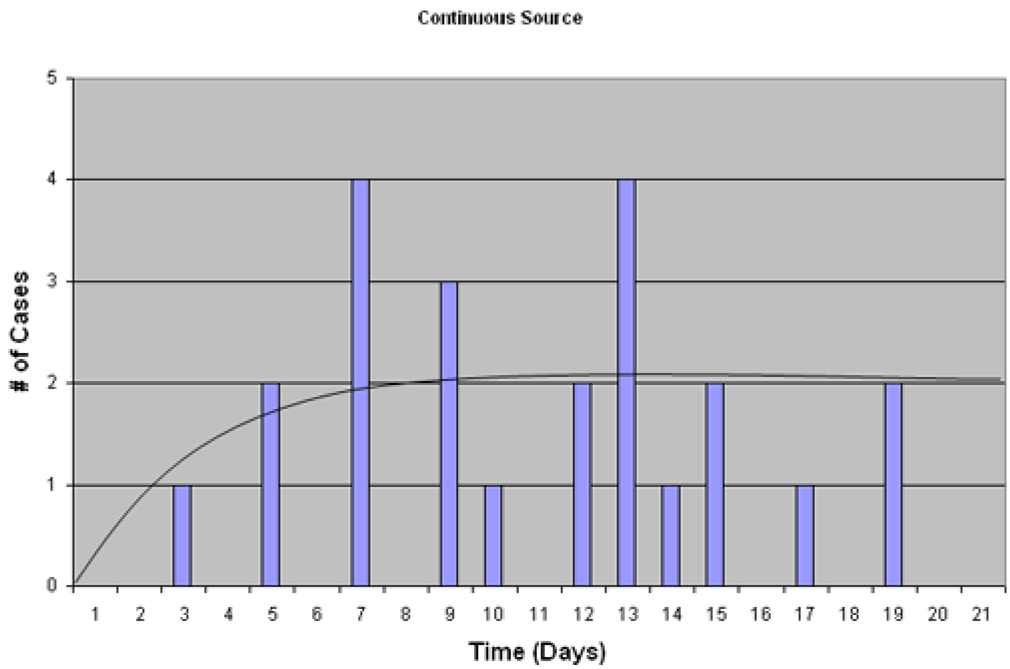


Assuming that a new point source outbreak will follow a similar lognormal distribution allows us to predict the projected severity of the epidemic in near real-time. For example, if in the above graph we only had information on the number of new cases through 11/15, we could fit a lognormal curve to 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. (see below).



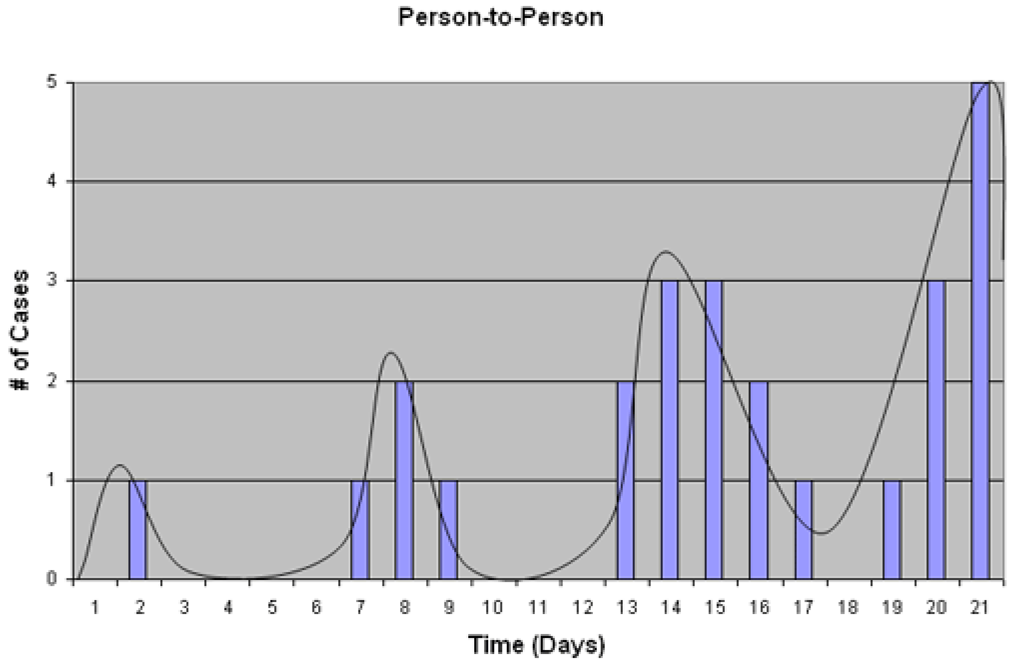
<u>Continuous Source Epidemic</u>

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.



<u>Person-to-Person Transmission</u> (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.



The Epiville Epidemic Curve

For a complete list of cases which appeared in the Amoy Apartment Complex and at the Star Hospital look here.

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

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. Look here.

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
Incorrect. Incubation period is not a particular number of days but rather a range of days, reflecting differences in the intensity of exposures and/or differing immune responses among the exposed.

b. 5 to 12 days
Incorrect. This is not the correct time interval between exposure to an infectious agent and onset

of disease in our outbreak.

c. 2 to 20 days
Correct. Persons were first exposed to SARS on August 1 at the Amoy Apartment Complex luau party. The first cases appeared 3 days later. Thus, the incubation period for the outbreak in the Amoy Apartment Complex is from 2 to 12 days. As we know from the data collected during the outbreak investigation, the first exposure at Star Hospital occurred on August 3, with the admission of an elderly patient from the Amoy Apartment Complex who then infected attending staff members. Based on the data plots presented above, the incubation period of SARS in Star Hospital ranged from 7 to 20 days. Therefore, the correct incubation period for the entire outbreak in Epiville is from 2 to 20 days.

3. Should we combine cases from the Amoy Apartment Complex and Star Hospital? Why or why not?

a. Yes
Incorrect. We should not combine cases from the Amoy Apartment Complex with cases from the Star Hospital because Star Hospital was the secondary wave of transmission. Combining all cases together will cause us to overestimate the incubation period.

b. No
Correct. By plotting the cases from the Amoy Apartment Complex and Star Hospital separately we can see that this is not a point source outbreak, but rather primary and secondary outbreaks of a person-to-person transmission outbreak.

	Amoy Apartment Complex Outbreak	Star Hospital Outbreak
Number of people at risk	600	110
Number of SARS cases from 08/03-08/23	66	22
Number of deaths	12	3
Number alive / ill	54	19

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).
65+1 = # cases of SARS at Amoy Apartment Complex
600 = # at risk (residents of the Amoy Apartment Complex including those that came to the

luau party and those who did not)

(66/600)*1,000 = 110 cases of SARS per 1,000 population at risk of SARS

Note: this is the same answer as that which you obtained

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

23-1 = # cases of SARS at the Star Hospital

111-1 = # at risk (employees of the Star Hospital who came in contact with the index case – an elderly man from the Amoy Apartment Complex)

((22) / (110))*1,000=200 per 1,000 population at risk of SARS

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

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.

Correct answer: (12/66)*100=18.18%

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
- Out of the remaining 54 sick patients 34 recovered and 20 patients are still ill as of August 23rd and their outcome (recovery or death) is unknown.

Correct answer: (12/(66-20))*100=26.09

c. Calculate the case-fatality ratio for the Star Hospital assuming the following:

- We know the outcome of all infections.
- All infected subjects recover

Correct answer: (3/22)*100=13.64

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 if the remaining 19 sick personnel 5 are still ill and the outcome of their illness in unknown.

Correct answer: (3/(22-5))*100=17.64

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
Incorrect. a and c (in question 6) are not more conservative because calculating the case-fatality ratio assuming that all those who are still ill will recover inflates the denominator and produces an underestimate of the case-fatality ratio.

b. B and D (in question 6) - exclude those with the unknown outcome from the denominator
Correct. b and d (in question6) are more conservative because calculating the case-fatality ratio using only those cases whose final outcome is known (died or recovered) before the outbreak is over, gives an overestimate.

Intellectually curious?

Learn about other ways to calculate case-fatality.

Step 5: Outbreak Control

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, 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:

$$R_0 = \beta * c * D$$

where:

β = 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_o would you expect each of these to alter?**	
a.	Wearing masks	B
b.	Closing schools	C
c.	Public advisory on attending public gatherings (cinemas were closed in Hong Kong during the SARS epidemic)	C
d.	Precautionary measures at the hospitals (negative pressure wards and properly clothed personnel)	B
e.	Travel advisories	C
f.	Early identification and treatment of symptoms	D

Exercise:

The objective of this exercise is to understand how R_o changes with varying of its parameters: β, c, and D

Directions for this exercise:

- The interactive map in the link below, 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.

[Open Exercise in New Window]

Step 6: Discussion Questions

1. 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 were not SARS but HIV/AIDS?

2. 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?

3. 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?

Intellectually curious?

Why do you think SARS did not return in the Spring of 2005?