CDC Science Ambassador Workshop
2014 Lesson Plan

Have You “Herd”? Modeling Influenza’s Spread

Developed by

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CENTERS FOR DISEASE CONTROL AND PREVENTION

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Have You “Herd”? Modeling Influenza’s Spread

Summary

During the 2009 influenza A H1N1 pandemic in the United States, an estimated 61 million cases of influenza were reported, resulting in an estimated 12,500 deaths.[1] Guidance has been developed to prepare, plan, and practice for the next influenza (flu) pandemic. Mathematical models have been designed to enable public health officials, policymakers, and students of infectious disease to examine influenza’s spread through communities. Models also facilitate identification of strategies to slow influenza transmission (e.g., school closures), allow hospital administrators and public health officials to estimate the surge in demand for hospital-based services during the next flu pandemic, and make possible laboratory directors’ forecasting demands for specimen testing and developing response plans. The key topic in this lesson is pandemic preparedness, including the following subtopics: vaccine development and the logistics of vaccine administration, importance of influenza surveillance, predictions for influenza’s spread using mathematical modeling, and implementation of countermeasures to prevent a pandemic.

Students will be engaged in activities to increase their understanding of modeling as a tool for public health preparedness. In the first portion of the lesson, students will obtain simulated patient samples and perform a test to determine if these patients are positive for a simulated rapid influenza diagnostic test. By using this information, students will interpret their results, considering false-positive and false-negative test results. As the lesson progresses, the scale of the outbreak scenario will increase, and students will use mathematical models to calculate the transmissibility of the virus and countermeasures that would be needed to limit the spread of influenza. Students will examine the herd immunity threshold of a population by determining the vaccine efficacy. Final questions will challenge the students to analyze the benefits, limitations, and applications of modeling for preparing and responding to future pandemics.

The lesson is designed as an upper-level high school course. Before the lesson, students should have an understanding of the cause and symptoms of influenza.

Learning Outcomes

After completing this lesson, students should be able to

- employ mathematical models for influenza outbreak scenarios to calculate measures of disease spread and intervention effectiveness.
- synthesize effects of physical (e.g., social distancing or nonpharmaceutical interventions) and medical (e.g., vaccines) countermeasures for influenza outbreak scenarios.
- identify public health countermeasures that restrict the spread of an influenza outbreak.
- explain the importance of vaccinations and the monitoring cases of infectious diseases.

Duration

This lesson can be conducted as one-, 90-minute lesson, or divided into two-, 45-minute lessons.

[1] Shrestha SS, Swerdlow DL, Borse RH, et al. Estimating the burden of 2009 pandemic influenza A [H1N1] in the United States [April 2009–April 2010]. Clin Infect Dis. 2011;52 Suppl 1:75–82

Background

Importance of Modeling

Certain diseases are not transmitted from person to person (e.g., heart disease or cancer); these diseases are called noncommunicable diseases. However, certain infectious diseases, called communicable diseases, are inherently transmissible and can quickly create substantial public health problems (e.g., the number of cases of a disease can increase exponentially within a matter of weeks during an epidemic). Therefore, public health researchers often account for these characteristics of infectious diseases by using the transmission modeling methods introduced in this lesson. Modeling allows for analyses explicitly accounting for transmission of infectious diseases and the effect of interventions on disease transmission. Different models can be used to predict what future epidemics, including an influenza pandemic, might look like, assess the effect of interventions, and predict the course of an ongoing epidemic.

Basic Reproduction Number (R_0)

The basic reproduction number (R_0) is defined as the number of new infections originating from a single infectious person among a total susceptible population.

Although other methods for measuring transmissibility are available, R_0 is among the most useful. Some alternative methods can only be calculated after the epidemic has been completed, making those methods less timely. Other alternatives only address transmission in a single setting (e.g., the number of persons infected in a household after a single family member gets the flu). R_0 is used as a measure of transmissibility that measures how many persons one infected person would infect if (1) no one had immunity, and (2) no treatment, quarantine, or other interventions were available.

Knowledge of R_0 can help predict the scale of an outbreak or epidemic and assess the level of countermeasures required for containment. An R_0 less than 1 (<1) means <1 new infection will result from each current infection. The number of resulting infections will decline until the disease is no longer spreading throughout the population. An R_0 greater than 1 (>1) might indicate that an epidemic will occur. The greater the $R_{0,}$ the larger the expected epidemic is among a given population. In the activity, students will calculate R_0 values of 2.20, 1.88, or 1.43 (depending on scenario). A pathogen with an R_0 of 2.20 would cause a larger epidemic than one with an R_0 of 1.43.

Effective Reproduction Number (R_E)

The effective reproduction number (R_E) is defined as the average number of cases produced by a typical infectious person among a population with limited immunity or interventions.

This concept is introduced to the students in a set of assessment questions at the end of the lesson. R_E is similar to R_0, but it accounts for immunity and countermeasures. For example, a pathogen that has an R_0 >1 among a population can lead to an epidemic. If the number of infected persons is increasing, the number of new infections among a population must be greater than the number of persons recovering from infection; thus, the R_E is >1. As the epidemic spreads, countermeasures (e.g., vaccination or treatment) can be put in place, and persons can become immune through becoming infected and recovering. The increasing level of immunity among the population will slow the spread of the infection. If each person only infects 1 other person, $R_E = 1$ when the number of new infectious cases reaches a plateau and equals the number of persons who are recovering. As transmission rates decrease even more, R_E will decline to <1, which implies that more persons are recovering than becoming infected among the population, and prevalence of infection will decline. At this stage, the transmission rate is decreasing and $R_E = 0$ when transmission stops (Figure 1).

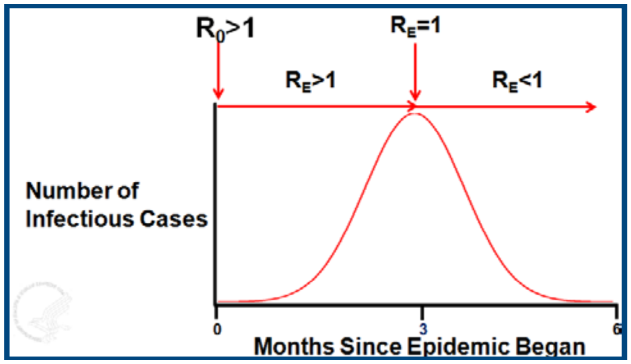


Figure 1. Epidemic rates relative to basic reproduction number and effective reproduction number. Source: O'Hagan J and Carias C. Modeling Influenza Outbreaks. Presented at CDC Science Ambassador Workshop July 22, 2014

Herd Immunity Threshold (HIT)

HIT is the fraction of a population that is needed to be immune to avoid widespread outbreaks, or, in the case of influenza, a pandemic. A pandemic is an epidemic occurring over a widespread area (multiple countries or continents) and usually affecting a substantial proportion of the population. The conditions necessary for a pandemic of influenza to occur include the emergence of a new influenza virus that can transmit readily from person to person and against which only a small percent of the population has immunity. Although HIT creates a target for vaccination programs, it assumes all members of a population are the same. Therefore, HIT is a theoretical value and can differ, depending on the characteristics of the population (e.g., access to health care or population density) (Figure 2).

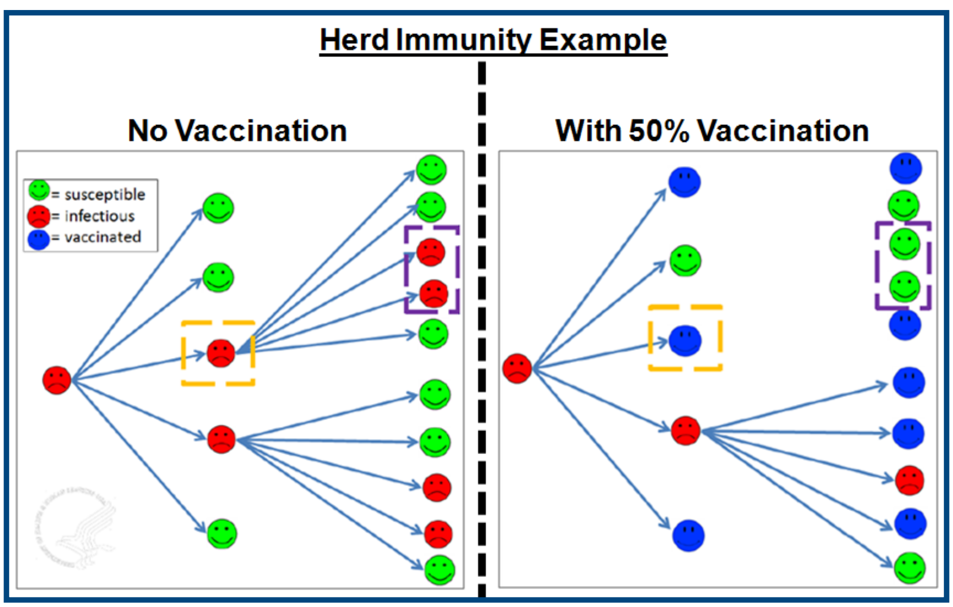


Figure 2. Herd immunity example displaying differences with vaccination rates for resulting infections. Source: Image developed by Justin O'Hagan and Cristina Carias for Modeling Influenza Outbreaks. Presented at CDC Science Ambassador Workshop July 22, 2014.

Procedures

Day 1: Modeling Influenza’s Spread, 45 minutes

Preparation

Before Day 1,

- Prepare simulated influenza tests. Note: To save 10 minutes of preparation time and 1 minute classroom time, the test swab that yields positive test result, high viral load (Preparing Simulated Influenza Tests, step 4) can be omitted. Students will test 4 swabs, 3 of which will have a positive result.
- Assign online preactivity homework (Appendix 1A: Preactivity Homework: Familiarizing Yourself with Influenza). Before the activity, students will review influenza basic information. Assign the online assignment option(s) below as homework.
    - Students should review CDC’s Website, Seasonal Influenza (Flu), How Flu Spreads. They can explore the Flu Basics section among others. By using the preactivity homework, students can familiarize themselves with key ideas, and take notes as they read. Students should be instructed to examine Weekly US Map: Influenza Summary Update, then examine a graph displaying the cases of different strains of influenza during the 2013–14 flu season.
    - Students should review CDC’s Website, FluView Interactive. Either in laboratory notebook or separate sheet of paper, students should write brief descriptions of the 3 types of influenza viruses. Students should also be able to explain the differences of the 2 subtypes on the basis of the 2 surface proteins, hemagglutinin (H) and neuraminidase (N).
- Make copies of Worksheet 1: Modeling Influenza (Appendices 2A, 2B, 2C). Students will work in pairs. One-third of the pairs will be given Worksheet 1: Scenario A — Modeling Influenza; one-third will be given Worksheet 1: Scenario B — Modeling Influenza; and the remaining third will be given Worksheet 1: Scenario C — Modeling Influenza. Make enough copies for each student to have a personal worksheet that matches the group they have been assigned.

Materials

- Student laboratory materials that are needed/group are as follows
    - Single 10-mL acidic (clear) phenolphthalein solution in either of the following formats:
    - 1 prepared simulated influenza test (see Preparation section) with 5 cotton-tipped swabs, 5 test tubes, and 1 test tube rack; or
    - 1 dropper bottle or 50-mL beaker with a plastic pipette.
    - Calculator(s).
- Worksheet 1: Part 1, Modeling Influenza (Appendices 2A, 2B, 2C).
    - Scenario A (Appendix 2A): Students are given an outbreak scenario that occurs in an urban area characterized by dense populations. Students are guided through completing a laboratory test on patient samples, analyzing results, calculating basic reproduction numbers for the virus, and critical thinking questions. 1 copy per student in Group A.
    - Scenario B (Appendix 2B): Students are given an outbreak scenario that occurs in a suburban area characterized by moderate-density populations. Students are guided through completing a laboratory test on patient samples, analyzing results, calculating basic reproduction numbers for the virus, and critical thinking questions. 1 copy per student in Group B.
      Scenario C (Appendix 2C): Students are given an outbreak scenario that occurs in a rural area characterized by low-density populations. Students are guided through completing a laboratory test on patient samples, analyzing results, calculating basic reproduction numbers for the virus, and critical thinking questions. 1 copy per student in Group C.

Preparing Simulated Influenza Tests

Materials

- 10 mL of 0.1 M HCl.
- 10 mL of 0.1 M NaOH.
- 1 mL of 1.0 M NaOH.
- 5 cotton-tipped swabs/group.
- 5 test tubes/group.
- 1 test tube rack/group.

Procedures

1. Acquire or prepare phenolphthalein solution. If no phenolphthalein solution is available, mix 0.35 g phenolphthalein powder into 50 mL 95% ethanol until dissolved.
2. If phenolphthalein solution is pink (indicating basic), mix titrate 0.1 M HCl into the phenolphthalein solution until solution is clear (indicating acidic).
3. Aliquot 10 mL of clear phenolphthalein into dropper bottles or beakers for each group.
4. Refer to Figure 3 while completing steps a-c as follows:
   a. Place 1 cotton-tipped swab into a test tube for each group. Place this negative-test swab into a single test tube.
   b. Dip 1 cotton-tipped swab into 1.0 M NaOH. Place each single positive with high viral load test swab into a single test tube.
   c. Dip 3 cotton-tipped swabs into 0.1 M NaOH. Place each single positive test swab into a single test tube.
5. Make sure that each group has 1 positive with high viral load test swab, 3 positive test swabs, and 1 negative test swab in their test tube rack. Do not label the swabs positive or negative.

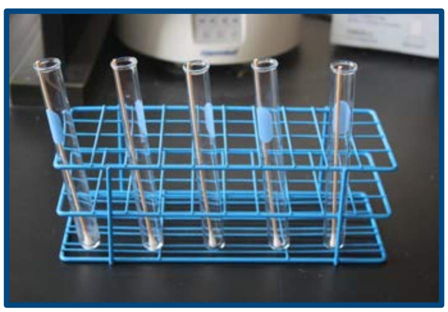


Figure 3. A sample setup for each student group that will be used in Part 1 of the activity. These represent simulated nasopharynx swab samples of 5 hospitalized patients presenting with acute respiratory infections. Image used with permission by photographer, Kelley Tuel.

Online Resources

- Influenza (Flu)
  URL: http://www.cdc.gov/flu/.
  Description: Links to CDC resources, including Flu Basics, Prevention, Treatment, News and Highlights, and more.
- FluView Interactive
  URL: http://www.cdc.gov/flu/weekly/fluviewinteractive.htm.
  Description: CDC FluView report provides weekly influenza surveillance information in the United States. This series of dynamic visualizations allow any Internet user to access influenza information collected by CDC's monitoring systems. Links on the left side of the page for this site include Current United States Flu Activity Map, Antigenic Characterization, and more.
- Understanding R Nought
  URL: https://www.youtube.com/watch?v=jKUGZvW99os.
  Description: The Khan Academy provides an explanation of the R_0 value as the reproductive rate for a particular virus.

Activity

1. Divide students into pairs. Assign each pair a letter A, B, or C. Distribute Worksheet 1: Modeling Influenza (Appendices 2A, 2B, 2C), accordingly.
2. Show the Understanding R Nought video to the class to introduce R_0 concepts.
3. Have students complete Worksheet 1: Part 1, Modeling Influenza (Appendices 2A, 2B, 2C). Refer to Figure 4 for sample student results from simulated nasopharynx swabs.
4. Conclude with a brief class discussion about countermeasures.
   - Brainstorm: Give the students 1 minute to write as many countermeasures as they can think of on the backside of Worksheet 1 or another piece of paper. Students can start with the countermeasures they listed for Question 8 of Worksheet 1. Their goal is to be writing down ideas for the full minute; any spoken ideas should be written down.
   - Evaluate: Give students 2 minutes to review the list that they generated. Evaluate how effective the countermeasures would be at preventing the spread of influenza. Decide as a group what the 2 most effective countermeasures are and circle them.
   - Discuss: As a class, have each group share 1 of the countermeasures they identified as the most effective. Do not repeat countermeasures. Continue until all groups have shared their circled countermeasures. During the discussion, have 1 student compile a list of the most effective countermeasures shared on the board.

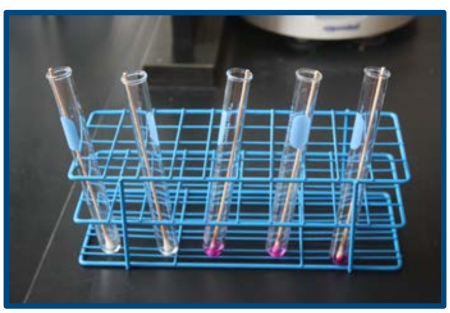


Figure 4. Sample student results from simulated nasopharynx swabs. Image published with permission by photographer, Kelley Tuel.

Day 2: Influence of Vaccinations, 45 minutes

Preparation

- Make copies of Worksheet 2: Influence of Vaccinations (Appendix 3A), 1 copy per student.

Materials

- Worksheet 2: Influence of Vaccinations (Appendix 3A)
  Description: Students will calculate the influence of vaccine effectiveness on herd immunity threshold through calculations and processing questions. Critical thinking questions examine the logistics of pandemic preparedness and the applications of theoretical models in the real world. Each student will need their own Part 2 worksheet.
- Calculator(s)

Activity

1. Reassemble students into pairs from Part 1 activity.
2. As a class, review the causes for nonsusceptibility. The review should lead the students to vaccination as the primary cause. Use vaccination as a lead in to Part 2 of the activity.
3. Hand out Worksheet 2: Influence of Vaccinations (Appendix 3A), 1 copy per student.
4. Have students complete the worksheet in pairs, by using information calculated in Part 1. If students have their copies of Worksheet 1: Modeling Influenza (Appendices 2A, 2B, 2C, respectively) they can fill in the values by conversing with their peers. If Worksheet 1: Modeling Influenza (Appendices 2A, 2B, 2C, respectively) has already been turned in, post the following R_0 values for the students to reference: Scenario A, R_0 = 2.20; Scenario B, R_0 = 1.88; and Scenario C, R_0 = 1.43. An R_0 of 2.20 means that on average an infected person will transmit illness to 2.20 other persons among a population in which no one has immunity and no countermeasures are available.
5. When all groups have completed Part 2, provide an opportunity to answer clarification questions.
6. Lead a brief class discussion about the value of vaccinations. Questions that might guide the discussion include the following:
   - How many students have received an influenza vaccination for ≤5 years? During the last year?
   - How many students will receive a vaccination this year or encourage others to get vaccinated?
   - Using what you have learned in this activity, do you think a personal decision to receive a vaccination has only personal consequences?
   - After completing the activity, why are vaccinations important to public health?
   - To reach a herd immunity threshold, the public must be informed about the importance of vaccinations and how they can receive vaccinations. How can we increase vaccination awareness?
   - What other diseases have vaccines available? Are you aware of any current outbreaks of diseases in which vaccines are available?

Extensions

Extension 1: Primary Literature Reading, 30–45 minutes

Materials

- Computer and Internet access for each student.

Online Resource

- Skountzou I, Koutsonanos DG, Kim JH, et al. Immunity to pre-1950 H1N1 influenza viruses confers cross-protection against the pandemic swine-origin 2009 A (H1N1) influenza virus. J Immunol 2010;185:1642–9.
  URL: http://www.jimmunol.org/content/185/3/1642.long.
  Description: By using primary literature from a peer-reviewed source, students can read online about the structure of the influenza virus, hemagglutinin protein function, and neuraminidase function. The different types of influenza (A, B, and C) are briefly explained. The 2009 influenza A (H1N1) pandemic resulted in limited (<5%) affected persons aged >62 years. Research is outlined of a study with mice that were exposed to a lethal challenge of 1947 or 1934 H1N1 viruses. Humans with previous exposure to either 1947 or 1934 H1N1 influenza had induction of cross-reactive antibodies to the H1N1 virus, which might explain protection against the 2009 pandemic.

Activity

1. Direct students to read the journal article online, taking notes on notebook paper (or in a laboratory notebook). While reading, students should focus on two key ideas, (1) what is cross protection, and (2) what implications does cross-protection have on the overall susceptibility of the public. If students are not experienced in reading primary literature, advise them to omit the Materials and Methods and Results sections.
2. Lead a discussion to aid students' understanding. Discussion points (as class or each group assigned multiple questions) might include the following:
   a. What was this research trying to determine? Why or how did persons aged >62 years have a lower than expected incidence of 2009 H1N1 influenza A?
   b. Describe the function of the H protein in H1N1. Answer is in the *Introduction* section of article: The hemagglutinin (HA) protein is "responsible for attachment of the virus to sialic acid-containing receptors on the host cell surface."
   c. Describe the function of the N protein in H1N1. Answer is in the *Introduction* section of article: "…the neuraminidase (NA) is a receptor-destroying enzyme, which has important functions in viral release and cell-to-cell spread."
   d. Where are the HA and NA proteins located on the virus? Answer is in the *Introduction* section of article, which explains that the proteins are located on the viral lipid envelope.
   e. What is the cause of shifts in HA or NA proteins, which can potentially lead to influenza pandemics? Answer is in the *Introduction* section of article and includes information about the rapid evolution of viral genome RNA that can cause surface glycoproteins to change, which leads to poorer recognition of the virus by the immune system. These mutations are called antigenic drift, occur routinely, and lead to seasonal influenza epidemics. Greater genetic and antigenic changes (which occur by the exchange of genes among different influenza viruses) are called antigenic shifts and can lead to pandemics (i.e., epidemics occurring worldwide and affecting a large number of people).
   f. Why was the 2009 H1N1 virus novel? Answer is in the second paragraph of article, and includes information that H1N1 was a "quadruple reassortment virus" that had gene segments from 4 different sources. This pandemic spread rapidly and had a substantial number of deaths

(~12,500) during a limited period.

g. Epidemiologic data indicated that persons aged >60 years, a group that is typically susceptible to influenza, had low incidence of the 2009 H1N1 flu. This data prompted an immunological study to determine "the extent to which pre-existing immunity to representative H1N1 viruses that appeared in the human population from 1930 to 2000 protects against the 2009 pandemic virus." How did they go about testing this? Answer is most directly located in the *Discussion* section. Laboratory mice were exposed to various historical H1N1 viruses (1943 and 1947). Surviving mice were later exposed to 2009 H1N1 virus with high incidence of immunity (cross-reactivity).
h. Describe what previous exposure to H3N2 viruses (e.g., 1968) might have to do with persons exposed to the 2009 H1N1 virus. Answer is most directly located in the *Discussion* section, and includes "indirect evidence in humans of cross-protection against influenza strains due to cross-reactive T cells and even Abs [antibodies]." This is likely because of the cross-protection role of CD8 T cells.
i. Should the historical viruses described in the article be used for vaccine production for next year's influenza outbreak? Justify your decision. Answer: Yes, since continued circulation of the pandemic strain is likely. Note that influenza vaccines contain 3-4 antigens, one for 2009 H1N1, one for an H3N2 virus, and 1-2 for an influenza B virus.

Conclusions

After this lesson, students will have improved skills in mathematical modeling. Using information collected from a laboratory test simulation, students use mathematical modeling in a variety of ways to explore influenza pandemic preparedness, including the following subtopics: vaccine development and the logistics of vaccine administration, importance of influenza surveillance, predictions for influenza's spread using mathematical modeling, and implementation of countermeasures to prevent a pandemic. Through discussion, students will be able to engage in arguments regarding vaccination. They will be able to discuss infectious disease transmission and spread, and use data to evaluate the effectiveness of countermeasures implemented, including vaccination.

Assessment

- Assessment: Have You Herd (Appendix 4A)
  Learning Outcomes Assessed:
  - employ mathematical models for influenza outbreak scenarios to calculate measures of disease spread and intervention effectiveness;
  - synthesize effects of physical (e.g., social distancing or nonpharmaceutical interventions) and medical (e.g., vaccines) countermeasures for influenza outbreak scenarios;
  - identify public health countermeasures that restrict the spread of an influenza outbreak; and
  - explain the importance of vaccinations and the monitoring cases of infectious diseases.

  Description: Includes 4 short-answer and 4 multiple-choice questions that can be incorporated into an exam or used as a separate assessment. The questions are extensions of the activity and require students to apply concepts learned during the activity and applied in a new situation. Questions include figure and graph analyses. Each question will require 2–4 minutes to complete. The entire assessment should take students approximately 20–30 minutes to complete.

Educational Standards

In this lesson, the following CDC Epidemiology and Public Health Science (EPHS) Core Competencies for High School Students[1], Next Generation Science Standards[*] (NGSS) Science & Engineering Practices[2], and NGSS Cross-cutting Concepts[3] are addressed:

HS-EPHS2-3. Use models (e.g., mathematical models, figures) based on empirical evidence to identify patterns of health and disease in order to characterize a public health problem.

NGSS Key Science & Engineering Practice[2]
Analyzing and Interpreting Data Analyze data using tools, technologies, and/or models (e.g., computational, mathematical) in order to make valid and reliable scientific claims or determine an optimal design solution.
NGSS Key Crosscutting Concept[3]
Patterns Mathematical representations are needed to identify some patterns.

HS-EPHS3-4. Make a claim about an association between an exposure and disease with consideration of a mathematical analysis of empirical data

NGSS Key Science & Engineering Practice[2]
Constructing explanations and designing solutions Make a quantitative and/or qualitative claim regarding the relationship between an independent and dependent variable
NGSS Key Crosscutting Concept[3]
Scale, Proportion, and Quantity Algebraic thinking is used to examine scientific data and predict the effect of a change in one variable on another.

HS-EPHS 4-1: Describe a model illustrating how scientific, social, economic, environmental, cultural, and political systems influence intervention performance patterns. .

NGSS Key Science & Engineering Practice[2]
Developing and Using Models Develop, revise, and/or use a model based on evidence to illustrate and/or predict the relationships between systems or between components of a system.
NGSS Key Crosscutting Concept[3]
Patterns Patterns of performance of designed systems can be analyzed and interpreted to reengineer and improve the system.

[*]Next Generation Science Standards is a registered trademark of Achieve. Neither Achieve nor the lead states and partners that developed the Next Generation Science Standards was involved in the production of, and does not endorse, this product.

[1] Centers for Disease Control and Prevention (CDC). Science Ambassador Workshop—Epidemiology and Public Health Science: Core Competencies for high school students. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. Not currently available for public use.

[2] NGSS Lead States. Next Generation Science Standards: For States, By States (Appendix F–Science and Engineering Practices). Achieve, Inc. on behalf of the twenty-six states and partners that collaborated on the NGSS. 2013. Available at: http://www.nextgenscience.org/sites/ngss/files/Appendix%20F%20%20Science%20and%20Engineering%20Practices%20in%20the%20NGSS%20-%20FINAL%20060513.pdf

[3] NGSS Lead States. Next Generation Science Standards: For States, By States (Appendix G–Crosscutting Concepts). Achieve, Inc. on behalf of the twenty-six states and partners that collaborated on the NGSS. 2013. Available at: http://www.nextgenscience.org/sites/ngss/files/Appendix%20G%20-%20Crosscutting%20Concepts%20FINAL%20edited%204.10.13.pdf.

Appendices: Supplementary Documents

Appendix 1A: Preactivity Homework: Familiarizing Yourself with Influenza

Familiarizing Yourself with Influenza

Name: ____________________________ Date: ____________

Directions: Complete this worksheet before the Have You Herd lesson.

Part 1: Review the Centers for Disease Control and Prevention (CDC) website for Influenza (Flu) available at: http://www.cdc.gov/flu/index.htm. Explore the Flu Basics section and familiarize yourself with the following key ideas. Take notes as you read.

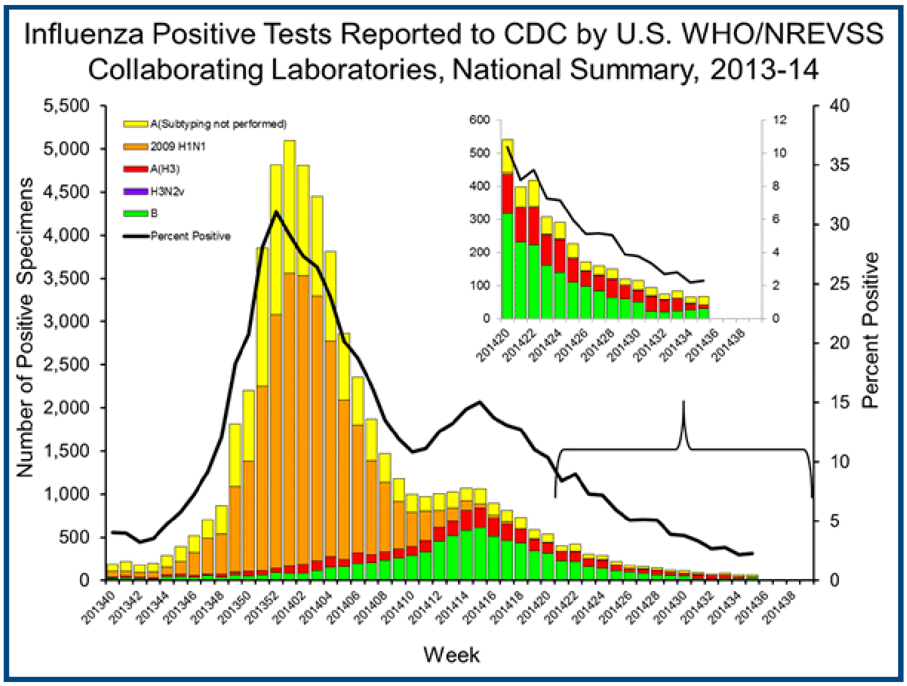
Cause	**Influenza virus**
Symptoms and complications	
Persons at high risk from flu	
How flu spreads	
Treatment and prevention	
Misconceptions about seasonal flu and flu vaccines	
Flu season (i.e., peak circulation of the virus)	

Part 2: Examine the CDC's Weekly US Map: Influenza Summary Update available at http://www.cdc.gov/flu/weekly/usmap.htm.

1. Which states have widespread cases of influenza being reported?

2. Predict how the map would differ if this review was being done during February. Explain why these differences would be observed.

Part 3: Examine the following graphic. Weeks are displayed on the x-axis as year-week (i.e., 201402 is the second week of January 2014).The key displays the presence of 5 different strains of influenza.



Center for Disease Control and Prevention. Weekly U.S. Influenza Surveillance Report. Available at: http://www.cdc.gov/flu/weekly/index.htm#whomap

3. What was the most common influenza type reported during the 2013–14 flu season?

4. Describe any difference in the strains of influenza observed during the 201340–201410 period, compared with 201420–201438.

5. Data displays influenza cases reported during the 2013–14 flu season. However, one of the influenza strains is labeled 2009 H1N1. Provide a possible explanation for this observation.

Appendix 1B: Preactivity Homework: Familiarizing Yourself with Influenza, Answer Key

Familiarizing Yourself with Influenza

Name: ______Answer Key__________________ Date: ________________

Directions: Complete this worksheet before the Have You Herd lesson.

Part 1: Review the Centers for Disease Control and Prevention (CDC) website for Influenza (Flu) that is available at http://www.cdc.gov/flu/index.htm. Explore the Flu Basics section and familiarize yourself with the following key ideas. Take notes as you read.

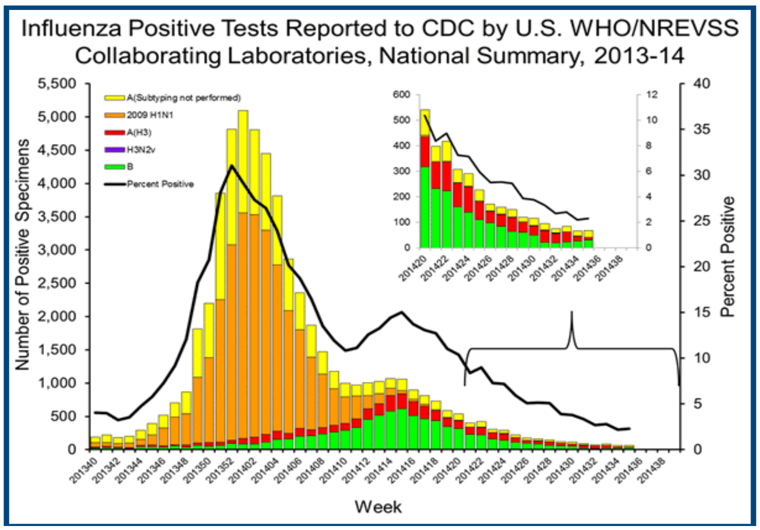
Cause	**Influenza virus**
Symptoms and complications	• Fever, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, and certain persons might have vomiting or diarrhea. • Certain complications (e.g., pneumonia, bronchitis, and sinus or ear infections) can develop. Certain complications can result in death. The flu can make chronic health problems (e.g., congestive heart failure or asthma) worse.
Persons at high risk from flu	• Everyone is at risk. • Persons at high risk for serious complications include those aged ≥65 years, persons of any age with certain chronic medical conditions (e.g., asthma, diabetes, or heart disease), pregnant women, and children.
How flu spreads	• Influenza is most commonly spread by droplet. • Droplets can be spread when a person sneezes, coughs, or talks. • Influenza can also be spread by touching a surface or object that has the flu virus on it and then touching their own mouth or nose.
Treatment and prevention	• Prevent the seasonal flu by getting vaccinated. The vaccine typically protects against 3–4 different strains of influenza. The vaccine is available as a shot or nasal spray. Practice recommended health habits, which include avoiding close contact with other persons and staying at home when you are sick, covering your mouth and nose when coughing or sneezing, cleaning your hands thoroughly, avoid touching your eyes, nose or mouth, and other recommended habits. • Influenza can be treated with antiviral drugs (pills, liquid, or an inhaled powder).
Misconceptions about seasonal flu and flu vaccines	• The flu vaccine cannot give you the flu. • Getting the flu is NOT preferable to receiving the flu vaccine to avoid possible vaccine-related complications. • Studies have not demonstrated a benefit of receiving >1 flu shot during a season. Except for some children aged 6 months to 8 years, only one flu vaccine dose is recommended each season.
Flu season (i.e., peak circulation of the virus)	• Flu season is during October–March in the Northern hemisphere. Flu activity typically peaks during January-March (in the United States).

Part 2: Examine the CDC's Weekly US Map: Influenza Summary Update that is available at http://www.cdc.gov/flu/weekly/usmap.htm.

1. Which states have widespread cases of influenza being reported?
   Answer: Review map and answer will depend on current reports.

2. Predict how the map would differ if this review was being done during February. Explain why these differences would be observed.
   Answer: During February, the number of states with widespread cases of influenza would be likely greater because this is often the peak of flu season in the United States.

Part 3: Examine the following graphic. Weeks are displayed on the x-axis as year-week (i.e., 201402 is the second week of January 2014). The key displays the presence of 5 influenza type/subtype possibilities.



Center for Disease Control and Prevention. *Weekly U.S. Influenza Surveillance Report.* Available at: http://www.cdc.gov/flu/weekly/index.htm#whomap

3. What was the most common influenza type reported during the 2013–14 flu season?
   Answer: Influenza A.

4. Describe any difference in the strains of influenza observed during the 201340–201410 period, compared with the 201420–201438 period.
   Answer: During the first half of the flu season, the most prevalent findings strains were influenza A (typing not performed) and 2009 H1N1. During the second half of the flu season influenza B and influenza A (H3) increase in prevalence

5. Data displays influenza cases during the 2013–14 flu season. However, one of the influenza strains is labeled 2009 H1N1. Provide a possible explanation for this observation.
   Answer: The 2009 H1N1 strain of influenza was first identified during 2009. In 2009 it was a pandemic virus, but it became established in the population and in subsequent years it circulated as a seasonal virus. In 2013-2014 2009 H1N1 was the predominant seasonal influenza virus.

Modeling Influenza's Spread
Scenario A

Name: ________________________________ Date: _______________

Directions: Read the following scenario. Then, complete the laboratory activity and record your results. Answer the discussion questions in complete sentences.

Scenario A

In every state in the United States, locations known as sentinel sites are monitored. These sites report routine influenza testing results to determine what the typical illness level (i.e., baseline) is for that time of year.

The site of the outbreak is an urban area characterized by dense populations.

You are a clinical laboratory scientist working in a hospital that is a sentinel site. During a 24-hour period, you received nasopharynx swab samples from 5 hospitalized patients presenting with acute respiratory infections. To determine if each patient is positive for influenza, you will complete the first step of a rapid influenza diagnostic test, which will indicate the presence of influenza antigens. Use the procedures to the right to complete the test and record your results in the data table.

Laboratory Activity

1. Have each group collect the following materials:
   - 1 test tube rack with 5 test tubes, and
   - influenza testing reagent.
2. Label test tubes as Patient 1, Patient 2, Patient 3, Patient 4, and Patient 5, respectively.
3. Without removing the nasopharynx swabs, place 3–5 drops of influenza testing reagent into each test tube, allowing the reagent to drip down along the inner wall of the test tube.
4. Identify if patients are positive or negative for influenza. Note: if the patient sample is positive for influenza, an immediate color change will be apparent. A negative result will be concluded if no color change is observed.
5. If a test sample has a more vibrant color than others, record that observation.

Laboratory Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Test results					
Diagnosis					

Your results are sent to the local public health laboratory. The local public health laboratory is responsible for reporting unusual disease occurrences that are higher than the expected baseline. Anything >1 case/24 hours is considered higher than the baseline for influenza, and information will be sent on to the state public health laboratory and the Centers for Disease Control and Prevention (CDC) for additional testing and research.

Discussion Questions

1. On the basis of your data, should you report influenza to the state public health laboratory and CDC? Support your conclusion by using your laboratory results.

2. Although the rapid influenza diagnostic test is a quick way of checking for influenza, on average it has a false-positive rate of 5%–10% in which persons without influenza receive a positive result. On average, it has a false-negative rate of 30%–50% in which persons who have influenza receive a negative result. Explain one way a false-positive or a false-negative test result might occur?

Two weeks later, additional information about the number of influenza cases, hospitalizations and deaths was collected and reported through normal procedures to CDC. By using this information, transmission modelers at CDC are working to estimate countermeasures that would be needed to avoid a pandemic. The basic reproduction number (R_0) is used to determine the ability of the virus to spread.

$$R_0 = (k) \times (d) \times (p)$$

R_0 = average number of persons each infected person will infect.

k = number of contacts a person has during 1 day.

d = duration of infectiousness for a person.

p = probability of transmission/contact.

3. Assume that the average number of contacts a person has per day is 15.7, and a determination is made that the influenza virus is transmitted among 1 of every 50 contacts. Knowing that a person remains infectious for 7 days, calculate R_0 for the current outbreak. Show your work.

4. Using the formula to guide your answer, determine what the unit is for the basic reproduction number (R_0)? Explain how you got this answer.

5. A value of R_0 <1 will not lead to an epidemic, whereas a value of R_0 >1 indicates an epidemic is possible. Considering the formula you have used to calculate R_0, explain why an R_0 >1 can lead to an epidemic.

6. Does your model provide evidence to support the possibility of an epidemic? (Yes or No)

7. Compare your results with a group who has Scenario B. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Despite the probability of transmission/contact being the same for both groups, your R_0 values differed. What variable differed between the 2 scenarios? List 2 reasons why this variable might have differed.

8. Compare your results with a group who has Scenario C. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Do the R_0 values provide information about the speed at which influenza will spread in each scenario? Use your understanding of the R_0 equation to support your response.

Although this R_0 calculation allows scientists to predict influenza pandemics, factors are present that are not accounted for. It does not account for countermeasures already in place, and for persons who are not susceptible to influenza.

9. List 3 possible countermeasures that persons can use to avoid transmitting or contracting the flu, and 1 cause for nonsusceptibility.

Modeling Influenza's Spread
Scenario B

Name: ___________________________________ Date: ________________

Directions: Read the following scenario. Then, complete the laboratory activity and record your results. Answer the discussion questions in complete sentences.

Scenario B

In every state in the United States, locations known as sentinel sites are monitored. These sites report routine influenza testing results to determine what the typical illness level (i.e., baseline) is for that time of year.

The site of the outbreak is a suburban area characterized by moderate density populations.

You are a clinical laboratory scientist working in a hospital that is a sentinel site. During a 24-hour period, you have received nasopharynx swab samples from 5 hospitalized patients presenting with acute respiratory infections. To determine if each patient is positive for influenza, you will complete the first step of a rapid influenza diagnostic test, which will indicate the presence of flu antigens. Use the procedures to the right to complete the test and record your results in the data table.

Laboratory Activity

1. Have each group will collect the following materials:
   - 1 test tube rack with 5 test tubes, and
   - influenza testing reagent.
2. Label test tubes as Patient 1, Patient 2, Patient 3, Patient 4, and Patient5, respectively.
3. Without removing the nasopharynx swabs, place 3–5 drops of influenza testing reagent into each test tube, allowing the reagent to drip down along the inner wall of the test tube.
4. Identify if each patient is negative or positive for influenza. Note: if the patient sample is positive for influenza, an immediate color change will be apparent. A negative result will be concluded if no color change is observed.
5. If a test sample has a more vibrant color than others, record that observation.

Laboratory Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Test results					
Diagnosis					

Your results are sent to the local public health laboratory. The local public health laboratory is responsible for reporting unusual disease occurrences that are higher than the baseline. Anything >1 case/24 hours is considered higher than the baseline for influenza, and information will be sent on to the state public health laboratory and the Centers for Disease Control and Prevention (CDC) for additional testing and research.

1. On the basis of your data, should you report influenza to the state public health laboratory and CDC? Support your conclusion by using your laboratory results.

2. Although the rapid influenza diagnostic test is a quick way of checking for influenza, on average it has a false-positive rate of 5%–10% in which persons without influenza receive a positive result. On average, it has a false-negative rate of 30%–50% in which persons who have influenza receive a negative result. Explain one way a false-positive or a false-negative test result might occur?

Two weeks later, additional information about the number of influenza cases, hospitalizations, and deaths was collected, and reported through normal procedures to CDC. By using this information, transmission modelers at CDC are working to estimate countermeasures that would be needed to avoid a pandemic. The basic reproduction number (R_0) is used to determine the ability of the virus to spread.

$$R_0 = (k) \times (d) \times (p)$$

R_0 = average number of persons each infected person will infect.
k = number of contacts a person has during 1 day.
d = duration of infectiousness for a person.
p = probability of transmission/contact.

3. Assume that the average number of contacts a person has per day is 13.4, and a determination is made that the influenza virus is transmitted among 1 of every 50 contacts. Knowing that a person remains infectious for 7 days, calculate R_0 for the current outbreak. Show your work.

4. What are the units for the basic reproduction number (R_0)? Explain how you determined this conclusion.

5. A value of R_0 <1 will not lead to an epidemic, whereas a value of R_0 >1 indicates an epidemic is possible. Considering the formula you have used to calculate R_0, explain why an R_0 >1 can lead to an epidemic.

6. Does your model provide evidence to support the possibility of an epidemic? (Yes or No)

7. Compare your results with a group who has Scenario A. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Despite the probability of transmission or contact being the same for both groups, your R_0 values differed. What variable differed between the 2 scenarios? List 2 reasons why this variable might have differed.

8. Compare your results with a group who has Scenario C. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Do the R_0 values provide information about the speed at which influenza will spread in each scenario? Use your understanding of the R_0 equation to support your response.

Although this R_0 calculation allows scientists to predict influenza pandemics, factors are present that are not accounted for. It does not account for countermeasures already in place, and for persons who are not susceptible to influenza.

9. List 3 possible countermeasures that persons can use to avoid transmitting or contracting the flu and 1 cause for nonsusceptibility.

Modeling Influenza's Spread
Scenario C

Name: ___________________________________ Date: ________________

Directions: Read the following scenario. Then, complete the laboratory activity and record your results. Answer the discussion questions in complete sentences.

Scenario C

In every state in the United States, locations known as sentinel sites are monitored. These sites report routine influenza testing results to determine what the typical illness level (i.e., baseline) is for that time of year.

The site of the outbreak is a rural area characterized by low density populations.

You are a clinical laboratory scientist working in a hospital that is a sentinel site. During a 24-hour period, you have received nasopharynx swab samples from 5 hospitalized patients presenting with acute respiratory infections. To determine if each patient is positive for influenza, you will complete the first step of a rapid influenza diagnostic test, which will indicate the presence of flu antigens. Use the procedures to the right to complete the test and record your results in the data table.

Laboratory Activity

1. Have each group will collect the following materials
   - 1 test tube rack with 5 test tubes, and
   - influenza testing reagent.
2. Label each test tube as Patient 1, Patient 2, Patient 3, Patient 4, and Patient 5, respectively.
3. Without removing the nasopharynx swabs, place 3–5 drops of influenza testing reagent into each test tube, allowing the reagent to drip down along the inner wall of the test tube.
4. Identify if each patient is positive or negative for influenza. Note: if the patient sample is positive for influenza, an immediate color change will be apparent. A negative result will be concluded if no color change is observed.
5. If a test sample has a more vibrant color than others, record that observation.

Laboratory Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Test results					
Diagnosis					

Your results are sent to the local public health laboratory. The local public health laboratory is responsible for reporting unusual disease occurrences that are higher than the baseline. Anything >1 case/24 hours is considered higher than the baseline for influenza, and information will be sent on to the state public health laboratory and the Centers for Disease Control and Prevention (CDC) for additional testing and research.

1. On the basis of your data, should you report influenza to the state public health laboratory and CDC? Support your conclusion by using your laboratory results.

2. Although the rapid influenza diagnostic test is a quick way of checking for influenza, on average it has a false-positive rate of 5%–10% in which persons without influenza receive a positive result. On average, it has a false-negative rate of 30%–50% in which persons who have influenza receive a negative result. Explain one way a false-positive or a false-negative test result might occur?

Two weeks later additional information about the number of influenza cases, hospitalizations, and deaths was collected, and reported through normal procedures to CDC. By using this information, transmission modelers at CDC are working to estimate countermeasures that would be needed to avoid a pandemic. The basic reproduction number (R_0) is used to determine the ability of the virus to spread.

$$R_0 = (k) \times (d) \times (p)$$

R_0 = average number of persons each infected person will infect.
k = number of contacts a person has during 1 day
d = duration of infectiousness for a person.
p = probability of transmission/contact.

3. Assume that the average number of contacts a person has per day is 10.2, and a determination is made that the influenza virus is transmitted among 1 of every 50 contacts. Knowing that a person remains infectious for 7 days, calculate R_0 for the current outbreak. Show your work.

4. What are the units for the basic reproduction number (R_0)? Explain how you determined this conclusion.

5. A value of $R_0 < 1$ will not lead to an epidemic, whereas a value of $R_0 > 1$ indicates an epidemic is possible. Considering the formula you have used to calculate R_0, explain why an $R_0 > 1$ can lead to an epidemic.

6. Does your model provide evidence to support the possibility of an epidemic? (Yes or No)

7. Compare your results with a group who has Scenario A. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Despite the probability of transmission/contact being the same for both groups, your R_0 values differed. What variable differed between the 2 scenarios? List 2 reasons why this variable might have differed.

8. Compare your results with a group who has Scenario B. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values.

   B. Do the R_0 values provide information about the speed at which influenza will spread in each scenario? Use your understanding of the R_0 equation to support your response.

Although this R_0 calculation allows scientists to predict influenza pandemics, factors are present that are not accounted for. It does not account for countermeasures already in place, and for persons who are not susceptible to influenza.

9. List 3 possible countermeasures that persons can use to avoid transmitting or contracting the flu and 1 cause for nonsusceptibility.

Appendix 2D: Worksheet 1: Modeling Influenza, Answer Key

Modeling Influenza's Spread

Name: ________ **Answer Key**___________________________ Date: ________________

Laboratory Results

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Test results	**(+)**	**(+)**	**(+)**	**(+)**	**(–)**
Diagnosis	**Has influenza**	**Has influenza**	**Has influenza**	**Has influenza**	**Does not have influenza**

Note: Test results will vary, depending on how the students numbered the samples. However, 4 of the 5 samples should be positive.

Discussion Questions

1. On the basis of your data, should you report influenza to the state public health laboratory and CDC? Support your conclusion by using your laboratory results.
   Answer: Yes, the test results should be reported. The baseline for influenza is 1 case/24 hours and our results reported 4 cases/24 hours. Because this is higher than the baseline for influenza, the sentinel site should report their cases of influenza.

2. Although the rapid influenza diagnostic test is a quick way of checking for influenza, on average it has a false-positive rate of 5%–10% in which persons without influenza receive a positive result. On average, it has a false-negative rate of 30%–50% in which persons who have influenza receive a negative result. Explain 1 way a false-positive or a false-negative test result might occur?
   Sample Answer: A false-positive might occur because of contamination when collecting the sample, its transport to the laboratory, or in the laboratory itself. A false-negative test result might occur due to an inadequate sample or inappropriate specimen collection, storage or sample transpore; it could also occur if the person is recovering from influenza and is shedding a low virus count.

3. Assume that the average number of contacts a person has per day is 15.7, and a determination is made that the influenza virus is transmitted in one out of every fifty contacts. Knowing that a person remains infectious for 7 days, calculate R_0 for the current outbreak. Show your work.
   Scenario A Answer: R_0 = (15.7 contacts/day) × (7 days) × (1/50 contacts transmissible) = 2.20. On average, each infected person is expected to infect 2.20 other persons.
   Scenario B Answer: R_0 = (13.4 contacts/day) × (7 days) × (1/50 contacts transmissible) = 1.88. On average, each person is expected to infect 1.88 other persons.
   Scenario C Answer: R_0 = (10.2 contacts/day) × (7 days) × (1/50 contacts transmissible) = 1.43. On average, each person is expected to infect 1.43 other persons.

4. What are the units for the basic reproduction number (R_0)? Explain how you determined this conclusion.
   Answer: R_0 is most often reported as a unitless number and is implicit that it refers to transmissions. However, working through the formula reveals that it has units of transmissions because all the other units cancel. For example, using the calculations for Scenario A, 15.7 contacts/day × 0.02 transmissions/contact × 7 days = 2.20 transmissions.

5. A value of R_0 <1 will not lead to an epidemic, whereas a value of R_0 >1 indicates an epidemic is possible. Considering the formula you have used to calculate R_0, explain why an R_0 >1 will probably lead to an epidemic.
   Sample Answer: Because each person is infecting >1 other person, the number of infected persons will increase over time, and the disease will multiply exponentially. The exponential spread will reach a greater portion of the population and will be challenging to stop, likely leading to an epidemic.

6. Does your model provide evidence to support the possibility of an epidemic? (Yes or no)
   Answer: Yes.

7. Compare your results with a group who has Scenario B. Discuss the details of your scenario and your R_0 values.

   A. Write 1 sentence describing the similarities or differences between your R_0 values

   B. Despite the probability of transmission/contact being the same for both groups, your R_0 values differed. What variable differed between the 2 scenarios? List 2 reasons why this variable might have differed.

   Scenario A answers:
   A. **Answer:** Scenario A has a greater R_0 value than Scenario B (2.20 versus 1.88).
   B. **Answer:** Variable is the number of contacts/day, and possible reasons are differences in personal hygiene, population density, transportation method, age distribution, social behaviors, or cultural practices.

   Scenario B answers:
   A. **Sample Answer:** Scenario A has a greater R_0 value than Scenario B (2.20 versus 1.88).
   B. **Sample Answer:** Variable is the number of contacts/day, and possible reasons are differences in personal hygiene, population density, transportation method, age distribution, social behaviors, or cultural practices.

   Scenario C answers:
   A. **Sample Answer:** Scenario A has a greater R_0 value than Scenario C (2.20 versus 1.43).
   B. **Sample Answer:** Variable is the number of contacts/day, and possible reasons are differences in personal hygiene, population density, transportation method, age distribution, social behaviors, or cultural practices.

8. Compare your results with a group who has Scenario C. Discuss the details of your scenario and your R_0 values.

    A. Write 1 sentence describing the similarities or differences between your R_0 values.

    B. Do the R_0 values provide information about the speed at which influenza will spread in each scenario? Use your understanding of the R_0 equation to support your response.

    Scenario A answers:

    A. **Sample Answer:** Scenario A has a greater R_0 value than Scenario C (2.20 versus 1.43).
    B. **Sample Answer:** No. The equation provides an estimate of the number of additional cases that will occur from 1 infected person, but it does not provide any information about the speed at which the virus will spread.

    Scenario B answers:

    A. **Sample Answer:** Scenario B has a greater R_0 value than Scenario C (1.88 versus 1.43).
    B. **Sample Answer:** No. The equation provides an estimate of the number of additional cases that will occur from 1 infected person, but it does not provide any information about the speed at which the virus will spread.

    Scenario C answers:

    A. **Sample Answer:** Scenario B has a greater R_0 value than Scenario C (1.88 versus 1.43).
    B. **Sample Answer:** No. The equation provides an estimate of the number of additional cases that will occur from 1 infected person, but it does not provide any information about the speed at which the virus will spread.

9. List 3 possible countermeasures that persons can use to avoid transmitting or contracting the flu and 1 cause for nonsusceptibility.
    Sample Answer: Countermeasures can include coughing into your elbow instead of your hands, washing hands thoroughly and frequently, avoiding sick persons, eating a healthy diet and getting the recommended amount of sleep.
    Nonsusceptibility can come from being vaccinated against the current strain of influenza.

Appendix 3A: Worksheet 2: Influence of Vaccinations

Examining the Influence of Vaccinations on the Spread of Influenza

Name: ________________________________ Date: ______________

Directions: Answer the following questions. You are allowed to use a calculator.

Review Part 1 and fill in the R_0 value for your scenario and obtain values for the other scenarios. Record these values in the table.

	Scenario A	Scenario B	Scenario C
R_0			

For a population to be protected from a pandemic, a specific proportion of the population must be immune to the virus; this is called the herd immunity threshold (I_c). For example, if the herd immunity threshold is 0.5, a total of 50% of the population would need to be vaccinated to prevent the outbreak from becoming a pandemic.

$$I_c = 1 - 1/R_0$$

1. For each scenario, calculate the theoretical herd immunity threshold and record in the data table. Show your work for Scenario A.

	Scenario A	Scenario B	Scenario C
I_c			

Although you have calculated a proportion of the population that would theoretically need to be vaccinated to prevent the outbreak from becoming a pandemic, this assumes that the vaccine is 100% effective. The actual proportion of the vaccinations leading to nonsusceptibility is the vaccine effectiveness (E). By using the vaccine effectiveness, you can calculate the minimum proportion of a population that should be vaccinated to avoid an influenza pandemic; this is known as the critical vaccination level (V_c).

$$V_c = I_c \div E$$

I_c = herd immunity threshold.
V_c = critical vaccination level.
E = vaccine effectiveness.

Every February, a group of experts decide which influenza strains should be included in the vaccine for the coming flu season. This vaccine will be produced and shipped in the coming months and administered throughout the flu season (October–May). In this hypothetical scenario, assume that the vaccine is well-matched to the circulating strains and has an effectiveness of 0.65. Assume that the outbreak is caused by H1N1, a strain of seasonal influenza.

2. Use your previously calculated I_c values to determine the critical vaccination level for an H1N1 outbreak in each scenario.

   Show your work for Scenario A.

	Scenario A	Scenario B	Scenario C
V_c (H1N1)			

3. Examine the V_c values for each scenario if the influenza strain is H1N1.

   A. In which scenario would stopping the spread of the infection be the easiest? Explain why.

   B. In which scenario would stopping spread of the pandemic be the most challenging? Explain why.

4. At certain times, vaccines are produced and stockpiled for influenza strains that are considered to be of sufficient risk for producing a pandemic. Assume that the hypothetical outbreak being considered is caused by H5N1, a virulent strain of avian influenza. The vaccine was produced multiple years ago and during that time the virus has mutated, resulting in a vaccine effectiveness of 0.35.

   A. Why is the H5N1 vaccine effectiveness low, compared with the vaccine effectiveness of the H1N1 vaccine?

   B. Use your previously calculated I_c values to determine the critical vaccination level for the H5N1 outbreak in each scenario.

   Show your work for Scenario A.

	Scenario A	Scenario B	Scenario C
V_c (H5N1)			

5. Examine the V_c values for each scenario if the influenza strain is H5N1.

   A. Why is achieving a vaccination level >1 impossible (V_c >1)?

   B. Despite the V_c >1 of Scenario A and Scenario B, the possibility exists of stopping spread of the H5N1 pandemic. In 2–3 sentences, describe how this would be possible.

   C. Although V_c <1 is listed in Scenario C, reaching this vaccination level might not be possible. Explain why.

6. All of the values you calculated by using these models were theoretical values. If you were the epidemiologist following an epidemic, why might the number of cases you observe be different than what your model predicted?

7. The effective reproduction number (R_E) is the portion of the population who is susceptible to influenza. Unlike the basic reproduction number (R_0), R_E takes into account previously acquired immunity or other countermeasures (e.g., vaccination or quarantine) to combat disease transmission. Immunity can come from vaccinations (artificially acquired immunity) or from a person recovering from the virus (naturally acquired immunity).

   A. Would the R_E remain constant throughout the course of an epidemic? Explain why or why not.

   B. If R_E is >1, an epidemic is probable. If R_E is <1, an epidemic is declining. By using your understanding of how outbreaks occur, explain why this is logical.

8. When pandemics occur, 1 possible countermeasure is to close schools with substantial levels of infected persons. This is a controversial countermeasure. Using the following table, identify 1 positive and 1 negative consideration for both sides of the problem.

	Positive	Negative
Closing schools with infected students		
Schools remaining open with infected students		

Examining the Influence of Vaccinations on the Spread of Influenza

Name: ________ **Answer Key**____________________________ Date: ________________

Directions: Answer the following questions. You are allowed to use a calculator.

Review Part 1 and fill in the R_0 value for your scenario and obtain values for the other scenarios. Record these values in the table.

	Scenario A	Scenario B	Scenario C
R_0	**2.20**	**1.88**	**1.43**

For a population to be protected from a pandemic, a specific proportion of the population must be immune to the virus; this is called the herd immunity threshold (I_c). For example, if the herd immunity threshold is 0.5, a total of 50% of the population would need to be vaccinated to prevent the outbreak from becoming a pandemic.

$$I_c = 1 - 1/R_0$$

1. For each scenario, calculate the theoretical herd immunity threshold and record in the data table. Show your work for Scenario A.
   Answer: Scenario A, $I_c = 1 - (1 \div 2.20) = 0.55$

	Scenario A	Scenario B	Scenario C
I_c	**0.55**	**0.47**	**0.30**

Although you have calculated a proportion of the population that would theoretically need to be vaccinated to prevent the outbreak from becoming a pandemic, this assumes that the vaccine is 100% effective. The actual proportion of the vaccinations leading to nonsusceptibility is the vaccine effectiveness (E). By using the vaccine effectiveness, you can calculate the minimum proportion of a population that should be vaccinated to avoid an influenza pandemic; this is known as the critical vaccination level (V_c).

$$V_c = I_c \div E$$

I_c = herd immunity threshold.
V_c = critical vaccination level.
E = vaccine effectiveness.

Every February, a group of experts decide which influenza strains should be included in the vaccine for the coming flu season. This vaccine will be produced and shipped in the coming months and administered throughout the flu season (October–May). In this hypothetical scenario, assume that the vaccine is well-matched to the circulating strains and has an effectiveness of 0.65. Assume that the outbreak is caused by H1N1, a strain of seasonal influenza.

2. Use your previously calculated I_c values to determine the critical vaccination level for an H1N1 outbreak in each scenario.

   Show your work for Scenario A.

   Answer: Scenario A, $V_c = (0.55) \div (0.65) = 0.85$

	Scenario A	Scenario B	Scenario C
V_c (H1N1)	**0.85**	**0.72**	**0.46**

3. Examine the V_c values for each scenario if the influenza strain is H1N1.

   A. In which scenario would stopping the spread of the infection be the easiest? Explain why.
   Answer: Scenario C would be the easiest to prevent a pandemic because it has the lowest critical vaccination level. The smallest proportion of the population would have to be vaccinated.

   B. In which scenario would stopping spread of the pandemic be the most challenging? Explain why.
   Answer: Scenario A would be the most challenging for preventing a pandemic because it has the highest critical vaccination level. The largest proportion of the population would have to be vaccinated.

4. At certain times, vaccines are produced and stockpiled for influenza strains that are considered to be of sufficient risk for producing a pandemic. Assume that the hypothetical outbreak being considered is caused by H5N1, a virulent strain of avian influenza. The vaccine was produced multiple years ago and during that time the virus has mutated, resulting in a vaccine effectiveness of 0.35.

   A. Why is the H5N1 vaccine effectiveness low, compared with the vaccine effectiveness of the H1N1 vaccine?
   Answer: The strains of influenza that were circulating when the vaccine was produced have mutated and are probably less similar than to those strains that were collected during the previous months. Therefore, vaccines made from more recently circulating strains should be a better match than those vaccines made from older strains, and would provide a higher effectiveness.

   B. Use your previously calculated I_c values to determine the critical vaccination level for the H5N1 outbreak in each scenario. Show your work for Scenario A.

   Answer: Scenario A, $V_c = (0.55) \div (0.35) = 1.57$

	Scenario A	Scenario B	Scenario C
V_c (H5N1)	**1.57**	**1.34**	**.86**

5. Examine the V_c values for each scenario if the influenza strain is H5N1.

   A. Why is achieving a vaccination level >1 impossible ($V_c > 1$)?
   Answer: Achieving a vaccination level > 1 would imply that >100% of the population is vaccinated, which is mathematically impossible.

   B. Despite the $V_c > 1$ of Scenario A and Scenario B, the possibility exists of stopping spread of the H5N1 pandemic. In 2–3 sentences describe how this would be possible.
   Sample Answer: Critical vaccination levels are calculated by using R_0 values, which do not take into account any additional countermeasures in place (e.g., quarantine or closing schools). If a population puts in place extra countermeasures that decrease the spread of the virus, those actions can lower the percentage of the population that needs to be vaccinated to an achievable level.

   C. Although $V_c < 1$ is listed in Scenario C, reaching this vaccination level might not be possible. Explain why.
   Sample Answer: To stop the spread of H5N1 in Scenario C, 86% of the population would need to be vaccinated. This is a challenge because some people may decline vaccination for different reasons, including medical, financial, and personal beliefs.

6. All of the values you calculated by using these models were theoretic values. If you were the epidemiologist following an epidemic, why might the number of cases you observe be different than what your model predicted?
   Sample Answer: Environmental conditions might affect how a certain portion of contacts spread the virus. Also, the virus might mutate rapidly causing the vaccine to be ineffective. Additionally, at the beginning of the epidemic, the number of cases might have been underreported or overreported.

7. The effective reproduction number (R_E) is the portion of the population who is susceptible to influenza. Unlike the basic reproduction number (R_0), R_E takes into account previously acquired immunity or other countermeasures (e.g., vaccination or quarantine) to combat disease transmission. Immunity can come from vaccinations (artificially acquired immunity) or from a person recovering from the virus (naturally acquired immunity).

   A. Would the R_E remain constant throughout the course of an epidemic? Explain why or why not.
   Answer: R_E does not always remain constant throughout an outbreak. As an epidemic spreads, countermeasures might be put in place and persons might become immune by getting infected and recovering. Countermeasures and immunity will slow the spread of infection.

   B. If R_E is >1, an epidemic is probable. If R_E is <1, an epidemic is declining. By using your understanding of how outbreaks occur, explain why this is logical.
   Answer: If R_E is >1, each infected person is spreading it to >1 person. This means the number of infections will continue to increase. If R_E is <1, each infected person is spreading it to <1 person. This means that the number of infections will start to decrease.

8. When pandemics occur, 1 possible countermeasure is to close schools with high levels of infected persons. This is a controversial countermeasure. Using the following table, identify 1 positive and 1 negative consideration for both sides of the problem.

	Positive	Negative
Closing schools with infected students	Number of contacts a person has during a day should decrease	Disruption, loss of income, and extra expenditure resulting from the school closing for parents who stay home from work with their children
Schools remaining open with infected students	No disruption because of closure	Infected persons can more easily spread influenza in a high-density environment

Have You “Herd”? Assessment

Name: ___________________________________ Date: ________________

Directions: Answer the following questions by using complete sentences.

1. R_0 modeling can be used to predict the percentage of a population who will become infected with influenza, but it cannot predict the speed with which the epidemic will spread. Why is this a critical piece of information when using R_0 to plan for an epidemic response?

The Centers for Disease Control and Prevention has released information about a strain of influenza that could cause a pandemic if it changed so that it could be efficiently transmitted from person to person. “The eight genes of the H7N9 virus are closely related to avian influenza viruses found in domestic ducks, wild birds and domestic poultry in Asia. The virus likely emerged from ‘reassortment,’ a process in which two or more influenza viruses coinfect a single host and exchange genes. This can result in the creation of a new influenza virus.”

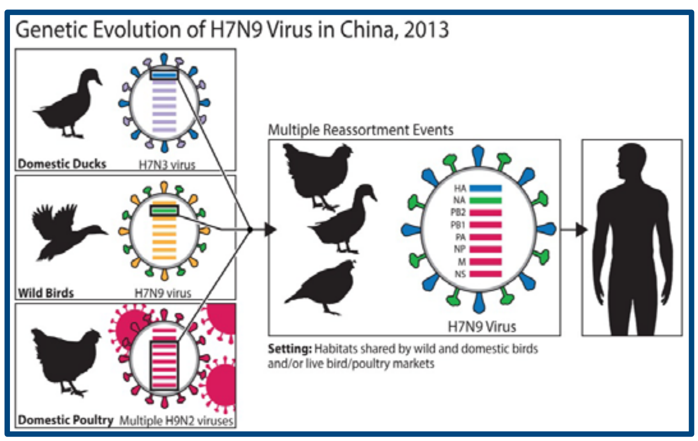


Figure 5 This diagram depicts the origins of the H7N9 virus from China and shows how the virus's genes came from other influenza viruses in birds. Source: Centers for Disease Control and Prevention: ***http://www.cdc.gov/flu/avianflu/h7n9-images.htm.***

2. Knowing this information, is preparing for an influenza pandemic easier or more challenging? Clearly explain and support your response.

3. Solving logistical problems are challenging in every pandemic situation. When an influenza pandemic occurs, vaccines are administered to reduce the spread of the disease. Describe 2 challenges for planning a vaccination program for residents of a city at the start of a pandemic.

4. Would incorporating the epidemic's doubling time (i.e., number of days needed for the number of cases to increase 2-fold) into the model of an influenza outbreak be valuable? Explain.

The figure below displays a classification system whereby different influenza viruses are arranged according to their transmissibility and clinical severity of influenza pandemics.

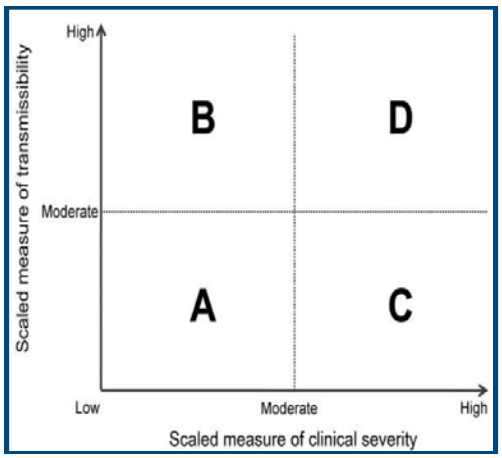


Figure 6: a classification system whereby different influenza viruses are arranged according to their transmissibility and clinical severity of influenza pandemics. Source: Reed C, Biggerstaff M, Finelli L, et al. Novel framework for assessing epidemiologic effects of influenza epidemics and pandemics. Emerg Infect Dis. 2013;19:85–91.

5. The viruses with the potential to generate the most catastrophic pandemic outbreaks would be found in which quadrant?
   A. Quadrant A.
   B. Quadrant B.
   C. Quadrant C.
   D. Quadrant D.

To answer Questions 6–8, the epidemic curve below displays the course of an influenza outbreak.

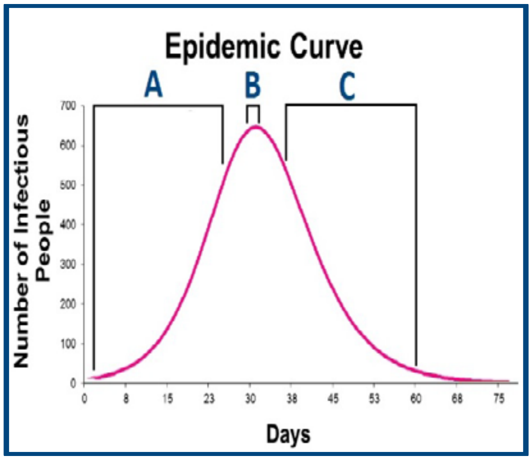


Figure 7. Epidemic curve. Adapted from: O'Hagan J and Carias C. Modeling Influenza Outbreaks. Presented to CDC Science Ambassador Workshop July 22, 2014

6. The region of the graph that displays when the effective reproduction number (R_E) is <1 is indicated by which section?
   A. A.
   B. B.
   C. C.

7. The region of the graph that displays when R_E >1 is indicated by which section?
   A. A.
   B. B.
   C. C.

8. The region of the graph that displays where the herd immunity threshold has been reached (and so $R_E = 1$) is indicated by which section?
   A. A.
   B. B.
   C. C.

Appendix 4B: Assessment 1: Have You “Herd”? Answer Key

Have You “Herd”? Assessment

Name: ______ Answer Key ________________ Date: ________________

Directions: Answer the following questions by using complete sentences.

1. R_0 modeling can be used to predict the percentage of a population who will become infected with influenza but it cannot predict the speed with which the epidemic will spread. Why is this a critical piece of information when using R_0 modeling to plan for epidemic response?
   Sample Answer: Without knowing the speed at which the virus will spread, effectively planning for and responding to an epidemic will be more challenging. Modelers will be unable to tell how rapidly vaccines must be produced and administered to reach the critical vaccination level in time to slow the spread of the virus.

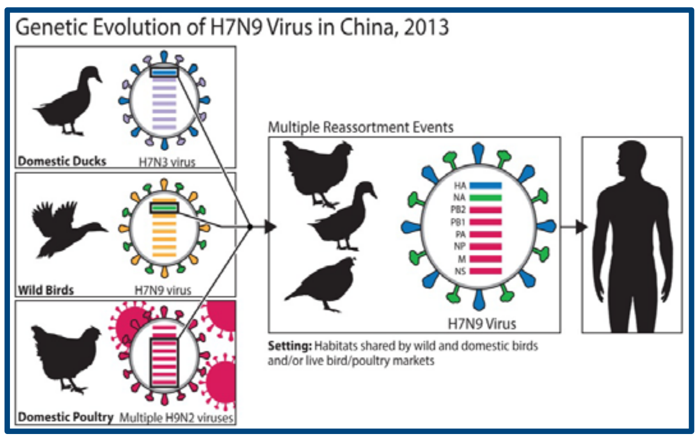


Figure 7 This diagram depicts the origins of the H7N9 virus from China and shows how the virus's genes came from other influenza viruses in birds. Source: Centers for Disease Control and Prevention: **http://www.cdc.gov/flu/avianflu/h7n9-images.htm.**

2. Knowing this information, is preparing for an influenza pandemic easier or more challenging? Clearly explain and support your response.
   Sample Answer: Knowing that the influenza virus can undergo reassortment makes it more challenging to prepare for pandemics. To prepare for an influenza pandemic, a vaccine must be made and stockpiled. If the virus mutates, the vaccine effectiveness will decrease, and it will become substantially more challenging to reach the critical vaccination level (i.e., vaccinate a sufficient number of persons to ensure that the epidemic begins to decline). To reach the critical vaccination level, a new vaccine might have to be produced and might not be able to be produced and administered rapidly.

3. Solving logistical problems are challenging in every pandemic situation. When an influenza pandemic occurs, vaccines are administered to reduce the spread of the disease. Describe 2 challenges for planning a vaccination program for residents of a city at the start of a pandemic.
   Sample Answer: Major challenges in a country like the United States include producing the vaccine within a meaningful timeframe, knowing how many doses should be available for each state or city, distributing the vaccine, and motivating the public to receive the vaccine. Also, a system is needed to administer both rounds of influenza vaccines that are typically required to produce a robust immune response among children. Additionally, education provided to the public about influenza symptoms, personal protective measures, and the importance of getting vaccinated is needed.

   Major challenges in countries with limited infrastructure for vaccine distribution include training staff to administer the vaccine; obtaining enough vaccine to reach the critical vaccination level; transporting staff and medical equipment to locations where the public can receive a vaccine, staffing, and facilities; tracking who has received the vaccine, particularly since it is thought that most pandemic vaccines require two doses to be fully effective, to determine when the critical vaccination level has been reached and to assess potential vaccine-associated adverse health events.

4. Would incorporating the epidemic's doubling time (i.e., number of days needed for the number of cases to increase 2-fold) into the model of an influenza outbreak be valuable? Explain.
   Sample Answer: Yes. Incorporating the doubling time into the model will allow for an estimation of the speed at which the virus will spread. This will allow for emergency planners to determine the speed at which countermeasures will need to be put in place, and having persons vaccinated to stop the outbreak spread.

The figure below displays a classification system whereby different influenza viruses are arranged according to their transmissibility and clinical severity of influenza pandemics.

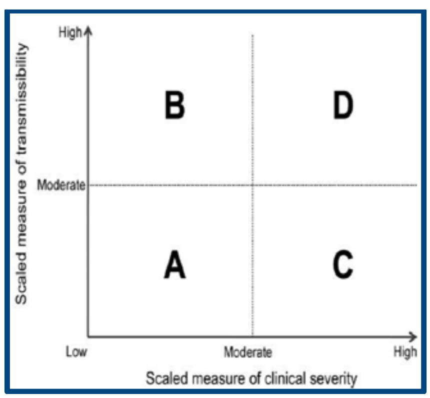


Figure 8: a classification system whereby different influenza viruses are arranged according to their transmissibility and clinical severity of influenza pandemics. Source: Reed C, Biggerstaff M, Finelli L, et al. Novel framework for assessing epidemiologic effects of influenza epidemics and pandemics. Emerg Infect Dis. 2013;19:85–91.

5. The most catastrophic pandemic outbreaks would be found in which quadrant?
   A. Quadrant A.
   B. Quadrant B.
   C. Quadrant C.
   D. **Quadrant D. (Answer)**

To answer Questions 6–8, the epidemic curve below displays the course of an influenza outbreak.

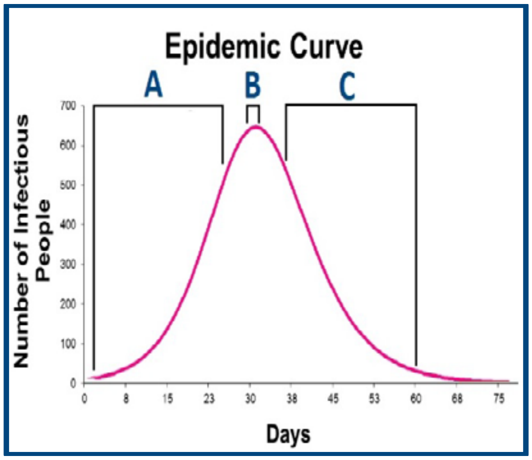


Figure 7. Epidemic curve. Adapted from: O'Hagan J and Carias C. Modeling Influenza Outbreaks. Presented to CDC Science Ambassador Workshop July 22, 2014

6. The region of the graph that displays when the effective reproduction number (R_E) is <1 is indicated by which section?
   A. A.
   B. B.
   C. **C. (Answer)**

7. The region of the graph that displays when R_E >1 is
   indicated by which section?
   A. **A. (Answer)**
   B. B.
   C. C.

8. The region of the graph that displays where the herd immunity threshold has been reached (and so $R_E = 1$)
   is indicated by which section?
   A. A.
   B. **B. (Answer)**
   C. C.