Learning Objectives
After completing this case study, the participant should be able to:

☐ Discuss the advantages and disadvantages of using a sensitive and/or specific case definition in an epidemic investigation;

☐ Calculate vaccine efficacy and discuss its interpretation; and

☐ Discuss the advantages and limitations of selecting a specific age as the recommended target date for administering vaccinations.

This case study is based on an investigation by Philip Landrigan, EIS ’70. The investigation is described in:

Landrigan PJ. Epidemic measles in a divided city. JAMA 1972; 221: 567-570.

This case study was originally developed by Philip Landrigan, Lyle Conrad and John Witte in 1971. The current version was updated by Richard Dicker in 2001 and 2003.
PART I

On Tuesday, November 3, 1970, the Center for Disease Control (CDC) in Atlanta received the weekly telegram of surveillance data from the Texas State Health Department. The telegram reported 319 cases of measles in the state during the previous week. In contrast, Texas had reported an average of 26 cases per week during the previous four weeks. In follow-up telephone calls, CDC learned from State health officials that 295 cases of measles had been diagnosed in the city of Texarkana, including 25 in children reported to have been previously immunized.

An invitation to investigate the situation was extended to the CDC on November 4, 1970. An EIS officer departed for Texarkana early on November 5.

Background

Texarkana is a city of roughly 50,000 that straddles the Texas-Arkansas state line.

Texarkana, Texas (Bowie County), had a population of 29,393 in the 1960 census; the population had been stable during the 1960s. Texarkana, Arkansas (Miller County), had a 1960 population of 21,088.

Although Texarkana is divided by the state line, it is a single town economically and socially. Persons of all ages on both sides of town have frequent contact. Churches, physicians, offices, movie theatres, and stores draw people from both the Arkansas and Texas sides of town. People cross the state line to attend social functions such as football games and school dances. Many families have friends and relatives who visit back and forth on both sides of town. Private nurseries and kindergartens receive children from both sides of town. The two sides of Texarkana, however, do have separate public school systems and separate public health departments.

Question 1: List the reasons to investigate a suspected outbreak. Which reasons may have prompted an investigation of this outbreak?
**Question 2a:** What would be the initial steps of your investigation, i.e., the steps before trying to find additional cases?

**Question 2b:** How might you look for additional cases?

**Question 2c:** Once you collected information about the cases, how would you characterize the outbreak?
PART II

The Investigation

The investigators obtained names of cases from the health departments, physicians, school and nursery records. They conducted a door-to-door survey. They also asked families of cases for names of other cases. They used the same methods of case-finding and epidemiologic investigation on both the Arkansas and Texas sides of town.

Clinical Picture

The illness was clinically compatible with measles. Typically, the patients had a 4- to 5-day prodrome with high fever, coryza (runny nose), cough, and conjunctivitis (red, irritated eyes) followed by the appearance of a bright maculopapular (red spots and areas) rash. The temperature usually returned to normal 2 to 3 days after appearance of the rash, while the rash persisted for 5 to 7 days.

Question 3: How might you define a case for purposes of this investigation?

Question 4: Describe the difference between a sensitive case definition and a specific case definition. What are the advantages and disadvantages of each? Provide an example of a situation where each would be helpful.
In Texarkana, the investigators defined a case as an "illness which is clinically compatible with measles."

**Question 5:** Critique this case definition.
The Outbreak

Between June 1970 and January 1971, 633 cases of measles were reported from Texarkana. Dates of onset were accurately determined for 535 cases. The epidemic curve is shown below.

Measles cases by week of onset, Texarkana, Texas and Arkansas, June 28, 1970 - January 29, 1971

Question 6: Discuss the key features of the epidemic that you can derive from the epidemic curve.
Though infants, adolescents, and adults were involved in the epidemic, the majority of cases occurred in children 1 to 9 years of age. Measles cases were not evenly distributed within the two counties. Table 1 displays the number of measles cases and population by age group for Bowie County, Texas and in Miller County, Arkansas.

Table 1. Number of measles cases and population (1960 census) by age group and county, Texarkana outbreak, 1970

<table>
<thead>
<tr>
<th>Residence</th>
<th>Urban/Rural</th>
<th>Age Group</th>
<th># Cases</th>
<th>Population</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowie Co., Texas</td>
<td>Rural</td>
<td>1-4 yr</td>
<td>47</td>
<td>2,452</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-9</td>
<td>178</td>
<td>3,242</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urban</td>
<td>1-4</td>
<td>195</td>
<td>2,481</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-9</td>
<td>73</td>
<td>3,010</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1-4</td>
<td>242</td>
<td>4,933</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>251</td>
<td>6,252</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miller Co., Arkansas</td>
<td>Total</td>
<td>1-4</td>
<td>19</td>
<td>2,671</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-9</td>
<td>6</td>
<td>3,345</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-9</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Question 7:** Calculate the totals and attack rates indicated in Table 1.

**Question 8:** Discuss the differences in attack rates for the Texas and Arkansas counties, for rural versus urban children, and for preschool versus school-age children.
Part III

Measles in Previously Vaccinated Children

Before this outbreak, the proportion of children vaccinated against measles on the Arkansas side was substantially higher than the proportion vaccinated on the Texas side. The Texas side had never had a community or school vaccination campaign for measles. In contrast, the Arkansas side had held mass community programs against measles for school and pre-school children in 1968 and 1969.

Based on health department and physician records, investigators estimated that over 99% of children aged 1-9 years in Miller County, Arkansas had received measles vaccine prior to the outbreak. The overall vaccination level in Bowie County, Texas, was estimated to be 57%.

In this outbreak, 27 of the measles cases in Bowie County and all 25 of the measles cases in Miller County gave a history of prior vaccination with live attenuated measles-virus vaccine. Parental history of vaccination was corroborated for all the cases by clinic or physician records. Local health authorities in both counties were very concerned that children who had previously received measles vaccine got the disease.

Question 9: Calculate attack rates among the vaccinated populations in both counties and comment on your findings.
Consider the use of a vaccine with 90% efficacy in four different hypothetical populations of 100 people each, with vaccine coverage of 0%, 20%, 60%, and 100%, respectively. Assume that every unvaccinated person will be exposed to, and will develop, measles.

**Question 10:** Complete Table 2.

**Question 11:** What do you conclude about the relationship between coverage and number of cases vaccinated? What might your public health message be for these data?
Vaccine Efficacy

The ability of a vaccine to prevent disease depends on its potency and proper administration to an individual capable of responding. The success of vaccination performed under field conditions may be assessed by measuring protection against clinical disease. Such field assessments can be very useful, particularly when doubt is cast on the efficacy of the vaccine because of the occurrence of disease among vaccinated persons.

Vaccine efficacy is measured by calculating the incidence (attack rates) of disease among vaccinated and unvaccinated persons and determining the percentage reduction in incidence of disease among vaccinated persons relative to unvaccinated persons. The greater the percentage reduction of illness in the vaccinated group, the greater the vaccine efficacy. The basic formula is written as:

\[ VE = \frac{ARU - ARV}{ARU} \times 100 \]

where

- \( VE \) = vaccine efficacy,
- \( ARU \) = attack rate in the unvaccinated population; and
- \( ARV \) = attack rate in the vaccinated population.

**Question 12:** Using the basic formula, calculate vaccine efficacy for Bowie County, Texas.

**Question 13:** Was inadequate vaccine efficacy primarily responsible for this outbreak? If not, what is your alternative explanation?

**Question 14:** What are the possible causes for the failure of the vaccine to protect vaccinated children from acquiring disease?
Part IV

In previously vaccinated children aged 1-9 years in Bowie County, the measles attack rate in this outbreak was 4.2 per 1000; the comparable rate in unvaccinated children was 96.9 per 1000. From these data, a vaccine efficacy of 95.7 percent was calculated. This is a minimum figure since it has been assumed that all 27 children were correctly vaccinated and that all of the cases therefore represent vaccine failure.

In actuality some of these patients did not receive vaccine under ideal conditions. Eight of the 27 previously vaccinated patients had been vaccinated by nurses from the Texarkana/Bowie County Health Unit at a day nursery. The vaccine for these eight children had been carried back and forth to the nursery from the Health Unit in a cooler in a car on three separate days in June and July 1970. Although a lapse in technique which allowed warming of the vaccine cannot be documented here, it is a possible explanation.

An additional seven patients had been vaccinated under the age of 1 year. These children were vaccinated in the years 1963-67 when it was recommended that measles vaccine be given at age 9 months. It has since been learned that a vaccine failure rate as high as 15% may accompany vaccination at 9 months in the United States.

Question 15: What is the WHO recommended age for measles vaccination in developing countries? Why is the recommended age for vaccination different in the United States?
PART V - CONCLUSION

Prior to the development of a vaccine, about 500,000 people developed measles in the United States annually; 50% of persons contracted the disease by age 6 years and 90% by age 15 years. In 1963 both a killed measles vaccine (KMV) and a live, attenuated vaccine were licensed. Since 1969 only live attenuated vaccine has been used in this country.

At the time of original licensure in 1963, the recommended age of vaccination in the United States was 9 months. The recommended age was raised to 12 months in 1965 and to 15 months in 1976.

 Compared with the pre-vaccination era, the occurrence of measles in the U.S. declined by more than 99% by the late 1980s. However, measles cases increased in 1989–1991, and a two-dose strategy was adopted. The recommended age for the first dose is 12–15 months; the recommended age for the second dose is 4–6 years. After the adoption of the two-dose strategy and a substantial increase in immunization program resources, measles cases again declined. Since 1997, fewer than 140 cases of measles have been reported each year in the United States, almost all of which could be traced to imported cases. The provisional totals for 2002 and 2003 were record lows of 44 and 42 cases, respectively.

REFERENCES

1. Landrigan PJ. Epidemic measles in a divided city. JAMA 1972; 221: 567-570.


ADDITIONAL READING
