



Centers for Disease Control and Prevention Case Study on Folic Acid and Neural Tube Defects

Instructor's Guide

Duration of Exercise:

120 minutes

Learning Objectives:

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

- Describe differences in population-based and hospital-based case ascertainment.
- Estimate the prevalence for neural tube defects by type of case ascertainment;
- Describe why there may be differences in the prevalence estimates for neural tube defects by ascertainment method;
- Describe the impact of folic acid fortification on neural tube defects prevalence;
- Describe a secular birth defects trend;
- Identify factors that could impact the prevalence of a health condition;
- Identify uses of public health data;
- Describe how data can be reported to varying audiences.

Part 1:

Population-based birth defects surveillance programs capture pregnancy outcomes (live births and stillbirths) from a source population (for birth defect surveillance, the population is resident mothers), living in a defined catchment area (geographical area) within a defined time period.

To calculate an estimated birth prevalence*, the numerator should include the total number of births, (including live births and stillbirths) with birth defects, occurring in hospitals, maternity hospitals, and at home to resident mothers. The denominator should include the total number of births (live births and stillbirths, with or without birth defects) to resident mothers in the population.

It is important to understand how a country defines residency, in order to identify which births to include in both the numerator and the denominator. Some countries define residency as having lived in the country for at least 1 year.

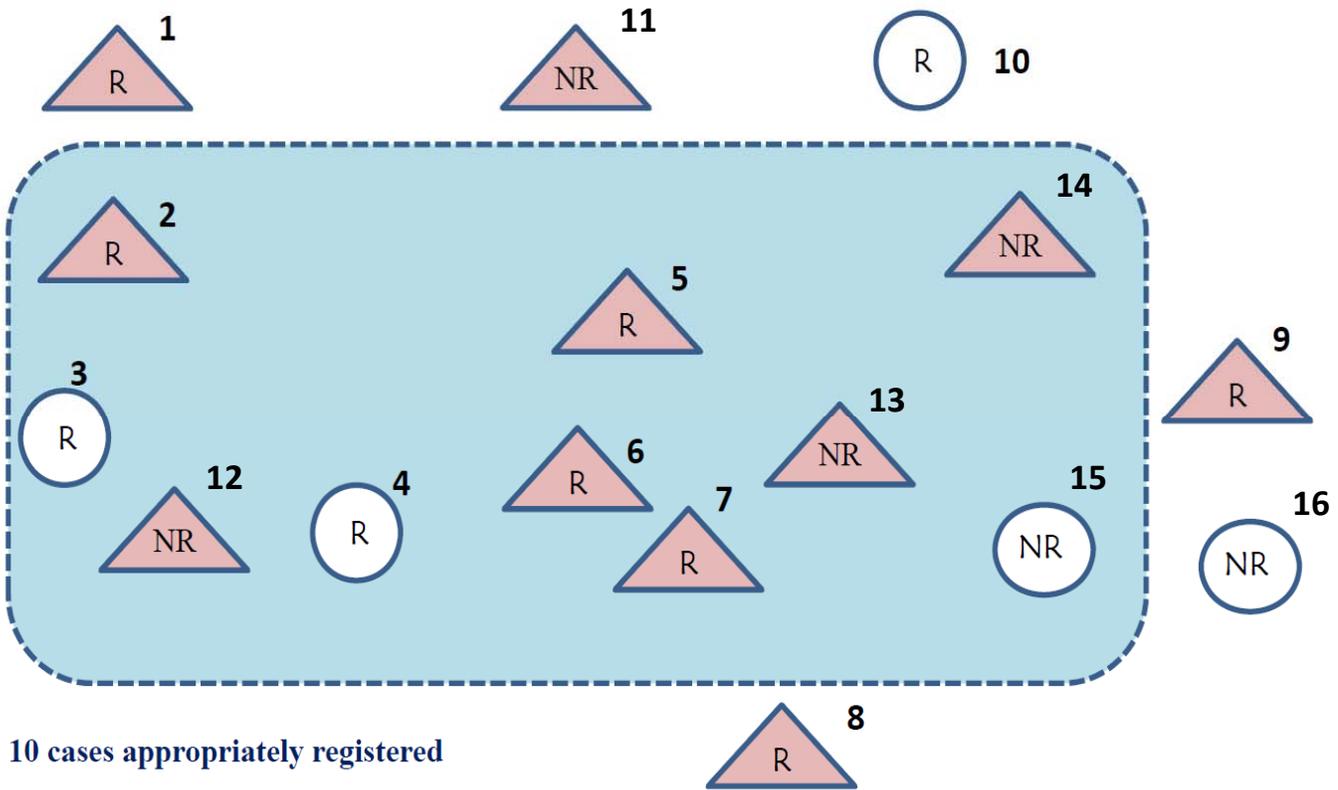
* **Prevalence:** a measure of disease frequency, for a given point in time or period, and among a given population; prevalence is also an indicator of the magnitude of the occurrence of a disease in the population; although prevalence is a proportion of the number of existing cases, regardless of whether or not they are new cases, during a period of time in a defined population, prevalence is sometimes referred to as a rate.

In birth defects epidemiology, the terms birth prevalence and total prevalence are used:

- **Birth prevalence:** includes new cases of a birth defect observed among a defined cohort of births (live births and stillbirths).
- **Total prevalence:** includes new cases of birth defects observed among a defined cohort of births and elective terminations of pregnancy for fetal anomaly.

Figure 1 illustrates an example of a population-based surveillance program.

Figure 1: Example, Population-based surveillance program



 = Geographic boundary defining residence (catchment area)
 = Hospital, clinic, or treatment facility
 = Home births

R= fetus/newborn with a birth defect whose mother is a resident (R)
 NR= fetus/newborn with a birth defect whose mother is a non-resident (NR)

Question 1:

Based on Figure 1, what is the numerator (cases that should be registered)?

Answer 1:

10 cases in total. All fetuses or newborns identified with a birth defect born to mothers residing *within* the catchment area (dashed area) are included in the program (#2 to #7 in Figure 1). Similarly, a fetus or newborn with a birth defect who is born outside of the defined catchment area (including one who is born at home while the mother is visiting a family member living outside of the catchment area, for example) would still be included if the mother is herself a resident of the catchment area (#1, #8, #9, and #10 in Figure 1). Fetuses or newborns identified with a birth defect and born to *non-resident mothers* are not included (#11–16 in Figure 1) even though they are born in hospitals within the catchment area.

Question 2:

Is maternal residence important for this type of surveillance?

Answer 2:

Yes.

Question 3:

Are home births with birth defects counted in this type of surveillance?

Answer 3:

Yes, if the mother is a resident. No, if the mother is not a resident.

Question 4:

What are some examples of data sources that would be used to capture birth defects in a population-based program?

Answer 4:

Data sources include all health facilities within the catchment area where births occur, vital records (e.g., birth and death registries), referral treatment centers for individuals with birth defects (up to the defined age period for inclusion), administrative databases (e.g., medical insurance, hospital discharge, hospitalization, and laboratory information), and any health facility that identifies a fetus or newborn with a birth defect.

Hospital-based birth defects surveillance programs capture pregnancy outcomes (live births and stillbirths) with birth defects that occur in selected hospitals in a defined geographic area (e.g., a state, province, or county) within a defined time period.

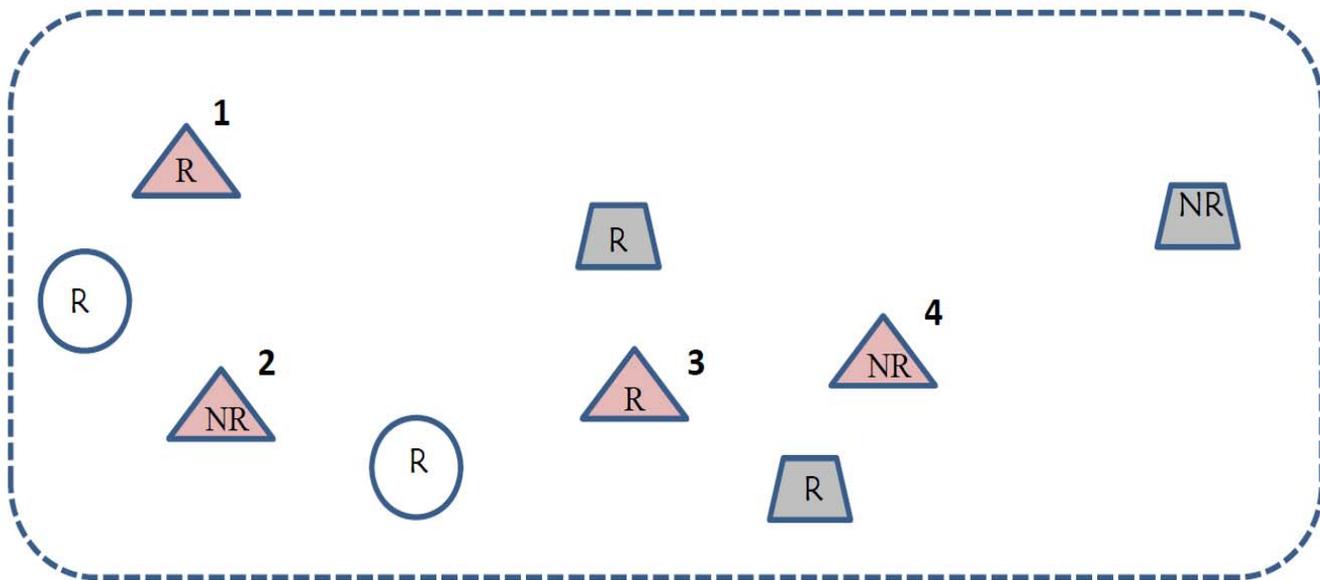
To calculate birth prevalence, the numerator should include the total number of deliveries (including live and stillbirths) with birth defects, occurring only in participating hospitals. The denominator should include the total number of births (including live births and stillbirths) occurring in the participating hospitals. Fetuses or newborns with birth defects who are delivered at home are not included, even if they are identified and captured in participating hospitals for treatment (because they are not part of the denominator).

Because the inclusion in a hospital-based program depends on where the birth occurred rather than on the residence at birth, the source population of cases is difficult to establish. This becomes an issue in the surveillance of birth defects when referral patterns skew the likelihood that a fetus or newborn with a birth defect is delivered at a particular hospital in the system. Thus, a major concern in hospital-based programs is referral bias of cases, that is, the selective delivery of affected pregnancies with a birth defect in hospitals participating in the hospital-based program. For example, if a mother knows that she will be delivering a baby with a birth defect, she might prefer to deliver at a participating hospital that offers specialized care for children born with birth defects, rather than in the hospital closer to her or at home. The impact or magnitude of the referral bias also can vary over time, either because referral patterns change or because hospitals are added or removed from the surveillance program. These attributes of hospital-based surveillance systems limit using hospital-based data longitudinally for monitoring.

Hospital-based programs typically collect data on live births and stillbirths. Because newborns are discharged from maternity hospitals within days following birth, hospital-based programs typically capture only those birth defects that are evident during the hospital stay, unless those newborns readmitted to the hospital for surgery or other procedures are captured and the program has the capacity to do follow up of those newborns. Note that newborns diagnosed after delivery in a hospital participating in a hospital-based program are not included for the purpose of surveillance *unless* they were also delivered at a participating hospital.

Figure 2 illustrates an example of participating and non-participating hospitals in a hospital-based surveillance program.

Figure 2: Example, Hospital-based surveillance program



4 cases appropriately registered



= Geographic boundary for participating hospitals



= Participating hospital



= Home births



= Non-participating hospital

R= fetus/newborn with a birth defect whose mother is a resident (R)

NR= fetus/newborn with a birth defect whose mother is a non-resident (NR)

Question 5:

Based on Figure 2, what is the numerator (cases that should be registered)?

Answer 5:

4 cases in total. All fetuses or newborns with birth defects born to mothers in participating hospitals, regardless of maternal residency, are included in the program (#1 to #4 in the Figure 2). Fetuses or newborns with birth defects born to resident mothers *but born outside of a participating hospital* (#5–7) or *at home* (#8–9) are not included. Fetuses or newborns with birth defects born to *non-resident mothers* are included if born in a participating hospital.

Question 6:

Is maternal residence important for this type of surveillance?

Answer 6:

No

Question 7:

Are home births with birth defects counted in this type of surveillance?

Answer 7:

No, only births that occur in participating hospitals.

Question 8:

What are some examples of data sources that would be used to capture birth defects in a hospital-based program?

Answer 8: Ascertainment of fetuses or newborns identified with birth defects in participating hospitals can vary. While some participating hospitals are primary hospitals, others might be specialized centers for certain conditions or for prenatal diagnosis and care and serve as referral hospitals for patients outside the catchment area. Such hospitals would disproportionately serve fetuses or newborns with birth defects, thus introducing bias in the calculation of their birth prevalence.

Part 2:

The United States National Birth Defects Prevention Network collects state-specific birth defects surveillance data for annual publication of prevalence estimates and collaborative research projects. In 2010, data for 21 birth defects from 2004–2006 were presented as national birth defects prevalence estimates. The data presented in Table 1 are from population-based programs that have different types of case ascertainment: active, hybrid, and passive. Active ascertainment occurs when there is active review of multiple data sources to identify cases. Active ascertainment usually requires that the program hire trained personnel to conduct abstraction from data sources. Passive ascertainment occurs when hospital staff report cases directly to the program without verification of cases by the program staff. An example of hybrid ascertainment is when hospital staff report cases and program staff verify them.

Table 1. Cases of neural tube defects by type of ascertainment, United States, 2004–2006

| Neural Tube Defects | Active Ascertainment (11 Programs)^a | Hybrid Ascertainment (6 Programs)^b | Passive Ascertainment (7 Programs)^c | National |
|----------------------------|---|--|---|-----------------|
| | Cases | Cases | Cases | Cases |
| Anencephaly | 697 | 211 | 192 | 1,100 |
| Spina Bifida | 1,162 | 561 | 820 | 2,543 |
| Encephalocele | 261 | 125 | 184 | 570 |
| Total Neural Tube Defects | 2,120 | 897 | 1,196 | 4,213 |

Source: Parker SE et al.: Updated national birth prevalence estimates for selected birth defects in the United States 2004-2006: Birth Defects Research 2010; (part A) 88:1008-1016.

Data from programs with active, hybrid, or passive ascertainment

^a Number of live births in the active ascertainment programs: 3,120,605

^b Number of live births in the hybrid ascertainment programs: 2,075,973

^c Number of live births in the passive ascertainment programs: 2,145,287

Question 1:

- Estimate the national prevalence for each neural tube defect and for the total neural tube defects per 10,000 live births.
- Estimate the birth prevalence for each neural tube defect per 10,000 live births by type of ascertainment.
- Estimate the birth prevalence for total neural tube defects per 10,000 live births by ascertainment.

Answer 1:

Table 1. Estimated prevalence of neural tube defects by type of ascertainment, United States, 2004–2006

| Neural Tube Defects | Active Ascertainment (11 Programs) ^a | | Hybrid Ascertainment (6 Programs) ^b | | Passive Ascertainment (7 Programs) ^c | | National | |
|---------------------------|---|-------------|--|-------------|---|-------------|----------|-------------|
| | Cases | Prevalence | Cases | Prevalence | Cases | Prevalence | Cases | Prevalence |
| Anencephaly | 697 | 2.23 | 211 | 1.02 | 192 | 0.89 | 1,100 | 1.50 |
| Spina Bifida | 1,162 | 3.72 | 561 | 2.70 | 820 | 3.82 | 2,543 | 3.46 |
| Encephalocele | 261 | 0.84 | 125 | 0.60 | 184 | 0.86 | 570 | 0.78 |
| Total Neural Tube Defects | 2,120 | 6.79 | 897 | 4.32 | 1,196 | 5.57 | 4,213 | 5.74 |

Source: Parker SE et al.: Updated national birth prevalence estimates for selected birth defects in the United States 2004-2006: Birth Defects Research 2010; (part A) 88:1008-1016.

N = Number of surveillance systems with active, hybrid, or passive ascertainment

^a Number of live births: 3,120,605

^b Number of live births: 2,075,973

^c Number of live births: 2,145,287

Question 2:

Describe the differences in prevalence by ascertainment method, and provide some reasons for why differences might exist.

Answer 2:

1. The prevalence of specific defects varied by ascertainment method.
2. Prevalence of anencephaly varied considerably by ascertainment method.
3. Prevalence of encephalocele was higher among the passive ascertainment method than among the hybrid or active ascertainment methods.
4. Possible reasons for differences include:
 - a. Some programs might include elective terminations.
 - b. Some programs might include stillbirths.
 - c. Some programs might have conducted specialized prenatal ascertainment.

Question 3:

What are some possible reasons why the passive and hybrid ascertainment methods have different prevalence estimates for spina bifida than the active ascertainment method?

Answer 3:

1. Misclassification of cases at birth

2. Reporting problems/Birth defects not reported e.g, biased reporting, underreporting or selective reporting
3. Hybrid ascertainment methods are able to assess probable cases during follow-up and provide a definitive diagnosis

In 1996, folic acid fortification of cereal grain products labeled as enriched became voluntary in the U.S. In 1998, a mandate was passed requiring that these products be fortified with folic acid to ensure an adequate supply of folate for women of childbearing age.

The United States National Birth Defects Prevention Network collects information on neural tube defects by three major race/ethnic groups, and has data from the time period prior to mandatory folic acid fortification (1995–1997) and following the folic acid fortification mandate (1998–2010). The estimated annual neural tube defects prevalence for nine hospitals in the United States during these time periods is presented in Table 2.

Table 2: Prevalence of neural tube defects per 10,000 births by race/ethnicity, United States, 1995–2007

| | Year | | | | | | | | | | | | |
|-----------|------|-------|------|------|------|------|------|------|------|------|------|------|------|
| | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 |
| Hispanic | 9.20 | 10.84 | 9.69 | 7.37 | 7.83 | 6.45 | 6.63 | 6.98 | 6.95 | 6.63 | 6.27 | 5.69 | 6.04 |
| Black | 4.89 | 5.75 | 3.59 | 4.78 | 4.80 | 4.49 | 4.81 | 5.16 | 4.17 | 3.68 | 3.89 | 3.37 | 3.74 |
| Caucasian | 7.1 | 7.8 | 6.7 | 5.5 | 5.5 | 5.3 | 5.1 | 4.6 | 4.6 | 5.2 | 4.6 | 4.9 | 5.3 |

Source: [CDC Grand Rounds: Additional Opportunities to Prevent Neural Tube Defects with Folic Acid Fortification. MMWR 2010; 59\(31\): 980-984.](#)

Question 4:

Has folic acid fortification impacted the prevalence of neural tube defects?

If so, how has folic acid fortification impacted the prevalence of neural tube defects?

Answer 4:

1. Folic acid fortification is most likely responsible for the majority of the decline in neural tube defects prevalence. The observable decline in the prevalence of neural tube defects is likely due to fortification.

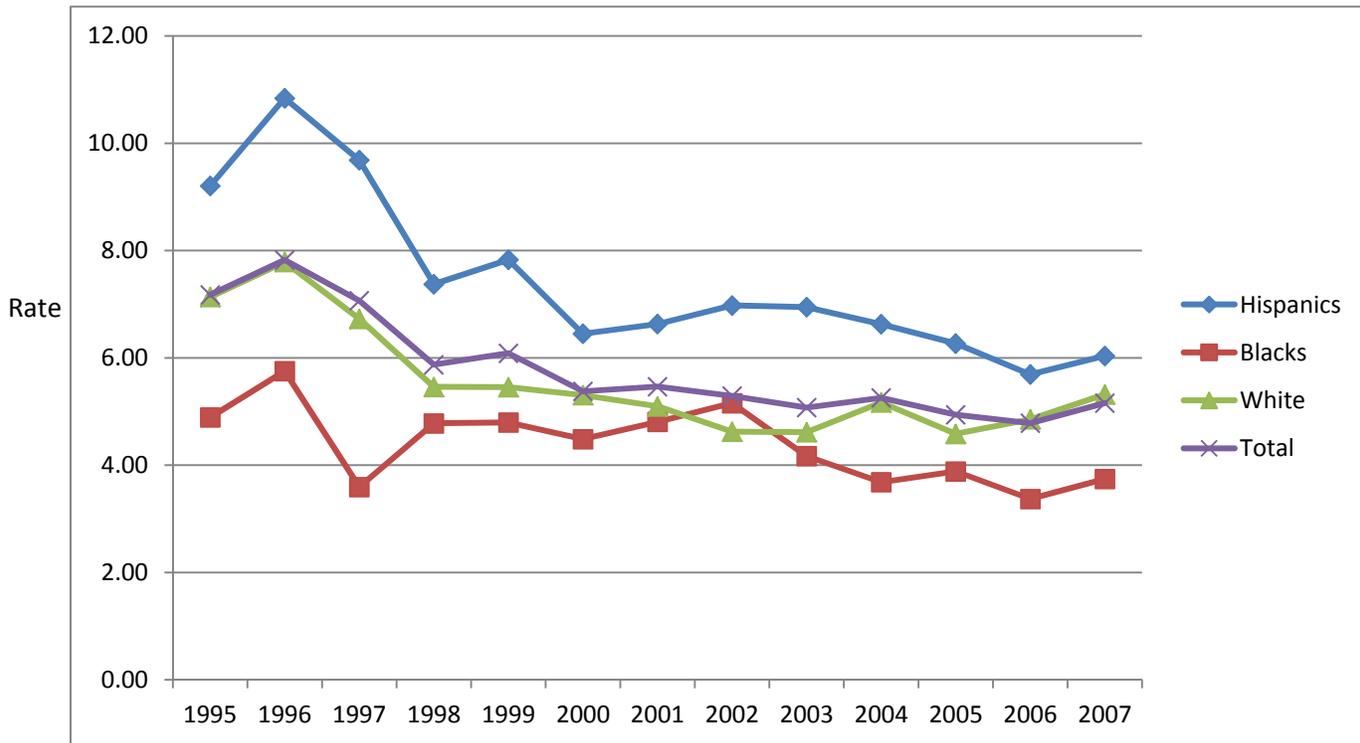
Instructor's Note: If students have a computer and access to Excel, ask students to make a graph with the data provided.

1. Remind students about the:
 - Need for a meaningful scale on the Y-axis to improve understanding of the use of a time scale on the x-axis to show trends
 - Importance of axis labeling
 - Use of highlighting effects or factors of interest, such as year in which fortification started in the United States (voluntary and mandatory)
 - Need for clear and descriptive titles

Public health agencies have a long tradition of monitoring trends in rates of disease and death, and in medical, social, and behavioral risk factors that may contribute to these adverse events. Trends in observed rates provide information for needs assessment, program planning, program evaluation, and policy development activities. Examining data over time also allows for making predictions about future frequencies and rates of occurrence.

Typically in public health, trend data are presented as population-based rates. These data are accessed from large database systems such as national vital records, and show how rates change over relatively long periods of time, e.g., ten or more years. Trend data can be visually presented through tables and graphs. Figure 3 shows secular trend data for neural tube defect prevalence in the United States by race/ethnicity.

Figure 3: Neural tube defects prevalence (per 10,000 births) by race/ethnicity, United States, 1995-2007



Source: National Birth Defects Prevention Network. Neural tube defect ascertainment project 2010. Available at http://www.nbdpn.org/current/resources/ntd_fa_info.html.

Question 5:

Describe the neural tube defects prevalence and the secular (long term) trend. Is there a change in the neural tube defects prevalence? What is the direction of the change?

Answer 5:

There is a decline in the prevalence of neural tube defects.

Question 6:

When was this change first evident?

Answer 6:

The change in prevalence started in the year 1997. After that point, the decrease in neural tube defects prevalence accelerates through 2004, followed by a leveling off of neural tube defects prevalence.

Question 7:

What are some possible reasons for some of the changes observed in neural tube defects prevalence?

Answer 7:

1. The introduction of folic acid fortification
2. The neural tube defect prevalence was already declining and it is only a continuation of such decline, possibly due to other unmeasured factors.
3. Improved surveillance, more accurate data, fewer misclassifications
4. Changes in ascertainment

Question 8:

What are some factors that could impact the prevalence of a health condition?

Answer 8:

1. Population changes due to migration
2. Improved diagnostic procedures
3. Enhanced reporting techniques
4. Changes in the surveillance system or methods
5. Changes in prevalence of other risk factors for the condition
6. Changes in intervention

Part 3:

One of the most important steps in public health surveillance is the distribution or dissemination of relevant findings to appropriate audiences in a timely manner. Possible audiences include partners, stakeholders, health care providers, and the public. It is important to remember who your target audiences are when preparing data for dissemination. What message or messages do you want to convey? What do your target audiences need to know? In what format should you present the data so that it is well understood?

Other important points to keep in mind when reporting surveillance data are the timeline for dissemination, the usefulness of disseminated information, and the channel for data dissemination. It is important to ensure that the data have been reviewed and validated prior to dissemination, and that the timing has been considered. For example, holding data for a longer period of time than necessary could lead the public to believe that the results of a study are being purposely hidden. Examples of channels are written reports, the Internet, media, or a combination of these.

Question 1:

What do you think are some of the uses of neural tube defects surveillance data?

Answer 1:

1. Planning, implementing, and assisting with the evaluation of evidence-based interventions for the prevention of neural tube defects, and minimizing complications and adverse outcomes among those

affected by neural tube defects.

- 2.
3. Informing policymakers and government officials about neural tube defects and the need for prevention efforts
4. Informing clinical/public health practitioners, NGOs, and the public about neural tube defects
5. Identifying and referring children living with a neural tube defect to medical care services
6. Identifying trends in neural tube defects prevalence so a sudden increase or decrease in the rates of neural tube defects can be identified.

Table 3 shows prevalence of select birth defects by ethnic group. Divide students into two or four small groups. Assign a target audience (groups 1 and 2 below) to each group. Using the hypothetical sample surveillance data, have groups discuss how they would communicate and disseminate the surveillance data information to their assigned group. After groups have had enough time to complete the activity, discuss results as a larger group.

Target Audience

Group 1: General public health professionals and health care providers

Group 2: Health care providers and institutions **participating** in a birth defects surveillance program

Table 3: Example: Prevalence of birth defects per 10,000 population by ethnic group

Ethnic group

| Birth Defect | Ethnic group 1 | | 2 | | Ethnic group 3 | |
|-------------------------|----------------|------------|---------|------------|----------------|------------|
| | Cases | Prevalence | Cases | Prevalence | Cases | Prevalence |
| Cleft Lip | 15 | 0.50 | 2 | 0.19 | 2 | 0.57 |
| Spina Bifida | 97 | 3.23 | 41 | 3.90 | 7 | 2.00 |
| Club Foot | 11 | 0.37 | 6 | 0.57 | 1 | 0.29 |
| Anencephaly | 6 | 0.20 | 5 | 0.48 | 0 | 0 |
| Encephalocele | 6 | 0.20 | 6 | 0.57 | 1 | 0.29 |
| Total Population | 300,500 | | 105,000 | | 35,000 | |

Question 2:

What would you include in a report designed for general public health professionals and health care providers?

Answer 2:

1. A description of the condition, its severity and related disability
2. Analyses and interpretation of public health surveillance results

3. Recommendations stemming from the results
4. Suggestions for how the public health professionals and health care providers can become involved in supporting prevention initiatives

Question 3:

What would you include in a report designed for health care providers and institutions participating in a birth defects surveillance program?

Answer 3:

1. Analyses and interpretation of public health surveillance results
2. Ways to improve reporting
3. Comparison of prevalence between geographic areas or populations
4. Detailed information related to program progress in participating hospitals and health care systems
5. Overall program progress

The examples just completed focused on communicating information about surveillance to public health professionals and health care providers. Communicating a diagnosis to parents is a separate issue and should be left to the family's doctor to discuss with the parents; however, it is important for all surveillance program staff to understand that this is a sensitive issue.

Only health care providers who have been appropriately trained should communicate the diagnosis and prognosis of a birth defect to the parents. Other surveillance program staff should NOT communicate information about diagnoses or prognosis to parents.

Parents can be effective advocates of the surveillance program and help maintain interest among government officials and others on the importance of having a birth defects surveillance program. Parents can also help advocate for new services or improvement of current services for children born with birth defects.

Conclusion:

CDC is working with the World Health Organization and country Ministries of Health to assist with the development and/or enhancement of birth defects surveillance programs. The goal of this surveillance is to collect data that can help support birth defects prevention initiatives, improve the quality of life for those children and families affected by birth defects, and ultimately decrease the prevalence of neural tube defects and other birth defects.