Using Epidemiology in TB Prevention & Control

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Why learn about epidemiology?
- Assist TB program staff to analyze and make practical use of data
- Assess current and evolving trends in TB morbidity, identify risk groups, and determine where to allocate staff and resources
- Assist all TB program staff in working towards effective TB control

What is epidemiology?

Epidemiology

“The study of the distribution and determinants of health-related states in specified populations, and the application of this study to control health problems.”

Source: http://www.cdc.gov/excite/

What is Epidemiology?

- Descriptive epidemiology concentrates on examining the distribution of diseases in the population in terms of person (who gets the disease), place (where they get the disease) and time (when they get the disease)
- Analytic Epidemiology is concerned with studying the relationship between risk factors and a disease
How do we find descriptive data?

Public Health Surveillance

The systematic, ongoing collection, analysis, interpretation, and dissemination of health data. The purpose of public health surveillance is to gain knowledge of the patterns of disease, injury, and other health problems in a community so that we can work toward controlling and preventing them.

Source: http://www.cdc.gov/excite/

Two types of surveillance

Active surveillance is a system where the health department or other agency initiates the data collection activities.

Passive surveillance is used when the health care provider is asked or required to report information to the health department.

TB Surveillance

- Since 1953
- Newly reported cases of TB disease
- Primarily collected via the expanded TB case report introduced in 1993.

- TB case report (Report of Verified Case of Tuberculosis, or RVCT) is submitted electronically to the Division of Tuberculosis Elimination (DTBE), CDC, by 60 reporting areas (the 50 states, the District of Columbia, New York City, Puerto Rico, and seven other jurisdictions in the Pacific and Caribbean).
TB Surveillance Data Reports

- Descriptive Statistics
  - Person
  - Place
  - Time
  - Combined with Census Data to generate case rates

The number of cases that occur during a specified time period \( \times 100,000 \)
population at risk during that time period

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TB Surveillance

[Image of CDC logo]

Tuberculosis in the United States
National Tuberculosis Surveillance System
Highlights from 2007
Division of Tuberculosis Elimination
Centers for Disease Control and Prevention


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Descriptive Data: person

[Graph showing TB Case Rates by Age Group and Sex, United States, 2007]

- Less than 15 yrs
- 15–24 yrs
- 25–44 yrs
- 45–64 yrs
- >65 yrs

Cases per 100,000

- Male
- Female

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Descriptive Data: place

[Map showing TB Case Rates, United States, 2007]

- ≤ 3.3 (year 2000 target)
- 3.4–4.4
- > 4.4 (national average)

*Cases per 100,000.
Descriptive Data: time

Using TB Surveillance Data

- Provide the descriptive epidemiology of local and state TB programs.
  - A description of the gender, race, ethnicity, occupation, nationality and place of residence of TB cases can be summarized for state or local areas
  - Health information such as HIV status, history of substance use, prior diagnosis of TB, site of disease, sputum culture results, initial drug regimen, initial and final drug susceptibility results, type of health care provider and type of therapy received (Directly observed vs. self-administered)

Using TB Surveillance Data

- Information related to treatment outcomes that can be used to evaluate program performance and needs
  - E.g., date of treatment initiation may be compared with date that therapy was completed to see how long it takes patients to complete therapy
  - Other program performance goals can be set by the state TB Control Program

Sources of TB Surveillance Information

Reported Tuberculosis in the United States, 2007

- This publication, Reported Tuberculosis in the United States, 2007, presents the summary data for TB cases reported to CDC, verified, and counted for 2007.  

Tuberculosis in the United States, 2007 (Slide Set)

- This slide series was developed as an accompaniment to the document Reported Tuberculosis in the United States, 2007  

Online Tuberculosis Information System (OTIS)

- OTIS is a query-based system containing information on TB cases reported to CDC  
Key epidemiologic terms

- **Epidemic (or outbreak)**
  Unusual occurrence of disease

- **Endemic**
  Usual occurrence of disease

- **Pandemic**
  World-wide epidemic

Key epidemiologic measures: Incidence Rate

\[ \frac{\text{# of NEW cases of disease during a specified time period}}{\text{Population at risk of disease during the same time period (also measured as person-time)}} \times 1,000 \]

Key epidemiologic measures: Prevalence Ratio

\[ \frac{\text{Total # of (new and old) cases of disease during a time period (or at one point in time)}}{\text{Total (usually mid-period) population during the same time period)}} \times 1,000 \]

Comparing Incidence Rates and Prevalence Ratios

<table>
<thead>
<tr>
<th>INCIDENCE RATE</th>
<th>PREVALENCE RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Numerator</strong></td>
<td><strong>Numerator</strong></td>
</tr>
<tr>
<td>New Cases during a time period</td>
<td>NEW and OLD Cases At one point in time or during a time period</td>
</tr>
<tr>
<td><strong>Denominator</strong></td>
<td><strong>Denominator</strong></td>
</tr>
<tr>
<td>Population at risk or Person-Time</td>
<td>Total Population</td>
</tr>
<tr>
<td>Excluding pre-existing cases during a specified time period</td>
<td>At one point in time or during a time period</td>
</tr>
<tr>
<td><strong>Use</strong></td>
<td><strong>Use</strong></td>
</tr>
<tr>
<td>Estimate of risk</td>
<td>Burden of disease</td>
</tr>
</tbody>
</table>
What is a TB Case Rate? An incidence rate or a prevalence ratio?

The number of cases that occur during a specified time period x 100,000 population at risk during that time period

Note: cases are verified cases of TB. If TB recurs or if more than 12 months has elapsed since the person was discharged or lost to follow-up, then the person is counted as a new case.

Sample Problem: Calculating Incidence and Prevalence

- A county TB Controller would like to know how many people currently living in a local homeless shelter are TST positive
- A nurse administers and reads the TST test results. Out of 100 homeless shelter residents, 40 had a positive TST result.
- All 100 residents remained in this shelter for the next year at which time only those who did not have an initial positive TST result were tested again. Among these 60 residents, 20 had a positive test result.

Calculate:
- a. the baseline prevalence of TB infection at this homeless shelter
- b. an estimate of the risk of developing TB infection in this population

Sample Problem: Solution Calculating Incidence and Prevalence

- A nurse administers and interprets the TST test results. Out of 100 homeless shelter residents, 40 had a positive TST result.

Baseline Prevalence is 40/100 or 40%

- All 100 residents remained in this shelter for the next year at which time only those who did not have an initial positive TST result were tested again. Among these 60 residents, 20 had a positive test result.

b. an estimate of the risk of developing TB infection in this population

Incidence Rate = 20/60 or 33%

TB Control

- Assume that these two figures are good representations of the TB occurrence. What does it tell us about TB Control?
Assume that these two figures are good representations of the TB occurrence. What does it tell us about TB Control?

Since TB has a long period of latent infection, these new infections added to the pool of existing infections, which represents a source for potential TB cases in the years, and even decades, to come. One strategy for global TB control would be to implement an effective screening program in high-risk populations that would identify individuals with latent TB infection and treat them to prevent disease.

Source: Whalen, JAMA, June 8, 2005, p. 2785

Severity of illness and reporting of disease statistics: Iceberg Phenomenon

- Subjective
- Type of surveillance used (active vs passive)
- Only available if someone seeks care and the information about that care is recorded
- The most severe cases of disease are more likely to be reported than less severe cases of disease
- Validity of a test to identify infection and disease

Quality of Morbidity Data

Mortality
- Is easier to define than morbidity
- Main source of mortality data in the United States is the standard US death certificate
- Collected by states and is kept by the National Center for Health Statistics
- Since TB death rates are so low in US, less likely to see published mortality figures for the US
- TB is a major cause of death in developing countries

Analytic Epidemiology - Study Designs
- Cross-Sectional studies
- Case-Control studies
- Cohort studies
Cross-sectional studies

- Provide information on possible risk factors and disease outcomes at the same point in time
- Sometimes called prevalence studies, since they can provide prevalence ratios
- Cannot provide information on causes of diseases since it is unclear in these studies whether the disease or the supposed risk factor occurred first
- Sometimes descriptive, in that they describe the disease or condition in a population at a given time, in terms of person time or place

Case-control studies

- CASES are people with disease or infection while CONTROLS do not have the disease/infection
- Both are questioned about potential risk factors, which occurred in the past
- Estimate the amount of disease risk associated with a particular risk factor using the odds ratio
- Useful when the disease outcome being studied is rare
Case-control studies

♦ Results for travel to a high burden country
- Parents of all 300 children consented to be in this study.
- 22 of these 300 children had traveled to a “high burden” TB country during the 12 months prior to their tuberculin skin test.
- 12 of the 80 children with a positive skin test had traveled to a “high burden” TB country during the 12 months before their skin test.

♦ Using the information provided in the above paragraph, create a 2 x 2 table.

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>SKIN TEST RESULT</th>
<th>Odds ratio = ( \frac{ad}{bc} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Travel</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>No Travel</td>
<td>68</td>
<td>210</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>220</td>
</tr>
</tbody>
</table>

Cohort study

♦ Collect information on a group of EXPOSED* and UNEXPOSED individuals over time.

♦ Calculate incidence rates of disease outcome.

♦ Calculate the direct measure of association between a risk factor and an outcome called the relative risk.

♦ To a risk factor

Cohort study

The **Relative Risk** is calculated as:

\[
\text{Relative Risk} = \frac{\text{incidence rate in the group exposed to the risk factor}}{\text{incidence rate in the unexposed group}}
\]

Interpretation:
A relative risk of 2 means that the risk of developing a particular outcome or disease is \textbf{twice as high} as among those with the risk factor as among those without the risk factor.
Cohort Study\textsuperscript{2}

TB Outbreak in a Community Hospital

Exposure Status

“Hospital staff contacts who were determined from the index patient’s medical record and from hospital employment records were categorized as 1) direct-care providers, 2) workers assigned to the same ward but not involved in the patient’s medical care, or 3) other workers who spent time on the medical ward but were not assigned there.” (pg. 214).

Outcome- Results of Tuberculin Skin Testing (TST)

- 495 (63%) of 784 staff members were evaluated with TSTs
- 56 of 495 staff members tested positive
- 21 of 56 (38%) were direct-care providers
- 6 of 56 (11%) were ward-based staff
- 29 of 56 (52%) were other staff

**Clinical trial**

- A special type of cohort study
- Used to assess the effectiveness of clinical therapies (e.g., a new TB drug regimen),
- Individuals are assigned to different therapies and then followed over time to measure the outcome of the therapy.
- Most valuable
  - Random assignment
  - “Blinded” or “masked”
  - Placebo controlled

\textsuperscript{2}Cohort Study

<table>
<thead>
<tr>
<th>Assignment workers</th>
<th>No. evaluated</th>
<th>TST positive*</th>
<th>RR* (95% CP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct care</td>
<td>106</td>
<td>65</td>
<td>21 (33)</td>
</tr>
<tr>
<td>Ward-based</td>
<td>49</td>
<td>26</td>
<td>6 (23)</td>
</tr>
<tr>
<td>Other</td>
<td>620</td>
<td>404</td>
<td>29 (7)</td>
</tr>
<tr>
<td>Total</td>
<td>784</td>
<td>495</td>
<td>56 (11)</td>
</tr>
</tbody>
</table>

* A TST of \( \geq 5 \) mm during the investigation in a person with a documented negative TST during the preceding 2 years.

\( \text{RR} \) = Relative risk

\( \text{CI} \) = Confidence interval

Incidence TST + direct care = RR direct care
Incidence TST + other

- RR= 32/7=4.5. This means that the direct care employees were 4.5 times more likely to have a positive TST result compared with those described as other employees.
- This means that greater exposure was related to outcome (TB infection).
The Diarylquinoline TMC207 for Multidrug-Resistant Tuberculosis

In the first stage of a two-stage, phase 2, randomized, controlled trial, we randomly assigned 47 patients who had newly diagnosed multidrug-resistant pulmonary tuberculosis to receive either TMC207 (400 mg daily for 2 weeks, followed by 300 mg three times a week for 6 weeks) or placebo (48 patients) in combination with a standard first-line, second-line antituberculosis regimen. The primary efficacy end point was the conversion of sputum cultures, in liquid broth, from positive to negative.

As compared with placebo, the addition of TMC207 to the standard drug regimen for multidrug-resistant tuberculosis resulted in quicker conversion to a negative sputum culture... (Fig. 2) p. 2402

Molecular Epidemiology

- TB epidemiology enhanced by molecular strain typing
- Used to differentiate between the different TB mycobacterial isolates
- DNA fingerprinting could be used during contact investigations to confirm (or disprove) known epidemiological links between cases and determine connections among cases where obvious epidemiological links do not exist

Closing

- Epidemiologic methods can help us to identify local, state, and national patterns of disease and their impact on local control of tuberculosis
- Can use epidemiological surveillance data to improve both patient care outcomes and effectiveness of individual TB Programs

Footnotes

1. The hypothetical Case-Control Study was inspired by the study published by MARK N. LOBATO and PHILIP C. HOPEWELL. *Mycobacterium tuberculosis* Infection After Travel to or Contact with Visitors from Countries with a High Prevalence of Tuberculosis, Am. J. Respir. Crit. Care Med., Volume 158, Number 6, December 1998, 1871-1875. However the study design and data presented are not taken directly from this study.