SURVEILLANCE OF MAJOR BIRTH DEFECTS IN NON-LIVE BIRTH PREGNANCY OUTCOMES

EPIDEMIOLOGICAL CONSIDERATIONS

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Objectives

• Provide overview for calculation of birth defect prevalence
• Discuss benefits of including non-live birth data for data analysis and epidemiological assessments
• Present some of the challenges of using non-live birth data
• Present potential ways to address the challenges with non-live birth data
• Discuss the gold standard vs. realistic alternatives

Overview of Calculation for Birth Defect Prevalence

• Case counts
• Prevalence estimates (overall & stratum-specific)
• 95% confidence intervals
• Prevalence calculation
  * NBDPN recommendation:
  \[
  \frac{BD \text{ Cases} \times 10,000}{\text{All Live Births in Same Population}}
  \]
  \[
  \frac{42 + 33}{427,550} \times 10,000 = 1.75 \text{ cases per 10,000 live births}
  \]

Acronyms:

BD – Birth defects
NBDPN – National Birth Defects Prevention Network
NTD – Neural Tube Defects

(Mason et al., 2005; NBDPN Guidelines, 2004)
Benefits of Including Non-Live Birth Data

1) More complete case ascertainment
   • Reduces risk of under reporting that could occur with just live birth data
   • 1 BD case for every 33 pregnancies, yet 1 BD case for every 5 stillborn fetuses
   • Odds of elective termination are 126 times higher for fetuses with severe non-neurologic malformations
   • Odds of elective termination are 300 times higher for fetuses with serious neurologic malformations
   • Over 40% of pregnancies with neural tube defects were electively terminated after prenatal diagnosis (South Carolina, California)
   • Scant data in BD cases among miscarriages
     • Chromosomal abnormalities and NTDs

(Rynn, 2008; Hoyert, 2016; Gregory, 2013; Stillbirth Collaborative Research Network Writing Group 2011; Schechtman, 2002; Allen, 1996; Selvin, 1996)

Benefits of Including Non-Live Birth Data

1) More complete case ascertainment
   • Miscarriages…

National Birth Defects Prevention Network

Benefits of Including Non-Live Birth Data

1) More complete case ascertainment
   • Arizona example
     • Anencephaly prevalence estimate, 2011-2015

<table>
<thead>
<tr>
<th>BD live births</th>
<th>BD live births x 10,000 = Prevalence estimate</th>
<th>BD live births + BD fetal deaths x 10,000 = .93 cases per 10,000 live births</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>437,100</td>
<td>478.92</td>
</tr>
<tr>
<td>427,550</td>
<td></td>
<td>1.71 cases per 10,000 live births</td>
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</tbody>
</table>

National Birth Defects Prevention Network
**Benefits of Including Non-Live Birth Data**

1) More complete case ascertainment
   - Texas example
   - Study in 2002

*Excluding non-live birth data can lead to an underestimation of prevalence estimates*

2) More accurate evaluation of prevention efforts
   - If non-live births are excluded, it can lead to underestimation of prevalence estimates and possible overestimation of success of prevention efforts.

3) Reduces potential bias in epidemiologic studies of birth defects
   - If there are exposures and/or events of interest associated with the decision to terminate a pregnancy or a stillbirth, excluding non-live births could bias findings.

4) Assess & monitor terminations over time
   - Cannot assume a consistent proportion of BD cases will result in terminations; thus, exclusion of elective terminations can underestimate prevalence.

*NBDPN Guidelines, 2012; Cragan and Khoury, 2000*

**Some Challenges of Using Non-Live Birth Data**

1) Classification/categories for non-live birth outcomes
   - Not knowing, or being able to provide, accurate birth outcome (i.e. stillbirth vs miscarriage vs termination)

2) Inflation of prevalence estimates
   - Certain BDs need a post-delivery confirmation or are poorly identified prenatally (e.g. certain congenital heart defects, chromosomal abnormalities)

3) Missing data for individual cases
   - Race/ethnicity and sex are often missing
   - Occurs most often for miscarriages and terminations in comparison to stillbirths

4) Missing BD cases among non-live births (incomplete ascertainment)
   - Fetuses with certain BDs are more likely to undergo elective terminations early on, so may not have any record of the terminations

*NBDPN Guidelines, 2012*
Addressing Challenges of Using Non-Live Birth Data

1) Classification/categories for non-live birth outcomes
   - Ideally categorizing cases as:
     - Stillbirths (i.e. fetal deaths)
     - Spontaneous abortion (i.e. miscarriages)
     - Elective terminations
     - Unknown/unspecified non-live births
   - Alternate option for state &/or program restrictions - "other pregnancy loss"
   - At minimum, report any non-live birth case
     - Unknown/unspecified non-live birth
   - NBDPN guidelines important for accurately estimating birth-defect prevalence

2) Inflation of prevalence estimates
   - Gold standard: using only cases with confirmed BD
     - Confirmed through postnatal records (e.g. pathology, autopsy, lab records) whenever needed & possible
   - Lack of postnatal confirmation
     - Develop consistent criteria reflecting certainty of prenatal findings (e.g. precision codes used)
     - Review of prenatal findings by consultants knowledgeable about specific birth defects (e.g. clinical geneticist, pediatric cardiologist, etc.)
   - NBDPN Guidelines Appendix 12.2

3) Missing data for individual cases
   - Various data sources
     - Vital records, multiple surveillance sources (healthcare clinics, administrative databases)
   - Limiting case ascertainment to non-live birth outcomes with low rates of missing data
     - Arizona fetal deaths and vital records fetal death certificates
   - Displaying data for presentation
     - Breakdown of count data by birth outcome
     - When calculating stratum-specific prevalence estimates, exclude cases with missing values
     - Texas example
Addressing Challenges of Using Non-Live Birth Data

5) Missing data for individual cases (continued)
   • Texas example
     • Table 6. Case breakdown by birth outcome per BD
     • Table 4. Stratum-specific prevalence estimates – exclude cases with missing data

Addressing Challenges of Using Non-Live Birth Data

4) Missing BD cases among non-live births (incomplete ascertainment)
   • Very difficult to assess or measure
   • Awareness of the BD cases that are likely to result in elective terminations or miscarriages is crucial
     • Abdominal wall defects can be diagnosed 15-18 weeks (can be detected earlier)
     • Screening between 11-13 weeks of pregnancy: some heart defects, NTDs, and chromosomal disorders
   • Further individual research through state reports, peer-reviewed articles, etc.
   • NBDPN guideline: include as many confirmed non-live birth cases as possible in order to avoid under-reporting

Gold Standard vs. Reality

• Limited permissions and/or ability to obtain non-live birth cases
• Difficult to predict the:
  • Amount of missing data (or missing cases)
  • Variations in birth outcomes (especially elective terminations)
• Consistency within program data collection
  • Strengthen individual state BD analysis
  • Explain changes in processes within write-ups as needed
• Report and assess available BD data
  • Include descriptive information when possible (i.e., proportions of birth outcomes)
  • Exclude cases with missing information for specific analysis (stratum-specific prevalence calculations, etc.)
THANK YOU!

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References


