Follow-Up of Metabolic Cases for the First Three Years of Life: Results from a Population-Based Multi-State Pilot Project

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Project Overview

- 3 year pilot, year 2 data
- 2005-2007 population-based birth cohort
- CA: metabolic centers reporting to NBS program
- IA, NY, UT: partnership birth defect surveillance with NBS, multiple sources (including metabolic centers)
- 19 conditions (TMS, core panel minus tyrosinemia)
Public health surveillance:

- Ongoing, systematic
- Collection, analysis, and interpretation of health data
- Essential to the planning, implementation, and evaluation of public health practice,
- Closely integrated with the timely dissemination of these data to those responsible for prevention and control.
DHHS definition of research (from 45 CFR 46.102):

“A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.”

- attempt to make comparisons or draw conclusions from the gathered data;
- attempt to reach for generalizable principles of historical or social development;
- seek underlying principles or laws of nature that have predictive value and can be applied to other circumstances for the purpose of controlling outcomes;
- create general explanations about all that has happened in the past; or predict the future.
Core functions of public health in NBS: assessment, policy development, assurance

<table>
<thead>
<tr>
<th>Uses of public health surveillance</th>
<th>Assessment: what is going on?</th>
<th>Assurance: are we doing things right?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnitude of problem</td>
<td>Prevalence (VLCAD), mortality (MCAD), morbidity, disability (GA1), cost, QoL</td>
<td>Rates of complication by race/ethnicity, SES, geography, rural/urban, insurance status</td>
</tr>
<tr>
<td>Health disparities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemics, clusters of adverse events</td>
<td>Deaths (MCAD), neurologic complications (GA1), developmental delays</td>
<td></td>
</tr>
<tr>
<td>Effectiveness of control measures</td>
<td>Variations in frequency and severity of outcomes over time</td>
<td></td>
</tr>
<tr>
<td>Changes in health practices</td>
<td>Screening flow (# screens), diagnostic tests</td>
<td></td>
</tr>
<tr>
<td>Stimulate research</td>
<td>Genotype and GE interactions, diagnosis, treatment, education</td>
<td></td>
</tr>
</tbody>
</table>
Why birth defects surveillance programs?

- **Population-based, nationwide, ongoing**
  - Present already in most US states (and many countries),
  - typically population-based,
  - under the public health authority.
  - Also, integrated into health department and national network (NBDPN)

- **Data sources**
  - Many connections already made (hospitals, clinics, labs, administrative databases).
  - Will need to integrate NBS program, metabolic clinics, possibly additional labs.
Why birth surveillance (cont.)?

- **Data domains**
  - Already collecting usually extensive demographic and medical record information.
  - Will need to define specific elements for diagnosis and outcomes (longitudinal)

- **Data quality**
  - Several programs (not all) with active case ascertainment,
  - trained abstractors,
  - case tracking, clinical case review, and quality assessment procedures in place.
4 States for Pilot Project

- California, Iowa, New York, Utah
- Number of births at least 100,000 per state over pilot period
- Legal authority to collect newborn screening data
- Linkage in place with Vital Records
Year 1 spent defining Data Elements: General Categories Collected on Confirmed Cases

- Demographics
- Basic diagnostic information
- Morbidity/mortality
- Service encounters
- Treatments
- Hospitalizations
- Developmental assessments
“Confirmed Cases”

- As designated by each state program
  - An project to define cases for public health surveillance purposes is ongoing

- Clinical geneticists reviewed the cases of VLCAD and 3MCC
  - Devised standard case definition template
  - Evaluated cases status
  - Resulted in reclassification of cases, particularly for 3MCC
Pilot study of metabolic surveillance: 4 states, 1.35 million births, 261 cases

**excluding New York City**
## Confirmed cases of the 19 selected conditions from Newborn Screening, by type

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Cases</th>
<th>%</th>
<th>Rate/100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TOTAL</strong></td>
<td>261</td>
<td></td>
<td>19.4</td>
</tr>
<tr>
<td><strong>Organic Acid Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVA</td>
<td>4</td>
<td>1.5</td>
<td>0.3</td>
</tr>
<tr>
<td>GA1</td>
<td>11</td>
<td>4.2</td>
<td>0.8</td>
</tr>
<tr>
<td>MUT</td>
<td>15</td>
<td>5.7</td>
<td>1.1</td>
</tr>
<tr>
<td>3MCC</td>
<td>42</td>
<td>16.1</td>
<td>3.1</td>
</tr>
<tr>
<td>MMA</td>
<td>4</td>
<td>1.5</td>
<td>0.3</td>
</tr>
<tr>
<td>PROP</td>
<td>2</td>
<td>0.8</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Fatty Acid Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCAD</td>
<td>80</td>
<td>30.7</td>
<td>6.0</td>
</tr>
<tr>
<td>VLCAD</td>
<td>19</td>
<td>7.3</td>
<td>1.4</td>
</tr>
<tr>
<td>LCHAD</td>
<td>1</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>CUD</td>
<td>12</td>
<td>4.6</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Amino Acid Disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PKU</td>
<td>58</td>
<td>22.2</td>
<td>4.3</td>
</tr>
<tr>
<td>MSUD</td>
<td>7</td>
<td>2.7</td>
<td>0.5</td>
</tr>
<tr>
<td>CIT</td>
<td>2</td>
<td>0.8</td>
<td>0.1</td>
</tr>
<tr>
<td>ASA</td>
<td>4</td>
<td>1.5</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Birth prevalence compared to other studies

*CA, WI, MA, NC. Includes Significant Hyperphe.
Follow-up Status Variable

- Active
- Lost-to-follow-up
- Moved out of catchment area
- Parents refused follow-up
- Treatment deemed not necessary by clinician
- Died
- Unknown
What constitutes “active” status?

- “Taken for grantedness” of what is meant by “active” and “lost”
- The variable is from an administrative perspective versus a “censored” status from an epidemiologic perspective
  - How do we operationalize “follow-up status”?
- At what point is status measured?
  - At birthday
- Does it reflect what happened during the year?
- What about states that can link to hospital discharge data?
  - Child is still living in catchment area versus child is in care at metabolic center
Follow-Up Variable defined:

- **Active Status:**
  - Seen in genetics clinic at least once during the year
  - Does not include hospitalizations without genetics clinic visit during the year

- **Death, move, refuse, “treatment not needed” status reflected even if there was a clinic visit**

- **No clinic visit during year = lost to follow-up**
  - Grace period of a year
Where did they go?
Percent change from birth to end of Year 3.
"Active" cases compared to "Lost to follow up":
Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>% of Active</th>
<th>% of Lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCAD</td>
<td>27%</td>
<td>41%</td>
</tr>
<tr>
<td>3MCC</td>
<td>4%</td>
<td>32%</td>
</tr>
<tr>
<td>MMA</td>
<td>1%</td>
<td>6%</td>
</tr>
<tr>
<td>VLCAD</td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>CUD</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>IVA</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>GA1</td>
<td>3%</td>
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<tr>
<td>PKU</td>
<td>28%</td>
<td>3%</td>
</tr>
</tbody>
</table>
Maternal Characteristics of All Cases versus Lost to Follow-Up Cases

- % Total
- % Lost FU

1 mil +:
- Total: 64%
- Lost FU: 49%

Urban:
- Total: 43%
- Lost FU: 29%

<= H.S.:
- Total: 56%
- Lost FU: 48%

White:
- Total: 56%
- Lost FU: 59%

Medicaid:
- Total: 52%
- Lost FU: 38%

< 25 yrs old:
- Total: 47%
- Lost FU: 32%

Primigravid:
- Total: 21%
- Lost FU: 11%
Most likely to be Lost-to Follow-up:

- MCADD, 3MCC
- Mothers live in metro areas, 1 million pop +
- Medicaid
- <= High School Education
- < 25 years of age
- Primigravid
In Conclusion:

- A four-state pilot project compiled three years of follow-up data on 261 newborns diagnosed with metabolic conditions.
- Follow-up status needs to be carefully defined across states.
- Recommend using individual variables to compute follow-up status:
  - Death
  - Move
  - Clinical encounters
  - Hospitalizations
  - Etc.
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.