California Newborn Screening Program

Follow-up Status
During First Five Years of Life for Select Primary RUSP Disorders

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Background: RUSP

- Disorders on the Recommended Uniform Screening Panel (RUSP) have had to meet the criteria that a treatment exists and through early diagnosis, the treatment can halt or slow disease progression.

- Assumes that specialty care follow-up centers provide disease treatment and management services that are accessible to families in the early years of life.
Background:
California Newborn Screening Program (NBS)

• 1980:
  • California NBS Program began.
  • ~500,000 newborns/year.

• 2005:
  • MS/MS screening started.
  • Electronic data collection started (SIS).
  • Long-Term Follow-up (LTFU) data system using Annual Patient Summary (APS) reports started.
California Newborn Screening Program
Long-Term Follow Up Approach

Annual Patient Summary (APS) Reports:
• Collected for program evaluation purposes
• Data provided by state-contracted specialty care follow-up centers
• Once a year assessment of status of the child through fifth birthday
• Reports document whether child is still in active care
• Clinical management strategies
• Clinical outcomes
California Newborn Screening Program

Follow Up Model

Clinical case coordinators refer screen positive newborns to state-contracted specialty care follow-up centers

Follow-up centers responsible

Short Term Follow-Up: documentation of the services provided, health status of newborn & outcomes of confirmatory testing

No Disorder

Confirmed Disorder

Initiation of Long Term Follow-Up via Annual Patient Summary Data Collection (through age 5)
Study Questions

• What percent of children with disorders remain in care between the ages of one and five years old?
• What percent become lost to follow-up?
• What are the characteristics of lost to follow-up?
• What percent died?

Consensus public health questions based on:
(1) Hinton et al paper: What questions should newborn screening long term follow-up be able to answer…” Genetics in Medicine, Vol 13, No 10, Oct 2011
(2) Priority questions determined by Newborn Screening Translational Research Network
Methods

• 19 primary RUSP metabolic disorders
• 448 patients identified between 07/07/2005 through 12/31/2009
• Five years of follow-up data
• For data analysis including:
  • Newborn screening program routine data including metabolic disorder diagnosis, maternal race-ethnicity, and maternal age
  • APS data including follow-up status and child age at APS report
  • Birth certificate data including maternal education, and payment for delivery
Methods

• Follow-up categories on APS report:
  • Active Care: active, transferred to another center, followed up but no in-person visit
  • Lost to Follow-Up: lost to follow-up, refused follow-up
  • Other: child died, moved out of state, treatment deemed not necessary

• Assign follow-up status to missed APS reports
  • Assign ‘Active’ to a missed APS report if it is followed by an ‘Active’ APS in later years.
  • Assign ‘lost to follow-up’ if there are no more subsequent APS reports with patient visit.
  • Received 1,590 APS reports for the 448 patients over five-year follow-up.
Cumulative % of initial cohort remaining in active care by follow-up year (n=488)

Year of follow-up

- 1 year: 83% (374/448)
- 2 years: 73% (329/448)
- 3 years: 67% (300/448)
- 4 years: 61% (274/448)
- 5 years: 56% (250/448)
Comparison of one-year and five-year follow-up

<table>
<thead>
<tr>
<th>Category</th>
<th>One year</th>
<th>Five years</th>
</tr>
</thead>
<tbody>
<tr>
<td>In active care</td>
<td>83.5%</td>
<td>55.8%</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>7.8%</td>
<td>26.1%</td>
</tr>
<tr>
<td>Patient died</td>
<td>2.4%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Other</td>
<td>6.3%</td>
<td>14.8%</td>
</tr>
</tbody>
</table>

(n=374) (n=250) (n=35) (n=117) (n=11) (n=15) (N=28) (N=66)
Percent of children remaining in active care in the following year:

- Year 1: 83% (374/448)
- Year 2: 88% (329/374)
- Year 3: 91% (300/329)
- Year 4: 91% (274/300)
- Year 5: 91% (250/274)
Reported reasons for discontinuation of care by follow-up year

<table>
<thead>
<tr>
<th></th>
<th>Lost to follow-up</th>
<th>Refused follow up</th>
<th>Treatment deemed not necessary</th>
<th>Move-out-of state</th>
<th>Child died</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1 (n=448)</td>
<td>5.6</td>
<td>2.2</td>
<td>2.9</td>
<td>3.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Year 2 (n=374)</td>
<td>5.6</td>
<td>1.6</td>
<td>1.6</td>
<td>2.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Year 3 (n=329)</td>
<td>5.2</td>
<td>0.3</td>
<td>0.9</td>
<td>1.8</td>
<td>0.6</td>
</tr>
<tr>
<td>Year 4 (n=300)</td>
<td>6.0</td>
<td>0.3</td>
<td>0.7</td>
<td>1.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Year 5 (n=274)</td>
<td>5.5</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>0</td>
</tr>
</tbody>
</table>
## Comparison of one-year and five-year active follow-up status by select disorder

<table>
<thead>
<tr>
<th>Disorder</th>
<th>One Year</th>
<th>Five Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCAD Deficiency</td>
<td>88.7%</td>
<td>90.0%</td>
</tr>
<tr>
<td>3MCC Deficiency</td>
<td>80.3%</td>
<td>98.3%</td>
</tr>
<tr>
<td>PKU (n=60)</td>
<td>71.1%</td>
<td>71.0%</td>
</tr>
<tr>
<td>VLCAD Deficiency</td>
<td>50.0%</td>
<td>62.5%</td>
</tr>
<tr>
<td>MMA (n=32)</td>
<td>62.5%</td>
<td>67.9%</td>
</tr>
<tr>
<td>CTD/CUD (n=31)</td>
<td>31.3%</td>
<td>38.7%</td>
</tr>
<tr>
<td>Galactosemia</td>
<td>89.3%</td>
<td>85.2%</td>
</tr>
<tr>
<td>GA1 (n=27)</td>
<td>81.3%</td>
<td>81.3%</td>
</tr>
<tr>
<td>MSUD (n=16)</td>
<td>62.5%</td>
<td>66.7%</td>
</tr>
<tr>
<td>IVA (n=16)</td>
<td>50.0%</td>
<td>93.8%</td>
</tr>
</tbody>
</table>
Percentage of missed APS reports among active patients in the following year:

- Year 1: 16.5% (74/448)
- Year 2: 9.9% (37/374)
- Year 3: 7.9% (26/329)
- Year 4: 2.7% (8/300)
- Year 5: 1.8% (5/274)
Maternal race-ethnicity for initial cohort and follow-up status

- **In active care (n=250)**: 34.0% White non-Hispanic, 33.2% Hispanic, 19.6% Black, 12.8% Asian, 12.8% Other/Multiple, 6.8% Unknown
- **Lost to follow-up (n=117)**: 44.4% White non-Hispanic, 29.9% Hispanic, 6.0% Black, 2.6% Asian, 6.8% Other/Multiple, 6.8% Unknown
- **Patients moved (n=39)**: 46.2% White non-Hispanic, 20.5% Hispanic, 12.8% Black, 15.4% Asian, 2.6% Other/Multiple, 12.8% Unknown
- **Patients died (n=15)**: 33.3% White non-Hispanic, 13.3% Hispanic, 0% Black, 0% Asian, 13.3% Other/Multiple, 0% Unknown
- **Treatment deemed not necessary (n=27)**: 22.2% White non-Hispanic, 29.6% Hispanic, 18.5% Black, 22.2% Other/Multiple, 7.4% Unknown
Maternal education (in years) for initial cohort and follow-up status

<table>
<thead>
<tr>
<th>Status</th>
<th>&lt;12</th>
<th>12</th>
<th>&gt;12</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>In active care (n=250)</td>
<td>26.8</td>
<td>20.4</td>
<td>51.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Lost to follow-up (n=117)</td>
<td>26.5</td>
<td>21.4</td>
<td>44.4</td>
<td>7.7</td>
</tr>
<tr>
<td>Patients moved (n=39)</td>
<td>28.2</td>
<td>15.4</td>
<td>7.7</td>
<td>0</td>
</tr>
<tr>
<td>Patients died (n=15)</td>
<td>46.7</td>
<td>26.7</td>
<td>26.7</td>
<td>0</td>
</tr>
<tr>
<td>Treatment deemed not necessary (n=27)</td>
<td>22.2</td>
<td>11.1</td>
<td>11.1</td>
<td>11.1</td>
</tr>
</tbody>
</table>
Health care coverage for delivery for initial cohort and follow-up status

- In active care (n=250):
  - MediCal: 42.4%
  - Other government: 52.4%
  - Private: 2.4%
  - Self: 0.8%
  - Other: 2.0%
  - Unknown: 0%

- Lost to follow-up (n=117):
  - MediCal: 50.4%
  - Other government: 40.2%
  - Private: 1.7%
  - Self: 5.1%
  - Other: 2.6%
  - Unknown: 0%

- Patients moved (n=39):
  - MediCal: 41.0%
  - Other government: 48.7%
  - Private: 7.7%
  - Self: 0%
  - Other: 2.6%
  - Unknown: 0%

- Patients died (n=15):
  - MediCal: 60%
  - Other government: 26.7%
  - Private: 6.7%
  - Self: 0%
  - Other: 0%
  - Unknown: 0%

- Treatment deemed not necessary (n=27):
  - MediCal: 40.7%
  - Other government: 59.3%
  - Private: 0%
  - Self: 0%
  - Other: 0%
  - Unknown: 0%
Summary: Active Care

- Of 448 newborns, 56% were in active care by the end of the fifth year of life.

- Certain disorders were associated with a higher percent staying in active care through age five: 90% of PKU, 68% for Galactosemia, 67% for GA1, and 63% for MSUD.

- Disorders associated with lower percent of active care status through age five: 44% for 3MCC, 39% for CTD/CUD and 31% for MMA.

- Most children (70%) who transferred care to another center stayed in active care in the following year.
Summary: Lost to Follow-Up

• More cases were lost to follow-up in the first year of life (8%) compared to subsequent years (5%-7%).
• Over the course of five years, 26% of children were lost to follow-up and 3.3% died.
• Out of a total of 15 deaths, 11 (73%) occurred in the first year of life.
• Two thirds (67%) of lost to follow-ups did not report any health problem in the APS of previous year.
Summary: Maternal Characteristics

• Compared to the Active Care group:
  • Hispanics were more likely to be Lost to Follow-Up.
  • Mothers with more than 12 years of education were less likely to be Lost to Follow-Up.
  • Mothers covered by private insurance were less likely to be Lost to Follow-Up.
Next Steps

• Further exploration of patients that became lost to follow-up
  • Distance to clinic (GIS mapping)
• Detailed analysis by specific disorders
  • Symptoms and developmental status
  • Treatments & services provided
• Affordable Care Act impact on service utilization
Conclusion

• Limitations:
  • Missing data
  • Doesn’t capture highly detailed clinical information

• Challenges:
  • Cost of data collection
  • Late-onset disorders
  • Data capture from multiple specialty care centers
Acknowledgement

• Special thanks to the team members at our California state-contracted metabolic centers who provide long term follow-up data for our newborn screening program!