California Newborn Screening Program
Long-Term Follow Up Data Collection

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Long-Term Follow Up for Newborn Screening

What is it?

• Systematic evaluation to determine if newborn screening is meeting its goal

Why do it?

• Assurance that condition-specific treatment & age-appropriate preventive care is available for individuals identified with a condition included in newborn screening *

California Newborn Screening Program
Development of Long-Term Follow Up System

• 2002: A framework for LTFU was created as part of the HRSA funded pilot study to examine the efficacy of MS/MS screening

• 2005: Implementation of a LTFU data system developed as part of a web-based Screening Information System (SIS)

• SIS supports all aspects of lab results reporting, mailer creation, patient referral tracking & coordination with specialty care follow-up centers

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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
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
- State pays for submission of APS reports using SIS
- Reports document whether child is still in active care
- Clinical management strategies
- Clinical outcomes

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Implementation of Long-Term Follow Up System Since 2005

- 2005: Metabolic LTFU
- 2007: Cystic Fibrosis LTFU
- 2011: Endocrine LTFU
- 2011: Hemoglobin LTFU
- 2013: SCID LTFU
- 2016: Coming: ALD LTFU
California Newborn Screening Program

10 Years of LTFU Data on Metabolic Disorders*

- Newborns Screened: 5,182,386
- Diagnosed Cases: 1,505
- Total Annual Patient Summaries: 5,208

* As of October 2015
## 10-Year Count of Annual Patient Summary Reports for Metabolic Disorders

<table>
<thead>
<tr>
<th>Disorder Name</th>
<th>Age of Child (Years)</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC Deficiency)</td>
<td>109 94 66 47 36 352</td>
<td></td>
</tr>
<tr>
<td>Biotinidase Deficiency Partial (BD)</td>
<td>63 57 37 27 19 203</td>
<td></td>
</tr>
<tr>
<td>Biotinidase Deficiency Profound (BD)</td>
<td>44 32 29 22 18 145</td>
<td></td>
</tr>
<tr>
<td>Carnitine Transporter Deficiency (CTD)/Carnitine Uptake Defect (CUD)</td>
<td>63 52 41 29 19 204</td>
<td></td>
</tr>
<tr>
<td>Duarte Galactosemia (D/G)</td>
<td>109 108 54 46 37 354</td>
<td></td>
</tr>
<tr>
<td>Galactosemia, classical</td>
<td>26 25 29 23 25 128</td>
<td></td>
</tr>
<tr>
<td>Glutaric Acidemia type I (GA1)</td>
<td>45 40 35 28 23 171</td>
<td></td>
</tr>
<tr>
<td>Hyperphenylalaninemia, benign</td>
<td>68 60 48 43 33 252</td>
<td></td>
</tr>
<tr>
<td>Hyperphenylalaninemia, variant</td>
<td>64 60 55 54 46 279</td>
<td></td>
</tr>
<tr>
<td>Isovaleric Acidemia (IVA)</td>
<td>35 26 23 20 15 119</td>
<td></td>
</tr>
<tr>
<td>Long Chain Hydroxy Acyl-CoA Dehydrogenase Deficiency (LCHAD deficiency)</td>
<td>8  8  6  7  5  34</td>
<td></td>
</tr>
<tr>
<td>Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD Deficiency)</td>
<td>182 173 136 112 86 689</td>
<td></td>
</tr>
<tr>
<td>Methylmalonic Acidemia mut 0 (MMA)</td>
<td>18  20 18  14 10  80</td>
<td></td>
</tr>
<tr>
<td>Methylmalonic Acidemia mut- (MMA)</td>
<td>22  19 11  8  6  66</td>
<td></td>
</tr>
<tr>
<td>Methylmalonic Acidemia, Cbl C, D, F (MMA)</td>
<td>36  36 33  31 28 164</td>
<td></td>
</tr>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>140 123 112 113 112 600</td>
<td></td>
</tr>
<tr>
<td>Short Chain Acyl-CoA Dehydrogenase Deficiency (SCAD Deficiency)</td>
<td>150 122 88  61 44 465</td>
<td></td>
</tr>
<tr>
<td>Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD Deficiency)</td>
<td>52  45 36  29 28 190</td>
<td></td>
</tr>
<tr>
<td><strong>All</strong></td>
<td><strong>1463 1277 986 814 668 5208</strong></td>
<td></td>
</tr>
</tbody>
</table>
How Has Long-Term Follow Up Data Been Used?

Collaborative Studies:

- MS/MS Study, Hinton C et al, 4-State Collaborative Study (CDC)
- VLCADD Study, Merritt JL et al. (WSRGC)
- SCADD Study, Galant N, et al. (UCLA)
- 3MCC Study, Lam C, et al. (UCLA)
- CF genotype-phenotype studies, Salinas D, et al (CHLA)
- MS/MS, NIH-funded U19 Study (UCSF)
Long-Term Follow Up Data Uses

What % of children with diagnosed disorders...

• are in care through age five?
• become lost to follow-up?
• have disorder-related complications?
• died and for what reasons?
• have developmental delay?
• have high rates of ER visits & in-patient hospitalizations?
• have more frequent visits to the specialty care follow-up centers?
What percent of children with RUSP Primary MSMS disorders remained in active care between the ages of one and five years old?

- 10 years of MS/MS screening: 2 five year cohorts
- 2,514,004 newborns screened between 07/07/2005 to 07/06/2015.
- 448 RUSP Primary Metabolic Disorders diagnosed
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)
Reported reasons for discontinuation of care by follow-up year

<table>
<thead>
<tr>
<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>
</tr>
<tr>
<td>Year 2 (n=374)</td>
<td>5.6</td>
<td>1.6</td>
<td>1.6</td>
<td>2.9</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>
</tr>
<tr>
<td>Year 4 (n=300)</td>
<td>6.0</td>
<td>0.3</td>
<td>0.7</td>
<td>1.3</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>
</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>53.9</td>
</tr>
<tr>
<td>3MC Deficiency</td>
<td>98.3</td>
<td>44.3</td>
</tr>
<tr>
<td>PKU (n=60)</td>
<td>90.0</td>
<td>62.5</td>
</tr>
<tr>
<td>VLCAD Deficiency</td>
<td>71.1</td>
<td>31.3</td>
</tr>
<tr>
<td>MMA (n=32)</td>
<td>50.0</td>
<td>38.7</td>
</tr>
<tr>
<td>CTD/CUD (n=31)</td>
<td>71.0</td>
<td>67.9</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>66.7</td>
</tr>
<tr>
<td>MSUD (n=16)</td>
<td>81.3</td>
<td>62.5</td>
</tr>
<tr>
<td>IVA (n=16)</td>
<td>93.8</td>
<td>50.0</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)
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

• LTFU provides data on impact of newborn screening programs
• A valuable resource for clinical collaborations and program evaluation
• 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
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