Quality Improvement of Follow Up Strategies Using Region 4 Post Analytical Tools to Evaluate VLCADD and CACT/CPTII Newborn Screening Results

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What’s the problem?

Time period for this project: 1/1/12 – 3/6/14
2 years and 2 months

- 122 positive screens for VLCADD
- 125 positive screens for CACT/CPTII

Outcomes of those positive screens:
- VLCADD: 9 (PPV 7.3%)
- VLCADD carriers: 14
- CACT/CPTII: 0
Large numbers of false positive results and the associated follow up cause the following for NBS staff, parents and other healthcare providers:
Time analysis

**VLCADD**
- Average amount of time follow up spends on the initial report of the abnormal results per case: 38.5 minutes
- Min: 9
- Max: 120

**CACT/CPT2**
- Average amount of time follow up spends on the initial report of the abnormal results per case: 71.9 minutes
- Min: 26
- Max: 180

These figures are based on a subset of the abnormal results and not the entire data set.
### Time Analysis

- **1.1 working days per month**
- **Does not include:**
  - repeat contacts to pediatrician
  - time spent discussing case with geneticists
  - coordinating referral to metabolic clinic
  - the time spent by primary care and neonatology to find, assess, and test their kids

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Average time per case</th>
<th>number of positive screens</th>
<th>Average total time spent</th>
</tr>
</thead>
<tbody>
<tr>
<td>VLCADD</td>
<td>38.5 minutes</td>
<td>122</td>
<td>78.3 hours</td>
</tr>
<tr>
<td>CACT/CPTII</td>
<td>71.9 minutes</td>
<td>125</td>
<td>149.8 hours</td>
</tr>
</tbody>
</table>
What are we doing currently?

**VLCADD**
- Single analyte algorithm: C14:1
- Follow up team uses R4S single condition post analytical tool
- Categorize results:
  - Low risk – repeat NBS
  - Medium risk – biochemical testing
  - High risk – biochemical and molecular testing, possible immediate referral to metabolic clinic

**CACT/CPTII**
- Co-primary algorithm: C16 and C18:1

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**Score Interpretation Guidelines**

- Score is $\geq 110$
  Condition is very likely VLCAD.
- Score is $50 \leq \text{Score} < 110$
  Condition is likely VLCAD.
- Score is $15 \leq \text{Score} < 50$
  Condition is possibly VLCAD.
- Score is $\text{Score} < 15$
  Profile is not informative for VLCAD.
Follow Up Recommendations

VLCADD
• 43 diagnostic testing
• 77 repeat NBS

CACT/CPT2
• 45 diagnostic testing
• 80 repeat NBS

Reminder of the outcomes:
VLCADD: 9
CACT/CPT2: 0
How can we make it better?

- R4S has additional tools: dual scatter plot
- For this analysis we used two of these tools:
  - VLCADD vs. VLCADD heterozygote
  - CACT/CPTII vs. high C16
How can we make it better?

- Could using these tools help us determine which kids are more likely to be false positives and which kids are more likely to be affected?

- Could we use this information to reduce time spent in follow up?

- Could we reduce our false positive rate from the state lab?
VLCADD vs VLCADD Het.

Condition is VLCADD Heterozygote

Cannot differentiate

Not consistent with either condition
VLCADD vs VLCADD het.

- It is reasonable to rule out all children who fall in the “VLCADD heterozygote” or the “not either condition” quadrants.

- Abnormal NBS reports and diagnostic testing are still appropriate for children who fall in the indeterminate or affected quadrants.
The combined scores are not sufficient to exclude CACT/CPT-II.

Not consistent with either condition.

Condition is CACT/CPT-II.

False Positives
The combined scores are not sufficient to exclude CACT/CPT-II.

This child was diagnosed with VLCADD and labeled as affected by VLCADD dual scatter plot.

Condition is CACT/CPT-II

Not consistent with either condition.

False Positives
• Confidence in making big changes?
  – No diagnosed cases in this group of children.

• Can we stop calling these positive screens?
• Should we take a less cold turkey approach and advise assessment then close if normal?
Why is this important?

• False Positive screens are a problem
  – Testing algorithms are stretched
  – Follow up algorithms are stretched
  – Providers are stretched
  – New conditions are coming: SCID, Pompe pilot, CCHD

• Resources are limited, demands increasing = need process improvement!

Dual Scatter plot tools may be our opportunity to reduce workload and be highly effective
• We will continue to evaluate these tools
• Partner with the state lab in utilizing tools
• Consider partnering with other states to evaluate tools
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