Normalization of Laboratory MS/MS Cutoffs using CDC NSQAP Quality Control Materials

Mary Seeterlin,1 Victor De Jesus,2
Christopher Haynes,2 Mark Morrissey,3
Adrienne Manning,4 Konstantinos Petritis,5
Sonal Bhakta,5 Patrice Held6

1. Michigan Department of Health & Human Services, Lansing, Michigan
2. US Centers for Disease Control and Prevention, Atlanta, Georgia
3. Wadsworth Center/New York State Department of Health, Albany, New York
4. Dr. Katherine A. Kelley State Public Health Laboratory, Connecticut Department of Public Health, Rocky Hill, Connecticut
5. Arizona Department of Health Services, Office of Newborn Screening, Phoenix, Arizona
6. Wisconsin State Laboratory of Hygiene, Madison, Wisconsin
Succinylacetone (SA)

TP TYR1

Reference Lab = 35.2 µmol/L

MI Neobase = 8.76 µmol/L
Goal:
- Accurately compare analyte cutoff values

Problem:
- Differences in testing methodologies
  - Derivatized vs. non-derivatized
  - Extraction techniques
  - Instrumentation
  - Internal Standards
  - Calibration Techniques
  - Standard Calibration Materials
Goal
- Accurately compare analyte cutoff values
- Accurately compare analyte concentrations for positive cases

Problem
- Differences in testing methodologies
  - Derivatized vs. non-derivatized
  - Extraction technique
  - Instrumentation
  - Internal Standards
  - Calibration Techniques
  - Standard Calibration Materials

Solution
- Normalization using method comparison experiment
  - Laboratories test the NSQAP QC Materials
  - Linear regression equations generated
  - Normalized cutoffs calculated
Method Comparison Analysis

- 332 Normal Patient samples
- 11 PT Samples
- True Positive samples
- High and Low Kit Controls

Methionine (Met)

- NeoGram ($\mu$mol/L)
- NeoBase ($\mu$mol/L)

Graph showing the comparison of NeoGram and NeoBase with Methionine (Met) concentration. The graph displays data points and trends, indicating comparisons with CDC NSQAP QC Materials and identifying specific sample sets.
Method Comparison Analysis

Methionine (Met)

<table>
<thead>
<tr>
<th>Slope</th>
<th>0.731</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.743</td>
</tr>
<tr>
<td>R</td>
<td>0.992</td>
</tr>
</tbody>
</table>

NeoBase (μmol/L) vs. NeoGram (μmol/L)

Averaged CDC NSQAP QC Materials
Method Comparison - SUAC

SUAC (μmol/L) CDC vs. SUAC (μmol/L) NBS Lab

- Points: 1421, 1422, 1423, 1424

Graph shows a linear relationship between SUAC values from CDC and NBS Lab.
Method Comparison - SUAC

CDC Equivalent Cutoff = Normalized Cutoff

1.8

1.4
Method Comparison - SUAC
Method Comparison - SUAC

SUAC (μmol/L) CDC

SUAC (μmol/L)

1.4  3.0  5.4
Collaborative

Methods:
- Derivatized
- Non-Derivatized
- Laboratory Developed Test
- Kit Method

Analytes:
- Arginine (Arg)
- Citrulline (Cit)
- Phenylalanine (Phe)
- Succinylacetone (SUAC)
- Free carnitine (C0)
- Octanoylcarnitine (C8)
- Malonylcarnitine (C3DC)
- Glutaryl carnitine (C5DC)
- Myristoylcarnitine (C14)
Method Comparison - Cit

Cit (μmol/L) Lab B

Cit (μmol/L) NBS Lab A

91

50
Conclusions:

Normalization Technique Using CDC NSQAP QC Materials + Method Comparison

• Provides normalized cutoff values
• Allows accurate comparison of cutoffs regardless of testing methodology.
• Provides a foundation for comparison and discussion.
Hypothetical Normalized Succinylacetone (SUAC) Cutoffs by Method
Hypothetical **Normalized** Succinylacetone (SUAC) Cutoffs by Method

95% UL

Mean

95% LL

- Deriv. MS/MS non-Kit
- Non-deriv. MS/MS non-Kit
- Deriv. MS/MS PerkinElmer NeoGran Kit
- Non-deriv. MS/MS PerkinElmer NeoBase Kit
- Deriv. MS/MS Chromsystems MassChrom Kit
- Non-deriv. MS/MS Chromsystems MassChrom Screening Kit
- MS Screening Neo (MS-Neo) Siemens
- Other
Acknowledgements:

Victor De Jesus – CDC NSQAP
Christopher Haynes – CDC NSQAP
Mark Morrissey – New York
Adrienne Manning – Connecticut
Konstantinos Petritis – Arizona
Sonal Bhakta – Arizona
Patrice Held – Wisconsin
MI NBS Team – Eleanor Stanley