Joint Committee for Traceability in Laboratory Medicine

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Analytic Bias

• Bias directly affects test values
• Small analytic changes can produce major shifts in frequency distributions of clinical test values
Daily Plot of Assay Control

+2SD ____________________________

-2SD ____________________________
PSA - 0.7 SD Shift

Z Values (Standard Deviations)

+0.7 SD

9.7%
2.3%
Specimen K-18 - PSA

Value

Frequency

Axysym
Access
"ACS 180 2
Centaur
Dim HM
IMX
ACS 180
Tandem E
Specimen K-19 - PSA

Value

Frequency

AxSYM
Access
Dim HM
Immuno-1
IMX
ACS 180 2
Centaur
Elecsys
Case Studies - Mayo

• Starting Point - Critical Analytes
  – Cholesterol, Triglycerides, HDL, LDL
  – Glycated Hemoglobin
  – Creatine Kinase, CK MB and Troponin
  – Prostatic Specific Antigen (PSA)
PSA Reference Range

Age (years)

ng/mL

False -

False +

PSA Reference Range
Effect of Positive Bias on PSA

- Number > age limit per 1000 Tested
- Bias
- % Increase from Expected

- 0%: 76
- 5%: 86, 13%
- 10%: 95, 25%
- 15%: 105, 38%
Effect of Low End Bias on PSA

Reoccurrences >0.2 ng/mL per 1000 post-radical men

% Increase from Expected

0% 50% 100% 150% 200% 250% 300% 350% 400% 450% 500%

0.00 0.05 0.10 0.15 0.20

Bias (ng/mL)

0 50 100 150 200 250 300 350 400 450 500

73 136 191 233 409

0% 86% 162% 219% 460%
PSA - Cost Comparison

Average charge at Mayo of prostate biopsy: $2,710

Charges for prostate bx/1000 lives, age 60-74, w/out age adjusted ref range: $406,500

Charges for prostate bx/1000 lives, age 60-74, with age adjusted ref range: $243,900

Total reduction in prostate bx charges/1000 lives with age adjusted reference range: $162,600
Preoperative Serum Prostate-specific Antigen (PSA) Below 10 µg/L Predicts Neither the Presence of Prostate Cancer Nor the Rate of Postoperative PSA Failure

Thomas A. Stamey

Stanford University, Department of Urology S-287, Stanford University School of Medicine, Stanford, CA
PSA Blinded Specimen

If Precision and Accuracy Improved

Abnormal

Current MHS Precision and Accuracy

43.0%

4.3%
Figure 1

Mayo method comparison prior to assay change

\[ y = 0.9717x - 0.0975 \]

\[ R^2 = 0.9941 \]
Figure 2

Trending of PSA Medians by Month

Median PSA, ng/mL

Months (Jan. 00 - Aug. 03)
Figure 3
Panel A

PSA WHO 96/670 at 4 ug/L

<table>
<thead>
<tr>
<th>Diluent</th>
<th>ACCESS</th>
<th>CENTAUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1% BSA</td>
<td>5.18</td>
<td>3.96</td>
</tr>
<tr>
<td>2% HSA</td>
<td>5.38</td>
<td>4.16</td>
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<tr>
<td>5% HSA</td>
<td>5.41</td>
<td>4.26</td>
</tr>
<tr>
<td>MultiDil 2</td>
<td>3.88</td>
<td>3.81</td>
</tr>
<tr>
<td>Tandem-R Zero</td>
<td>5.32</td>
<td>4.41</td>
</tr>
<tr>
<td>Synthetic Matrix</td>
<td>5.14</td>
<td>3.60</td>
</tr>
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</table>
Figure 3
Panel B

PSA WHO 96/670 at 10 μg/L

<table>
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<tr>
<td>1% BSA</td>
<td>12.5</td>
<td>9.80</td>
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<tr>
<td>2% HSA</td>
<td>12.5</td>
<td>9.80</td>
</tr>
<tr>
<td>5% HSA</td>
<td>11.9</td>
<td>8.60</td>
</tr>
<tr>
<td>MultiDil 2</td>
<td>9.00</td>
<td>8.80</td>
</tr>
<tr>
<td>Tandem-R Zero</td>
<td>13.0</td>
<td>10.4</td>
</tr>
<tr>
<td>Synthetic Matrix</td>
<td>12.8</td>
<td>8.50</td>
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</table>
Figure 3
Panel C

PSA WHO 96/670 at 80 µg/L

<table>
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<th>Diluent</th>
<th>ACCESS</th>
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<tbody>
<tr>
<td>1% BSA</td>
<td>94.5</td>
<td>86.5</td>
</tr>
<tr>
<td>2% HSA</td>
<td>94.3</td>
<td>88.4</td>
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<tr>
<td>5% HSA</td>
<td>97.0</td>
<td>86.0</td>
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<tr>
<td>MultiDil 2</td>
<td>71.9</td>
<td>76.5</td>
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<tr>
<td>Tandem-R Zero</td>
<td>92.7</td>
<td>84.1</td>
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<tr>
<td>Synthetic Matrix</td>
<td>92.2</td>
<td>69.0</td>
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</tbody>
</table>
Figure 4

Panel A

\[ y = 0.8901x - 0.0057 \]
\[ r = 0.9989 \]
Figure 4

Panel B

\[ y = 0.9253x + 0.3289 \]
\[ r = 0.9983 \]
Figure 4

Panel C

\[ y = 0.8947x + 0.2946 \]

\[ r = 0.9991 \]
Figure 4

Panel D

y = 0.8395x + 0.3581
r = 0.9985
Wisdom

“Have we thought enough of wisdom, which moves knowledge and makes it useful?”

William J. Mayo, 1938