Impact of Calibration Error and Measurement Uncertainty on Medical Decisions and Patient Care

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Metrological Traceability
Outline of Presentation

- Role of Lab Tests in Medical Decisions
- Integrated Health System Effects
- Effect of Analytic Bias on tests
  - Gaussian Model
  - Cholesterol
  - Calcium
- Cost Analysis Model for Calcium
Medical Decisions

- **Diagnostic**
  - Separation of patients into categories.
  - Evaluation of a patient’s single test value relative to distribution of values from patients having confirmed diagnoses (Reference data generally collected at a different time and often with a different assay).
Medical Decisions (continued)

- Monitoring
  - Tracking of a patient’s multiple test values over time (maybe hours, day, weeks, months or years)
  - Evaluation of test value relative to prior values and/or relative to therapeutic range (generally established with a different assay or different assay calibration)
Laboratory Performance Criteria

- Diagnostic Test
  - Major dependence on analytic bias for effects on health system performance. Dependence on both bias and precision for individual patient performance.

- Monitoring Test
  - Major dependence on both analytic bias and analytic precision for both health system performance and individual patient performance.
Health System “Outcomes Monitoring” Affected by Analytic Bias of Test Values
Tolerance Limits for Analytic Bias

- Bias directly affects test values

- Small analytic changes can produce major shifts in frequency distributions of clinical test values
Effect of Analytic Bias on Decisions

Gaussian Model

Original Positives 2.3%
With Bias 15.8%

+2.0 SD_{Biol}

FREQUENCY

STANDARD DEVIATES
Laboratory Tests as Key Indicators for Clinical Guidelines

- Cholesterol - Cardiac Disease Risk
- Serum Calcium-Hypercalcemia
Paradigm I: Cholesterol testing for identifying patients at risk for coronary artery disease (CAD)

National Cholesterol Education Program (NCEP-ATP III)

- Test adults > 20 years, every 5 years
- Follow-up if cholesterol \( \geq 200 \text{mg/ dL} \) or HDL Cholesterol < 40mg/ dL
- LDL cholesterol goal for persons with CAD is 100 mg/ dL
- LDL cholesterol goal for persons with 2+ risk factors is < 130 mg/ dL and < 160 mg/ dL for those with 0-1 risk factors
Cholesterol Frequency Distribution with ±2%, ±6% and ±20% Limits Around 200mg/dL
## Cholesterol Bias Effects on Positives per 1000 @ 200 mg/dL

<table>
<thead>
<tr>
<th>Bias</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10% bias</td>
<td>410</td>
<td>-31.0%</td>
</tr>
<tr>
<td>-3% bias</td>
<td>538</td>
<td>-9.4%</td>
</tr>
<tr>
<td>-1% bias</td>
<td>575</td>
<td>-3.2%</td>
</tr>
<tr>
<td>0% bias</td>
<td>594</td>
<td>0%</td>
</tr>
<tr>
<td>+1% bias</td>
<td>612</td>
<td>+3.0%</td>
</tr>
<tr>
<td>+3% bias</td>
<td>646</td>
<td>+8.8%</td>
</tr>
<tr>
<td>+10% bias</td>
<td>759</td>
<td>+27.8%</td>
</tr>
</tbody>
</table>
Paradigm II-Hypercalcemia

Re-check Calcium
Intact PTH
Chest X-ray

Non PTH-mediated
Evaluate for:
- Vitamin D Intoxication
- Hyperthyroidism
- Adrenal insufficiency
- Sarcoidosis
- Multiple Myeloma
- Lymphoma

PTH-mediated

Excretory Urogram

Check 24 Urine Calcium

Normal
Primary Hyperparathyroidism

Low
Evaluate for:
- Familial, Hypocalciuric
  Hypocalcemia

Primary Hyperparathyroidism
Calcium Frequency Distribution with $\pm 2\%$, $\pm 4\%$ and $\pm 10\%$
## Calcium Bias Effects on Positives per 1000

<table>
<thead>
<tr>
<th>Level</th>
<th>10.1 mg/dL</th>
<th>10.4 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-10% bias</td>
<td>2, -92%</td>
<td>1, -90%</td>
</tr>
<tr>
<td>-4% bias</td>
<td>7, -72%</td>
<td>4, -60%</td>
</tr>
<tr>
<td>-2% bias</td>
<td>13, -52%</td>
<td>6, -40%</td>
</tr>
<tr>
<td>0% bias</td>
<td>25, 0%</td>
<td>10, 0%</td>
</tr>
<tr>
<td>+2% bias</td>
<td>52, +108%</td>
<td>18, +80%</td>
</tr>
<tr>
<td>+4% bias</td>
<td>113, +352%</td>
<td>36, +260%</td>
</tr>
<tr>
<td>+10% bias</td>
<td>640, +2460%</td>
<td>329, +3190%</td>
</tr>
</tbody>
</table>
Model Building Process

- Medically identified the CPT4 procedures which were associated with the disease processes (hypercalcemia).

- Statistically determine the CPT4 codes that were more frequently found in patients with elevations of the index tests (serum calcium) using coded Mayo Clinic records.
Model Building Process cont.

- Defined **standardized** charges for these CPT4 codes using both Medicare pricing and private payor pricing.
- Calculated the aggregate Medical costs for these defined procedures for a cohort of patients.
- Developed a simulated cost model for calcium bias using regression equations.
# Procedures More Frequently Ordered in Patients with Hypercalcemia (1 of 3)

<table>
<thead>
<tr>
<th>CPT4</th>
<th>Description</th>
<th>Calcium, mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>8.9-10.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>#/pt</td>
</tr>
<tr>
<td>60512</td>
<td>Explore Parathyroid Gland</td>
<td>0.00056</td>
</tr>
<tr>
<td>71020</td>
<td>Chest X-Ray</td>
<td>1.11418</td>
</tr>
<tr>
<td>78070</td>
<td>Nuclear Scan of Parathyroid</td>
<td>0.00006</td>
</tr>
<tr>
<td>82040</td>
<td>Assay Serum ALB</td>
<td>0.63013</td>
</tr>
<tr>
<td>82150</td>
<td>Assay of Serum Amylase</td>
<td>0.12593</td>
</tr>
<tr>
<td>82164</td>
<td>Angiotensin Enzyme Test</td>
<td>0.02277</td>
</tr>
<tr>
<td>82310</td>
<td>Assay Calcium in Blood</td>
<td>0.61279</td>
</tr>
<tr>
<td>82340</td>
<td>Assay Calcium in Urine</td>
<td>0.01397</td>
</tr>
<tr>
<td>82374</td>
<td>Assay Blood Carbon Dioxide</td>
<td>0.11387</td>
</tr>
<tr>
<td>82435</td>
<td>Assay Blood Chlorides</td>
<td>0.12417</td>
</tr>
<tr>
<td>82550</td>
<td>Assay CPK in Blood</td>
<td>0.23521</td>
</tr>
</tbody>
</table>
Parathyroid Hormone tests
Females on Medicare

\[ y = -0.1195x^3 + 3.8169x^2 - 40.128x + 139.13 \]
Incremental Cost vs Calcium Females on Medicare

Percentage change in cost vs Analytic bias in calcium, mg/dL

- 9.9-10 Calcium
- 10.1-10.2 Calcium
- 10.3-10.4 Calcium
- ?10.5 Calcium
Incremental Cost due to Bias

Patients with Calcium > 9.8mg/dL
Extrapolation of Cost Impact to entire Nation

<table>
<thead>
<tr>
<th>Sub Segments</th>
<th>0.1 mg/dL</th>
<th>0.5 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private Insurance</td>
<td>0.55</td>
<td>1.81</td>
</tr>
<tr>
<td>Medicare</td>
<td>0.25</td>
<td>0.85</td>
</tr>
<tr>
<td>Total Weighted Average</td>
<td>0.40</td>
<td>1.33</td>
</tr>
</tbody>
</table>
Summary

- Analytic Traceability is important for both Diagnosis and Monitoring in an integrated Health System
- Analytic Bias can profoundly affect patient classifications (diagnoses) using guidelines
- Analytic Bias can Markedly Increase Costs
- Combined medical, government, and industry cooperation is needed to assure traceability and harmony of test values