MODULE 3. STRATUM-SPECIFIC LIKELIHOOD RATIOS

Henry Glick, Ph.D.
Decision Analysis Workshop
August 18, 2009
www.uphs.upenn.edu/dgimhsr

Outline

• In the last module, we reviewed methods for the identification of the optimal 2x2 table
• Here we address a second categorical approach to the interpretation of such scores, the development of stratum-specific likelihood ratios (SSLR)
• In what follows, we:
  – Describe the construction of SSLR
  – Demonstrate the calculation of post-test probabilities by use of SSLR
  – Describe the relationship between SSLR and the ROC curve
  – and briefly discuss the relationship between LR+ and LR- and the ROC curve

SSLR Approach

• In the 2x2 approach to continuous data, we break the continuous data up into a series of cumulative 2x2 tables
• In the SSLR approach, we calculate likelihood ratios for particular test results or ranges of test results (i.e., strata) and never aggregate the results of one stratum with those of another
• These strata can be large, like the five that we used in Table E1 to summarize the WBC data, or they can be infinitesimally small
  – e.g., if we plot the distribution of positive test scores and the distribution of negative test scores, we can define likelihood ratios for every point on the two curves
Formula for \( LR_i \):

\[
LR_i = \frac{\text{Probability of test result } i \text{ given } D^+}{\text{Probability of test result } i \text{ given } D^-}
\]

Graphical Interpretation of SSLR:

- Disease
  - High: 80%
  - Intermediate: 10%
  - Low: 10%
- No Disease
  - Intermediate: 20%
  - Low: 70%

SSLR and Post-Test Probabilities:
- SSLR greater than 1 indicate the test result occurs more frequently in those in whom disease is present than it does in those in whom it is absent.
- When we are considering 2 outcomes, these SSLR yield post-test probabilities that are greater than pre-test probabilities.
  - All else equal, the larger the SSLR, the greater the shift between pre- and post-test probabilities.
SSLR and Post-Test Probabilities (2)

- SSLR less than 1 indicate the test result occurs less frequently in those in whom disease is present than it does in those in whom disease is absent.
  - When we are considering 2 outcomes, these SSLR yield post-test probabilities that are less than pre-test probabilities.
  - All else equal, the smaller the SSLR, the greater the shift between pre- and post-test probabilities.
- SSLR that equal 1 yield post-test probabilities that equal pre-test probabilities (i.e., no information).

Three Methods for the Calculation of SSLR

- We review 3 methods for the calculation of SSLR.
  - All 3 are transformations of one another, and, except for possible differences due to rounding, all 3 give exactly the same results.
  - For all 3 methods, the first step is to establish the strata and tabulate the stratum specific test results.
  - Continue to illustrate the principles by use of data about white blood cell (WBC) counts for the diagnosis of bacteremia.

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Bact</th>
<th>No Bact</th>
<th>% Bact</th>
<th>% No Bact</th>
<th>SSLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25</td>
<td>6</td>
<td>26</td>
<td>0.23077</td>
<td>0.03027</td>
<td>7.6237</td>
</tr>
<tr>
<td>≥20, &lt;25</td>
<td>4</td>
<td>43</td>
<td>0.15385</td>
<td>0.05006</td>
<td>3.0733</td>
</tr>
<tr>
<td>≥15, &lt;20</td>
<td>7</td>
<td>129</td>
<td>0.26923</td>
<td>0.15017</td>
<td>1.7928</td>
</tr>
<tr>
<td>≥10, &lt;15</td>
<td>7</td>
<td>292</td>
<td>0.26923</td>
<td>0.33993</td>
<td>0.7920</td>
</tr>
<tr>
<td>≥0, &lt;10</td>
<td>2</td>
<td>369</td>
<td>0.07692</td>
<td>0.42957</td>
<td>0.1791</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>859</td>
<td>1.000</td>
<td>1.000</td>
<td>--</td>
</tr>
</tbody>
</table>
Method 2. \((axf) / (bxe)\)

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>Bact</th>
<th>No Bact</th>
<th>((axf) / (bxe))</th>
<th>SSLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25</td>
<td>6</td>
<td>26</td>
<td>(6x859) / (26x26)</td>
<td>7.6243</td>
</tr>
<tr>
<td>≥20, &lt;25</td>
<td>4</td>
<td>43</td>
<td>(4x859) / (43x26)</td>
<td>3.0733</td>
</tr>
<tr>
<td>≥15, &lt;20</td>
<td>7</td>
<td>129</td>
<td>(7x859) / (129x26)</td>
<td>1.7928</td>
</tr>
<tr>
<td>≥10, &lt;15</td>
<td>7</td>
<td>292</td>
<td>(7x859) / (292x26)</td>
<td>0.7920</td>
</tr>
<tr>
<td>≥0, &lt;10</td>
<td>2</td>
<td>369</td>
<td>(2x859) / (369x26)</td>
<td>0.1791</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>859</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Method 3. \((Se_{ji} - Se_{ji-1}) / (1 - Sp_{ji} - 1 - Sp_{ji-1})\)

<table>
<thead>
<tr>
<th>Cut-off</th>
<th>(Se_{j+1} - Se_{j+1})</th>
<th>(1 - Sp_{j+1} - 1 - Sp_{j+1})</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25</td>
<td>0.23077 - 0.00000</td>
<td>0.03027 - 0.00000</td>
<td>7.6237</td>
</tr>
<tr>
<td>≥20, &lt;25</td>
<td>0.38462 - 0.23077</td>
<td>0.08033 - 0.03027</td>
<td>3.0733</td>
</tr>
<tr>
<td>≥15, &lt;20</td>
<td>0.65385 - 0.38462</td>
<td>0.23050 - 0.08033</td>
<td>1.7928</td>
</tr>
<tr>
<td>≥10, &lt;15</td>
<td>0.92308 - 0.65385</td>
<td>0.57043 - 0.23050</td>
<td>0.7920</td>
</tr>
<tr>
<td>≥0, &lt;10</td>
<td>1.00000 - 0.92308</td>
<td>1.00000 - 0.57043</td>
<td>0.1791</td>
</tr>
</tbody>
</table>

SSLR and the Calculation Of Post-test Probability Of Disease

- Of the five methods for the calculation of the post-test probability of disease that we introduced in the 2x2 module, three used likelihood ratios:
  - Odds transformation method
  - Likelihood ratio and probability method
  - Nomogram
- We can use any of these three methods to calculate post-test probabilities by use of SSLR
- Below, we use the likelihood ratio and probability method

\[
\text{Pre-test probability } \times \text{LR}_i \\
\frac{\text{Pre-test probability } \times \text{LR}_i + (1 - \text{Pre-test probability})}{1 + \text{Pre-test probability } \times \text{LR}_i}
\]
Post-Test Probabilities

- For a pre-test probability of bacteremia of 10%, the post-test probabilities of bacteremia equal:

\[
\begin{align*}
\geq 25 & & 0.1 \cdot 7.6243 \\ (0.1 \cdot 7.6243) + 0.9 & = 0.76243 = 0.459 \\
20, <25 & & 0.1 \cdot 3.0733 \\ (0.1 \cdot 3.0733) + 0.9 & = 0.30733 = 0.255 \\
15, <20 & & 0.1 \cdot 1.7928 \\ (0.1 \cdot 1.7928) + 0.9 & = 0.17928 = 0.161 \\
10, <15 & & 0.1 \cdot 0.7929 \\ (0.1 \cdot 0.7929) + 0.9 & = 0.07929 = 0.081 \\
<10 & & 0.1 \cdot 0.1791 \\ (0.1 \cdot 0.1791) + 0.9 & = 0.01791 = 0.021
\end{align*}
\]

SSLR and ROC Curves

- SSLR and the ROC curve are related, and contain the information that allows us to identify the optimal 2x2 table (and thus the optimal cut-off for a positive test) for a particular patient or class of patients
- Recall that the formula for the third method for the calculation of SSLR is written in terms of sensitivity and 1-specificity:
  \[S_{SLR} = \frac{S_{p}}{1 - S_{p}} / \frac{1 - S_{p}}{1 - S_{p}}\]
- Also recall that in the ROC module we defined the slopes of the lines connecting each of the contiguous operating points by use of the same formula

SSLR=Slopes of ROC Curve

* x100/mm³; Cells
>0 and >5 combined
SSLR and ROC Curves (2)

- Finally, recall that a practical method for identifying a tangency is to compare the OOS and the slopes of the lines connecting each of the contiguous operating points.
- Thus, we don’t need to construct an ROC curve to identify the optimal cut-off for a particular patient or class of patients, but instead can compare the OOS to the test’s SSLR.
- For example, if the pre-test probability of disease is 20%, and the CFN is twice the CFP:
  - The OOS equals 2, which is larger than the SSLR of 1.7928 and smaller than 3.0733.
  - The common cut-off that defines these two slopes is <20 / >20, which is the same optimal cut-off we identified in the ROC module.

LR+ and LR- and ROC Curves

- There are also relationships between LR+, LR- and ROC curves.
- LR+ equals sensitivity / (1-specificity).
- The points on the ROC curve equal sensitivity and 1-specificity of each of the plotted 2x2 tables.
- Thus the slope of the line drawn from the origin to any point on the ROC curve equals the LR+ for the 2x2 table that is represented by the point.

LR+ and LR- and ROC Curves (2)

- Similarly, LR- equals (1-sensitivity) / specificity.
- The change in sensitivity between the point on the ROC curve and the upper right corner of the ROC curve (1,1) equals 1-sensitivity.
- The change in 1-specificity between the point on the ROC curve and the upper right corner of the ROC curve equals specificity.
- Thus, the slope of the line between a point on the ROC curve and the upper right corner of the ROC curve equals (1-sensitivity) / specificity, or LR-.
Summary

• In this module, we introduced stratum specific likelihood ratios, which are the extension of LR+ and LR- to multilevel test results
• We demonstrated 3 methods for calculating SSLR
• We demonstrated 1 of 3 methods for using SSLR to calculate post-test probabilities of disease
• All of these methods are generalizations of methods we first introduced in the 2x2 module when we described LR+ and LR-
• We also described the relationship between SSLR and slopes of the ROC curve, and indicated that when we compare the optimal operating slope to the SSLR, we can identify the optimal positive test cut-off for a particular patient or class of patients