INTRODUCTION TO LOGISTIC REGRESSION
SESSION 4

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OxPal Research Fellowship Series 2021

FEBRUARY, 2020
What will this session tell you?

🧩 Understand when to use logistic regression (LR).
🧩 Interpret a LR model with a binary exposure variable.
🧩 Assess model fit.
Your new friend

Jane Superbrain 2.0

- She steals the brains of top statisticians.
- She appears in red boxes to tell you really important things.
Content

1. From linear to logistic regression
   - The linear model
   - Redefining the dependent variable

2. The logistic regression model
   - The unadjusted model
   - Adjusting for confounders

3. Assessing model fit
   - Classification threshold
   - Performance of a classification model
1. From linear to logistic regression
   - The linear model
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Recap

Regression models are used to:
- Describe relationship between 2 or more variables where one of these is ‘dependent’ (‘response’, ‘outcome’).
- Predict the value of the dependent variable for a given value of the independent variable.

We can describe the linear relationship between \( y \) and \( x \) as:
\[
\hat{y}_i = \hat{\beta}_0 + \hat{\beta}_1 x_i
\]

We can use the linear model to investigate the association between number of hours studying and exam scores as:
\[
\text{exam score} = \hat{\beta}_0 + \hat{\beta}_1 \text{ hours studying}
\]
We could describe the linear relationship between hours studying and exam scores using the linear regression model:
\[ \hat{\text{score}} = \hat{\beta}_0 + \hat{\beta}_1 \text{ hours} \]

Figure 1: Exam scores versus hours studying.
Using the equation of the regression line, calculate the estimated exam score for hours studying = 6.

Figure 1 (Cont.): Exam scores versus hours studying.
Using the equation of the regression line, calculate the estimated exam score for hours studying = 6.

\[ \hat{\text{exam}} = 16.4 + 7.2 \times \text{hours} \]

**Figure 1 (Cont.):** Exam scores versus hours studying.
Let’s assume a student passes the exam if score $\geq 50$.

**Figure 1 (Cont.):** Exam scores versus hours studying.
How could we model this relationship between passing exam (0 vs 1) and hours studying?

Figure 2: Passing exam versus hours studying.
The line does not fit the data very well. It goes below 0 and above 1.

If we take values of Y between 0 and 1 to be probabilities, this does not make sense.

Figure 2 (Cont.): Passing exam versus hours studying.
How could we link the probability of passing exam to the continuous predictor ‘hours studying’? The risk is constrained to fall in the interval [0,1].

**Figure 3:** Probability of passing exam versus hours studying.
We can use a S-shaped curve to model the relationship between probability of passing and hours studying.

What’s the probability of passing for hours studying = 5?

Figure 3 (Cont.): Probability of passing exam versus hours studying.
We can use an S-shaped curve to model the relationship between probability of passing and hours studying.

What’s the probability of passing for hours studying $= 5$?

**Figure 3 (Cont.):** Probability of passing exam versus hours studying.
What’s the minimum number of hours studying required for \( \geq 50\% \) chance to pass exam?

**Figure 3 (Cont.):** Probability of passing exam versus hours studying.
What’s the minimum number of hours studying required for \( \geq 50\% \) chance to pass exam?

**Figure 3 (Cont.):** Probability of passing exam versus hours studying.
We need to transform the dichotomous $Y$ into a continuous variable $Y'$. We need a (link) function that takes a dichotomous $Y$ and gives us a continuous $Y'$. 
If we work with Y as a probability, what function $F(Y)$ goes from $[0,1]$ interval to the real line? We know at least one function that goes the other way round (but we won’t use that one!).
Let’s look at an alternative approach based on odds.

Taking the odds of Y occurring moves us from the $[0,1]$ interval to the half-line $[0, +\infty[$ (odds are always non-negative).
As a final step, let’s take the log of the odds. This is called the logit function:

\[ Y' = \text{logit}(Y) = \log(\text{odds } Y) = \log\left(\frac{Y}{1 - Y}\right) \]

\((Y \text{ as probability of disease})\).
The logistic model

The smooth S-shaped curve is known as the logistic (or logit) model.

Assuming a linear relationship between log(odds Y) and a predictor X, we can fit a linear regression model with log(odds Y) as the dependent variable and X as the independent variable.
Important points

Jane Superbrain 2.0

Properties of the logistic model:

- Allows for a smooth change in risk throughout the range of X.
- Has the property that risk increases slowly up to a threshold range of X, followed by a more rapid increase and a subsequent leveling off of risk.
- This shape is consistent with many dose response relationships (e.g. likelihood of toxicity response to varying levels of treatment).
1. From linear to logistic regression
   - The linear model
   - Redefining the dependent variable

2. The logistic regression model
   - The unadjusted model
   - Adjusting for confounders

3. Assessing model fit
   - Classification threshold
   - Performance of a classification model
Consider a prospective cohort study conducted for the purpose of studying the determinants of ischaemic heart disease (IHD) among 844 men without prior cardiovascular disease.

The men were subsequently followed-up for 10 years, at which point the investigators wanted to assess whether baseline levels of serum cholesterol were associated with IHD mortality.

The investigators conducted a nested case-control study of 68 IHD cases and 138 controls from the main cohort and measured cholesterol levels in these participants.
### 2x2 Contingency Table

The following Stata output shows the cross-tabulation of the number of participants with a diagnosis of IHD by baseline serum cholesterol (high versus low).

<table>
<thead>
<tr>
<th>Ischaemic heart disease</th>
<th>High serum cholesterol</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>73</td>
<td>65</td>
<td>138</td>
</tr>
<tr>
<td>1</td>
<td>24</td>
<td>44</td>
<td>68</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>97</strong></td>
<td><strong>109</strong></td>
<td><strong>206</strong></td>
</tr>
</tbody>
</table>

1. Calculate proportions with IHD in those with and without high cholesterol.
2. Calculate odds of IHD in those with and without high cholesterol.
2x2 Contingency Table (Cont.)

```
.tab ihd hichol1, m
```

<table>
<thead>
<tr>
<th>Ischaemic heart disease</th>
<th>High serum cholesterol</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>73</td>
<td>65</td>
</tr>
<tr>
<td>1</td>
<td>24</td>
<td>44</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>97</strong></td>
<td><strong>109</strong></td>
</tr>
</tbody>
</table>

**Proportions**

\[
P(ihd = 1 | \text{hichol} = 1) = \frac{44}{44 + 65} = 0.40
\]

\[
P(ihd = 1 | \text{hichol} = 0) = \frac{24}{24 + 73} = 0.25
\]
### 2x2 Contingency Table (Cont.)

<table>
<thead>
<tr>
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<th>Total</th>
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<tr>
<td><strong>Total</strong></td>
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<td><strong>109</strong></td>
</tr>
</tbody>
</table>

#### Odds

\[
\text{odds}(\text{ihd} = 1 | \text{hichol} = 1) = \frac{44}{65} = 0.68
\]

\[
\text{odds}(\text{ihd} = 1 | \text{hichol} = 0) = \frac{24}{73} = 0.33
\]

#### Odds ratio

\[
\text{odds ratio} = \frac{\text{odds}(\text{ihd} = 1 | \text{hichol} = 1)}{\text{odds}(\text{ihd} = 1 | \text{hichol} = 0)} = \frac{0.68}{0.33} = 2.06
\]
Suppose a logistic regression of ischemic heart disease (ihd) on high baseline serum cholesterol (hichol1) is performed:

\[ \log(\text{odds of ihd}) = \beta_0 + \beta_1 \times \text{hichol1} \]

Based on the equation above, what are \( \beta_0 \) and \( \beta_1 \)?

For an unexposed person (i.e. with low cholesterol), substitute hichol1 = 0 into the model:

\[ \log(\text{odds of ihd}) = \beta_0 + \beta_1 \times 0 = \beta_0 \]

\( \beta_0 \) is log odds in unexposed.
The simple logistic regression model (Cont.)

Suppose a logistic regression of ischemic heart disease (ihd) on high baseline serum cholesterol (hichol1) is performed:

\[
\log(\text{odds of ihd}) = \beta_0 + \beta_1 \times \text{hichol1}
\]

For an exposed person (i.e. with low cholesterol), substitute \( \text{hichol1} = 1 \) into the model:

\[
\log(\text{odds of ihd}) = \beta_0 + \beta_1 \times 1 = \beta_0 + \beta_1
\]

The calculation above could be rewritten as follows

\[
\beta_1 = \log(\text{odds in exposed}) - \beta_0
\]

\[
= \log(\text{odds in exposed}) - \log(\text{odds in unexposed})
\]

\[
= \log(\text{odds in exposed/odds in unexposed})
\]

\[
= \log(\text{odds ratio})
\]

\( \beta_1 \) is log odds ratio.
Based on our previous calculations (2x2 table):

$$OR = 2.06$$

odds in unexposed = 0.33

The logistic regression of ischemic heart disease (ihd) on high baseline serum cholesterol (hichol1) is given by:

$$\log(\text{odds of ihd}) = \beta_0 + \beta_1 hichol1$$

$$= \log(0.33) + \log(2.06) \times hichol1$$

$$= -1.11 + 0.72 \times hichol1$$
### Fitting a logistic regression model

```
. *--- log scale;
. logit ihd hichol1, noheader nolog
```

|     | Coef. | Std. Err. | z    | P>|z| | [95% Conf. Interval] |
|-----|-------|-----------|------|------|---------------------|
| ihd |       |           |      |      |                     |
| hichol1 | 0.722 | 0.306     | 2.36 | 0.018 | 0.123              1.321 |
| _cons| -1.112| 0.235     | -4.73| 0.000 | -1.574             -0.651 |

\[
\text{log(odds of ihd)} = -1.11 + 0.72 \times \text{hichol1}
\]
Interpretation

```
. *--- get ORs;
. logit ihd hichol1, or noheader nolog

|     | Odds Ratio | Std. Err. |    z |   P>|z|     |        [95% Conf. Interval] |
|-----|------------|-----------|------|--------|-----------------------------|
| ihd |            |           |      |        |                             |
| hichol1 | 2.059 | 0.630   |  2.36| 0.018  | 1.131                        | 3.749                        |
|   _cons | 0.329 | 0.077   | -4.73| 0.000  | 0.207                        | 0.521                        |

Note: _cons estimates baseline odds.
```

A person with high cholesterol have a 2-fold higher odds of IHD as compared to a person with low cholesterol (OR=2.06 [1.13, 3.75], p = 0.018).
In logistic regression, we model the log (odds of disease) as the outcome:

\[ \log(\text{odds of disease}) = \beta_0 + \beta_1 x \]

where

- \( \beta_0 \) = log odds in the unexposed
- \( \beta_1 \) = log OR

We use this model to estimate log OR and hence OR (with 95% CI, p-value).

We use a statistics package to fit logistic regression models.

Estimation is done using the method of maximum likelihood*. 

*Note: Maximum likelihood estimation is a statistical method used to estimate the parameters of a model. In the context of logistic regression, it helps in estimating the coefficients of the model by maximizing the likelihood of the observed data.
Study designs in which logistic regression may be used:

- A cross-sectional study
  Model parameters are interpreted as above.
  If outcome is not rare, then OR will overestimate the risk ratio.

- An unmatched case-control study
  Parameter $\beta_1$ is log OR, but $\beta_0$ (log odds in unexposed) is not interpretable.
Confounding by age

Looking at the regression results below, describe the impact of age on the association between IHD and baseline serum cholesterol.

```
. logit ihd hichol1, or noheader nolog

| ihd | Odds Ratio | Std. Err. | z   | P>|z| | [95% Conf. Interval] |
|-----|------------|-----------|-----|-----|----------------------|
| hichol1 | 2.059      | 0.630     | 2.36 | 0.018 | 1.131 - 3.749        |
| _cons  | 0.329      | 0.077     | -4.73| 0.000 | 0.207 - 0.521        |
```

```
. logit ihd hichol1 age, or noheader nolog

| ihd | Odds Ratio | Std. Err. | z   | P>|z| | [95% Conf. Interval] |
|-----|------------|-----------|-----|-----|----------------------|
| hichol1 | 1.884      | 0.596     | 2.00 | 0.045 | 1.014 - 3.502        |
| age   | 1.071      | 0.021     | 3.56 | 0.000 | 1.031 - 1.112        |
| _cons | 0.008      | 0.009     | -4.41| 0.000 | 0.001 - 0.069        |
```
Confounding by age (Cont.)

```
. logit ihd hichol1, noheader nolog

|      | Coef. | Std. Err. |    z |   P>|z| | [95% Conf. Interval] |
|------|-------|-----------|------|------|----------------------|
| ihd  |       |           |      |      |                      |
| hichol1 | 0.722 | 0.306     | 2.36 | 0.018| 0.123                |
| _cons | -1.112| 0.235     | -4.73| 0.000| -1.574               |

. logit ihd hichol1 age, noheader nolog

|      | Coef. | Std. Err. |    z |   P>|z| | [95% Conf. Interval] |
|------|-------|-----------|------|------|----------------------|
| ihd  |       |           |      |      |                      |
| hichol1 | 0.633 | 0.316     | 2.00 | 0.045| 0.014                |
| age   | 0.068 | 0.019     | 3.56 | 0.000| 0.031                |
| _cons | -4.808| 1.090     | -4.41| 0.000| -6.945               |
```

The confounding effect of age can be quantified by computing the percentage difference between the crude and adjusted coefficients 
\[
\frac{(\beta_{\text{unadjusted}} - \beta_{\text{adjusted}})}{\beta_{\text{unadjusted}}} \approx 12\%
\]
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### Hits and misses

What percent of the observation the model correctly predicts?

```bash
. qui logit ihd hichol11 age, noheader nolog
. lstat
Logistic model for ihd

<table>
<thead>
<tr>
<th>Classified</th>
<th>D</th>
<th>~D</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>14</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>-</td>
<td>54</td>
<td>128</td>
<td>182</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>138</td>
<td>206</td>
</tr>
</tbody>
</table>
```

Classified + if predicted Pr(D) $\geq .5$

True D defined as ihd $\neq 0$
Hits and misses (Cont.)

1. Use model to generate the probability $p$ that each observation will have the disease.

2. Use a cutoff $\pi = 0.5$. If $p \geq \pi$ predict $\text{ihd} = 1$, if $p < \pi$ predict $\text{ihd} = 0$.

3. Check predictions against the actual outcomes in the data.

```
. qui logit ihd hichol1 age, noheader nolog
. list
Logistic model for ihd

<table>
<thead>
<tr>
<th>Classified</th>
<th>True</th>
<th>~D</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>14</td>
<td>10</td>
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<td>68</td>
<td>138</td>
<td>206</td>
</tr>
</tbody>
</table>
```

Classified + if predicted $\text{Pr(D)} \geq 0.5$
True D defined as $\text{ihd} \neq 0$
Hits and misses (Cont.)

Output shows summary of correct and incorrect predictions.

<table>
<thead>
<tr>
<th></th>
<th>Formula</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classified + if predicted Pr(D) &gt;= .5</td>
<td>Pr( +</td>
<td>D)</td>
</tr>
<tr>
<td>True D defined as ihd != 0</td>
<td>Pr( -</td>
<td>~D)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Pr( +</td>
<td>D)</td>
</tr>
<tr>
<td>Specificity</td>
<td>Pr( -</td>
<td>~D)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>Pr( D</td>
<td>+)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>Pr( ~D</td>
<td>-)</td>
</tr>
<tr>
<td>False + rate for true ~D</td>
<td>Pr( +</td>
<td>~D)</td>
</tr>
<tr>
<td>False - rate for true D</td>
<td>Pr( -</td>
<td>D)</td>
</tr>
<tr>
<td>False + rate for classified +</td>
<td>Pr( -D</td>
<td>+)</td>
</tr>
<tr>
<td>False - rate for classified -</td>
<td>Pr( D</td>
<td>-)</td>
</tr>
<tr>
<td>Correctly classified</td>
<td></td>
<td>68.93%</td>
</tr>
</tbody>
</table>

Overall success rate = \(\frac{14 + 128}{206} = 68.93\%\)
We can imagine changing the cutoff point \( \pi \) continuously from 0 to 1. The ROC curve plots the sensitivity \( S_e = P(+|D) \) and 1–specificity \( S_p = P(-|\bar{D}) \) as \( \pi \) goes from 0 to 1.

Area under the curve is 0.6876.
Using logistic regression to make a classifier

The goal here is to model and predict if a given observation (row in dataset) has disease or not based on other variables/features in the dataset.

1. Split dataset into training, validation and test sets.
2. Build logistic (logit) model on the training set.
3. Tune the parameters of the classifier on the validation set.
What did this session tell you?

- Understand when to use logistic regression (LR).
- Interpret a LR model with a binary exposure variable.
- Assess model fit.
The relationship between IHD and baseline serum cholesterol (low versus high) was further investigated by identifying each individual who developed IHD and matching that person, based on age, to an individual who had not developed IHD.

The count data on the resulting matches are tabulated below.

<table>
<thead>
<tr>
<th>Developing IHD (cases)</th>
<th>Not developing IHD (controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High cholesterol</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>20</td>
</tr>
<tr>
<td>Low cholesterol</td>
<td>11</td>
</tr>
</tbody>
</table>

Based on these data, calculate the odds ratio for the association between IHD and serum cholesterol level (high versus low) among individuals of the same age.
This is a matched case-control study and the estimated odds ratio is based on the discordant pairs $b$ & $c$.

$b$ is the number of pairs in which emp developing IHD have high baseline serum cholesterol and their matched emp not developing IHD have low baseline serum cholesterol.

$c$ is number of pairs in which emp developing IHD have low baseline serum cholesterol and their matched emp not developing IHD have high baseline serum cholesterol.
### Advanced topics

**Matched case-control studies**

**Introduction to Logistic Regression**

#### Matching cases and controls based on age (Cont.)

<table>
<thead>
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</tr>
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</table>

**OR** = \( \frac{b}{c} = \frac{21}{11} = 1.9 \)