Statistics 305/605: Introduction to Biostatistical Methods for Health Sciences

Chapter 20, part 1: Logistic Regression Models

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Introduction to Logistic Regression

- In logistic regression we study the effect of explanatory variables on the odds of a binary outcome.
- This is a generalization of the analyses of odds ratios we have studied before.
- Think of the binary outcome Y as disease status (0=non-disease; 1=disease).
- The explanatory variables could be categorical (e.g., exposures), or quantitative variables.

Example Data

- In a sample of 223 low-birthweight infants from the neonatal ICU of a large hospital, 76 were diagnosed with bronchopulmonary dysplasia (BPD; $Y = 1$) and 147 were non-BPD ($Y = 0$).
- One factor that might affect the risk of BPD is birth weight (birthwt, in grams; X_1). Breaking birth weight into 3 categories, we have:

birthwt	BPD	no BPD	odds BPD	log-odds* BPD
0-950g	49	19	$49/19 = 2.58$	0.95
951-1350g	18	62	$18/62 = 0.29$	-1.24
1351-1750g	9	66	$9/66 = 0.14$	-1.99

* Use the natural logarithm.

- Consider the ratio of the odds at two values of X_1.
- To get the log of this odds ratio (the log-OR), we take the difference between the two log-odds.
  - E.G. The log-OR of BPD in babies with birthweight $< 950g$ relative to babies with birthweight between $1351 - 1750g$ is $0.95 - (-1.99) = 0.95 + 1.99 = 2.94$.

The Logistic Regression Model

- We may model the log-odds of $Y = 1$ (e.g. BPD) as a function of X_1 (e.g. birthwt):

$$\log\left[\frac{p}{1-p}\right] = \alpha + \beta_1 X_1, \quad \text{where}$$

  - log is the *natural logarithm* and
  - p is the probability of $Y = 1$ given X_1.

- Let $LO = \alpha + \beta_1 X_1$ be the linear predictor for the log-odds.
  - The logistic-regression parameters are α and β_1.

- It can be shown that

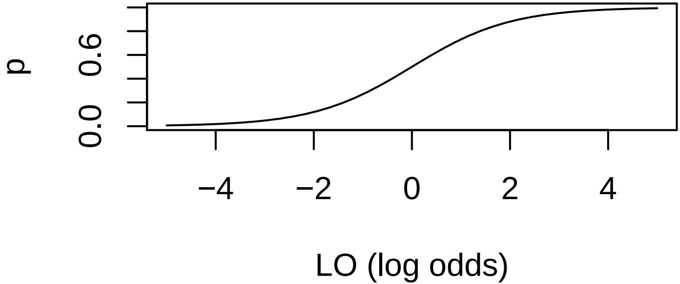
$$p = \frac{e^{LO}}{1 + e^{LO}}.$$

  - i.e., the probability p is the *logistic function* of the log-odds.

Graph of the Logistic Function

- Below, the y-axis shows p and x-axis shows LO; the curve is the function

$$p = \frac{e^{LO}}{1 + e^{LO}}.$$



- On the y-axis, p is constrained to be between 0 and 1 and, on the x-axis, LO is unconstrained.
  - As LO gets large and negative, p approaches 0.
  - As LO gets large and positive, p approaches 1.
  - At $LO = 0$, $p = 1/2$. ($LO = 0 \iff \text{odds} = 1$.)

Fitting the model to the data

- To fit this logistic-regression model to the data and get the parameter estimates, we use a technique called the method of *maximum likelihood*.
  - Likelihood methods for fitting statistical models to data and obtaining parameter estimates are beyond the scope of this course.
  - Instead, see STAT 475 on Applied Discrete Data Analysis, for which STAT 305 is a pre-requisite.
- For large sample sizes, we can make approximate inference about the slope parameter β_1 for X_1 that describes the association between Y and X_1.

Review of Natural Logarithms and Exponents

- Recall that if a is the natural logarithm of z, written $a = \log(z)$, then $e^a = e^{\log(z)} = z$.
- The logarithm of 1 is always zero;
  - e.g, $0 = \log(1)$ and $e^0 = 1$.
- Sums of exponents are multiples; that is, $e^{a+b} = e^a e^b$.
- Differences of exponents are ratios; that is, $e^{a-b} = e^a / e^b$.
  - We will make use of this as $e^a / e^b = e^{a-b}$.

Interpretation of β_1

- A one-unit (insert relevant units) increase in X_1 is associated with a change of β_1 in the log-odds of the outcome, or a e^{β_1}-fold change in the odds of the outcome.
- Need to take care with negative parameter values.
- E.G. Let's say that $\beta_1 = -2$ and X_1 is measured in grams. Then, literally:

  A one-gram increase in X_1 is associated with a change of -2 in the log-odds of the outcome, or a $e^{-2} = 0.135$-fold change in the odds of the outcome.

- But don't say this as it is too long and confusing. Instead, if X_1 is birthweight and the outcome is BPD, say something like:

  A one-gram increase in birthweight is associated with a 0.135-fold change in the odds of BPD.

Mathematical justification of interpretation

- Let p_1 be the probability of $Y = 1$ given $X_1 = x_1$.
- When $X_1 = x_1$, we have log-odds

$$\log\left[\frac{p_1}{1-p_1}\right] = \alpha + \beta_1 x_1.$$

- Let p_2 be the probability of $Y = 1$ given $X_1 = x_1 + 1$.
- When $X_1 = x_1 + 1$, we have log-odds

$$\log\left[\frac{p_2}{1-p_2}\right] = \alpha + \beta_1(x_1 + 1) = \alpha + \beta_1 x_1 + \beta_1.$$

- The odds at $X_1 = x_1$ and $X_1 = x_1 + 1$ are, respectively,

$$\frac{p_1}{1-p_1} = e^{\alpha+\beta_1 x_1} \quad \text{and} \quad \frac{p_2}{1-p_2} = e^{\alpha+\beta_1 x_1+\beta_1},$$

- Hence the odds-ratio for $X_1 = x_1 + 1$ relative to $X_1 = x_1$ is

$$\left(\frac{p_2}{1-p_2}\right) \Big/ \left(\frac{p_1}{1-p_1}\right) = e^{\alpha+\beta_1 x_1+\beta_1-(\alpha+\beta_1 x_1)} = e^{\beta_1}.$$

Interpretation of β_1 for a Binary Exposure

- If X_1 is a binary exposure that takes values 1 for exposed and 0 for unexposed, a one-unit increase in X_1 means going from unexposed to exposed.
- Set $x_1 = 0$ on the previous slide to find that e^{β_1} is the odds ratio for the exposed subjects relative to the unexposed subjects.
- In the homework assignment, you will be asked to interpret fitted coefficients from a logistic regression on a binary exposure variable.

BPD Example

- Let's read in the BPD data and look at it:

```r
uu <- url("http://people.stat.sfu.ca/~jgraham/Teaching/S305_18/Data/bpd.csv")
bpd <- read.csv(uu)
head(bpd)
```

```
##   bpd birthwt gestage toxemia steroid
## 1   1     850      27       0       0
## 2   0    1500      33       0       0
## 3   1    1360      32       0       0
## 4   0     960      35       1       0
## 5   0    1560      33       0       0
## 6   0    1120      29       0       1
```

Fit the Logistic Regression of BPD on Birth Weight

- To fit a logistic regression model to the data, we use the `glm()` function.
- Similar to the `lm()` function, `glm()` also requires a model formula.
  - The model formula is `bpd ~ birthwt`.
  - Response `bpd` on left-hand side of the $\sim$ in the formula and explanatory variable `birthwt` on the right-hand side are columns in the dataframe `bpd`.

```
bfit <- glm(bpd~birthwt,data=bpd,family=binomial)
coefficients(bfit)
```

```
## (Intercept)     birthwt
##  4.03429128 -0.00422914
```

- To three significant digits, the estimated parameters in the logistic regression are $\hat{\alpha} = 4.03$ and $\hat{\beta}_1 = -0.00423$

Software Notes

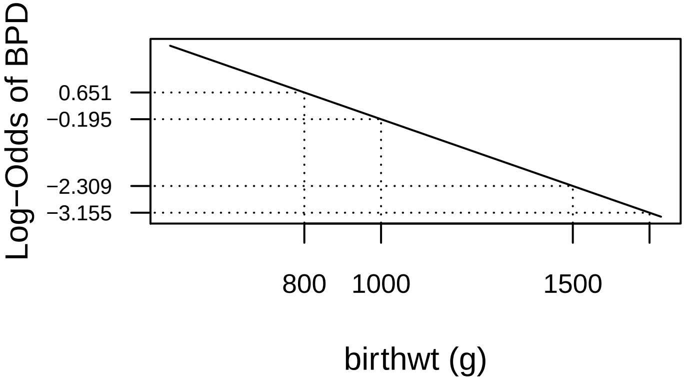
- When we fitted least-squares regression models to data, we used the *linear model* or `lm()` function.
- When we fit logistic-regression models to data, we use the *generalized linear model* or `glm()` function.
- In fact, `glm()` fits several types of models, including least-squares and logistic regression.
  - Specify the type of model with the `family` option. For example,
    - Regular least-squares is `family=gaussian`; same as using `lm()`.
    - Logistic is `family=binomial`.
- **BEWARE:** If you omit the `family=binomial` argument, `glm()` will use the default `gaussian`, and will fit a regular least-squares regression to your data.
  - You will get no warnings and your fitted model will be nonsense.

Interpretation of Birth-Weight Effect

- To three significant digits, $\hat{\beta}_1 = -0.00423$
- Model is for the log-odds, but interpret in terms of the odds.
- We estimate that a one-gram increase in birth weight is associated with a 0.00423 decrease in the log-odds of BPD.
- Report: "We estimate that a one-gram increase in birth weight is associated with a $e^{-0.00423} = 0.996$-fold change in the odds of BPD."
- As one-gram units are too fine-grained, can work with a 100-gram increase in birth weight ...
  - Then we estimate that a 100-gram increase in birth weight is associated with a $100 \times 0.00423 = 0.423$ change in the log-odds of BPD.
  - Report: "We estimate that a 100-gram increase in birth weight is associated with a $e^{-0.423} = 0.655$-fold change in the odds of BPD."

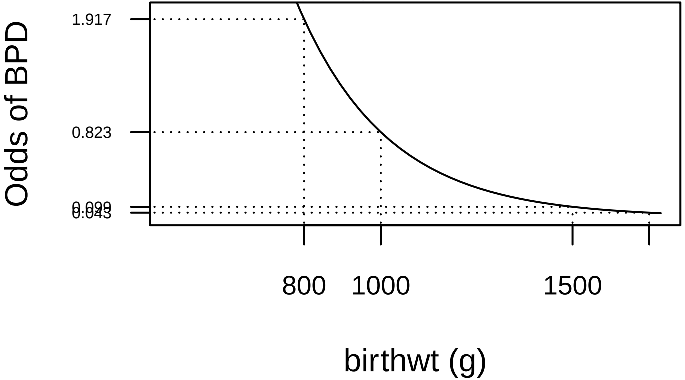
Log-Odds of BPD *vs.* Birthweight

- The logistic-regression model specifies a straight-line relationship between the log-odds of BPD and `birthwt`.



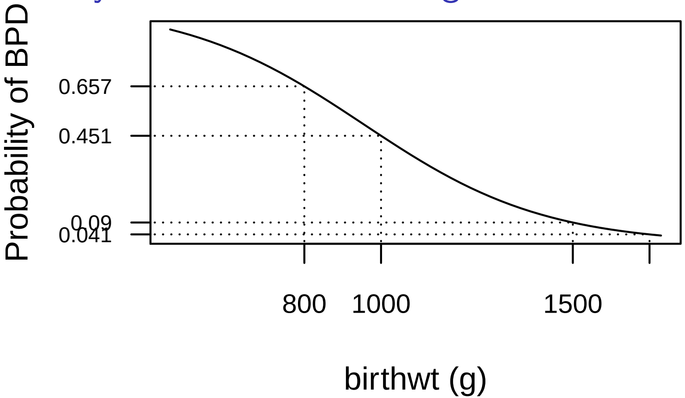
- E.G.: A 200g increase in `birthwt` is associated with an estimated $200 \times \hat{\beta}_1 = 200 \times -0.00423 = -0.846$ change in log-odds of BPD.
  - From plot, estimated log-odds of BPD in an 800g baby is 0.651.
  - So, for a 1000g baby, it is $0.651 - 0.846 = -0.195$

Odds of BPD *vs.* Birthweight



- Exponeniate to get odds. E.G.A 200g increase in `birthwt` is associated with an estimated $e^{200\times -0.00423} = e^{-0.846}$ or 0.429-fold change in the odds of BPD.
  - From plot, estimated odds of BPD in an 800g baby are $e^{0.651} = 1.92$.
  - For a 1000g baby, the odds are $e^{0.651-0.846} = e^{-0.195} = 0.823$

Probability of BPD *vs.* Birthweight



- Saw that estimated log-odds of BPD in an 800g and 1000g baby are, respectively, 0.651 and $0.651 - 0.846 = -0.195$.
  - Therefore, corresponding probabilities of BPD are $e^{0.651}/(1 + e^{0.651}) = 0.657$ for 800g babies and $e^{-0.195}/(1 + e^{-0.195}) = 0.451$ for 1000g babies.

Predicted Log-Odds and Probability of BPD

- We can use the `predict()` function to estimate the log-odds or the probability of the outcome at new values of the explanatory variable.
- The range of `birthwt` (in grams) in the `bpd` dataset is:

```
range(bpd$birthwt)
```

```
## [1]  450 1730
```

- Let's consider new values of `birthwt` towards the extremes of this range, for values 450.5g and 1729.5g

```
newdat <- data.frame(birthwt = c(450.5,1729.5))
library(dplyr)
newdat <- mutate(newdat,
          logodds = predict(bfit,newdata=newdat,type="link"),
          probability = predict(bfit,newdata=newdat,type="response"))
newdat
```

```
##   birthwt   logodds probability
## 1   450.5  2.129064  0.89369610
## 2  1729.5 -3.280006  0.03626351
```

Software Notes

In the above calls to `predict()`:

- specifying the `type` argument as **`type=link`** requests predictions on the scale of the linear predictor;
  - i.e. on the **log-odds scale**,
  - possible values of the log-odds are between $-\infty$ and ∞.

- specifying the `type` argument as **`type=response`** requests predictions on the scale of the response;
  - i.e. on the **probability scale**,
  - possible values are between 0 and 1.

Fitting a Logistic Regression to Case-Control Data

- The study of low-birthweight babies takes a simple random sample from a hospital ICU to see which babies have BPD.
- But what if, instead, we had a case-control study.
  - A case-control study does not take a SRS from the population but rather separate SRS's from cases and from controls.
  - Cases are typically over-sampled relative to their frequency in the population.
- This is called *biased sampling* and the case-control study design is called a *biased sampling design*.
- The biased sampling leads to biased estimates of the intercept parameter α in the linear predictor and therefore of the log odds, odds and probabilities.
  - We can't estimate any of these on an absolute scale.
- Fortunately, we **can** estimate the *changes* in the log odds and odds because estimates of the slope parameter β_1 turn out to be unbiased.

- Since the estimates of β_1 are not biased by the case-control sampling:
  - $\hat{\beta}_1$ can still be interpreted as the estimated effect of a one-unit increase in X_1 on the log-odds of the disease outcome.
  - $e^{\hat{\beta}_1}$ can still be interpreted as the estimated odds-ratio describing the multiplicative change resulting from a one-unit increase in X_1.
- The association between the binary disease outcome Y and the explanatory variable X_1 is our main interest, and $e^{\hat{\beta}_1}$ estimates an odds-ratio that describes this association.