Analysis of binary outcomes and logistic regression

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Eric S. Kawaguchi

Division of Biostatistics and Epidemiology
Department of Population and Public Health Sciences
University of Southern California

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Binary Outcomes

- $Y = 1$ if an event (i.e. outcome of interest) occurs and $Y = 0$ if it does not occur.
  - Might be inherently dichotomous: Dead/alive; Asthmatic/Non-asthmatic; Pass/Fail
  - Or can be created from a continuous variable: $Y = 1$ if SBP ≥ 140 mmHG and $Y = 0$ is SBP < 140 mmHG.
- Logistic regression is the most commonly-used regression model for binary outcomes.
- Goal of logistic regression is to identify if there is an association between X (set of predictors/covariates) and the Y (the binary outcome).

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Binary Outcomes and Proportions

- With $Y \in \{0, 1\}$, we are interested in the proportion of events;
- Population proportion is often defined as p;
- Sample proportion: $\hat{p}$:

$$\begin{aligned}\hat{p} &= \frac{\#\text{ of observations with } Y = 1}{\text{Total } \#\text{ of observations in our sample}} \\ &= \frac{\sum_{i=1}^{N} Y_i}{N} = \bar{Y}.\end{aligned}$$

  where N is the sample size and Y_i is the outcome for the ith individual.
- Second equality holds ONLY if $Y \in \{0, 1\}$, which is the typical coding.

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Binary Outcomes and Proportions

- The population proportion (p) is estimated by the sample proportion ($\hat{p}$).
- Assuming a random sample, the sample proportion is unbiased with estimated variance $\widehat{Var(\hat{p})} = \hat{p}(1-\hat{p})/N$.
- Given a "large enough N", a 95% confidence interval (CI) for $\hat{p}$ is given by:

$$\hat{p} \pm 1.96 \times \sqrt{\hat{p}(1-\hat{p})/N}.$$

- How large is "large enough"?
- One rule-of-thumb is $Np(1-p) > 5$.
- Exact methods exist when this condition is not met.

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Example: Children's Health Study (CHS) Data

- Outcome of interest: Asthma (Yes / No)
- Out of 996 children, 209 have reported asthma.
- $\hat{p} = 209/996 = 0.21$ (or 21%);
- A 95% confidence interval for $\hat{p}$ is (0.185, 0.235)

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Association Between Binary X and Binary Y

- We are interested in seeing if there is an association between biological sex (X) and asthma (Y).
- We can use a contingency table to look at associations between a categorical Y and categorical X variable.
  - When X and Y are binary we have a 2×2 table

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Association Between Binary X and Binary Y

- 2×2 tables have the following form:

	$Y = 0$	$Y = 1$	Total
$X = 0$	a	b	$a + b$
$X = 1$	c	d	$c + d$
Totals	$a + c$	$b + d$	N

- An association between X and Y means the proportion/frequency of the event $(Y = 1)$ "differs" between $X = 0$ and $X = 1$.

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Association Between Binary X and Binary Y

- CHS Data:

X/Y	No	Yes	Total
Female	418	99	517
Male	369	110	479
Totals	787	209	996

- Frequency of asthma among females: $99/517 \approx 0.19$

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Association Between Binary X and Binary Y

- CHS Data:

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Female	418	99	517
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- Frequency of asthma among females: $99/517 \approx 0.19$
- Frequency of asthma among males: $110/479 \approx 0.23$

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Association Between Binary X and Binary Y

- CHS Data:

X/Y	No	Yes	Total
Female	418	99	517
Male	479	110	479
Totals	787	209	996

- Frequency of asthma among females: $99/517 \approx 0.19$
- Frequency of asthma among males: $110/479 \approx 0.23$
- **Question: Is there an association between asthma and biological sex?**

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The Odds and Odds Ratio

- Let $p = \Pr(Y = 1)$ and $1 - p = \Pr(Y = 0)$.
- The odds (of an event occurring) is defined as $p/(1 - p)$ and can be estimated by $\hat{p}/(1 - \hat{p})$.
- Some examples:
  - The odds of getting heads with a fair coin are $0.5/0.5 = 1$.
  - The odds of winning the lottery jackpot are 1 in 3.5 million.
  - "May the odds be ever in your favor" -Effie Trinket
- Events range between $\{0, 1\}$;
- Probabilities/frequencies/proportions range between $[0, 1]$;
- Odds range between $[0, \infty)$.

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The Odds and Odds Ratio

- The odds ratio is a ratio of two odds
- Odds ratio (for binary $X \in \{0, 1\}$):

$$OR = \frac{\text{Odds of } Y = 1 \text{ when } X = 1}{\text{Odds of } Y = 1 \text{ when } X = 0} = \frac{\frac{p_1}{(1-p_1)}}{\frac{p_0}{(1-p_0)}}$$

- The odds that Y will occur ($Y = 1$) when $X = 1$ compared to the odds that Y will occur when $X = 0$.

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The Odds and Odds Ratio

Strength of association:

- $OR = 1$: Odds of $Y = 1$ are the same for $X = 0$ and $X = 1$ (no association between X and Y);
- $OR > 1$: Odds of $Y = 1$ are larger for $X = 1$ than for $X = 0$ (positive association between X and Y);
- $OR < 1$: Odds of $Y = 1$ are smaller for $X = 1$ than for $X = 0$ (negative association between X and Y);

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The Odds and Odds Ratio

	$Y = 0$	$Y = 1$	Total
$X = 0$	a	b	$a + b$
$X = 1$	c	d	$c + d$
Totals	$a + c$	$b + d$	N

- The odds ratio is estimated by:

$$\widehat{OR} = \frac{\hat{p}_1/(1-\hat{p}_1)}{\hat{p}_0/(1-\hat{p}_0)} = \frac{ad}{bc}$$

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CHS Example

- The estimated odds of having asthma ($Y = 1$) in females ($X = 0$) is:

$$\hat{p}_0/(1 - \hat{p}_0) = 0.19/0.81 = 99/418 \approx 0.24.$$

- The estimated odds of having asthma ($Y = 1$) in males ($X = 1$) is:

$$\hat{p}_1/(1 - \hat{p}_1) = 0.23/0.77 = 110/369 \approx 0.30.$$

- The odds ratio (males relative to females) is estimated to be:

$$\widehat{OR} = 0.30/0.24 \approx 1.25$$

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CHS Example

- The estimated odds ratio is 1.25.
- Interpretation: The odds of males having asthma is 1.25 times the odds of females having asthma.
- Can construct confidence intervals and test if this odds ratio is significantly different from 1 ($H_0 : OR = 1$) using data from the 2×2 table.
  - χ^2 test (Large n)
  - Fisher's exact test (Small n)

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The Odds Ratio

- Interpretation of the odds ratio is not as straightforward as with a relative risk;
- If the disease is rare, in the general population we are studying, then the odds ratio approximates the relative risk;
- Both odds ratio or relative risk can be directly estimated from a cohort study
- Only the odds ratio can be directly estimated when cases are over represented (case-control study).

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Logistic Regression

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Simple Logistic Regression

- Oftentimes X may be categorical (with more than 2 categories) or continuous:
  - Hard to tabulate the data as with a 2×2 table
- Assume, for now, we only have one covariate/predictor X.
- For simple linear regression, we model $E(Y|X) = \beta_0 + \beta_1 X$, where $E(Y|X)$ is the mean/average value of Y given X.
  - β_0 is the mean value of Y when $X = 0$;
  - β_1 is the change in the mean value of Y for a one-unit change in X.

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Simple Logistic Regression

The simple logistic regression model:

$$\log(\pi(X)) = \log\left(\frac{\Pr(Y=1|X)}{\Pr(Y=0|X)}\right) = \beta_0 + \beta_1 X,$$

- $\pi(X)$ is the odds of $Y = 1$ given X.
- We assume linearity on the *logit* (i.e. log-odds) scale;
- It can be shown that:

$$\Pr(Y=1|X) = \frac{\exp(\beta_0 + \beta_1 X)}{1 + \exp(\beta_0 + \beta_1 X)}.$$

- $f(t) = \frac{\exp(t)}{1+\exp(t)}$ is called the *logistic* function.

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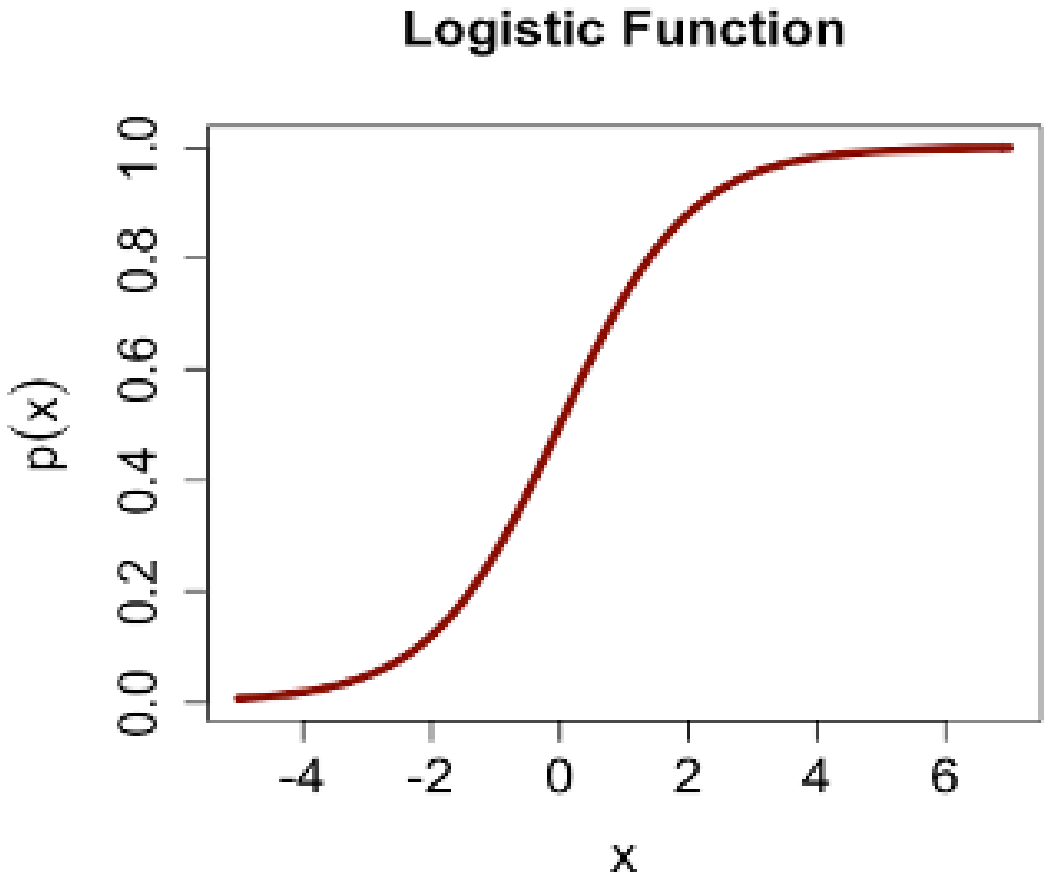
Plot of the logistic function



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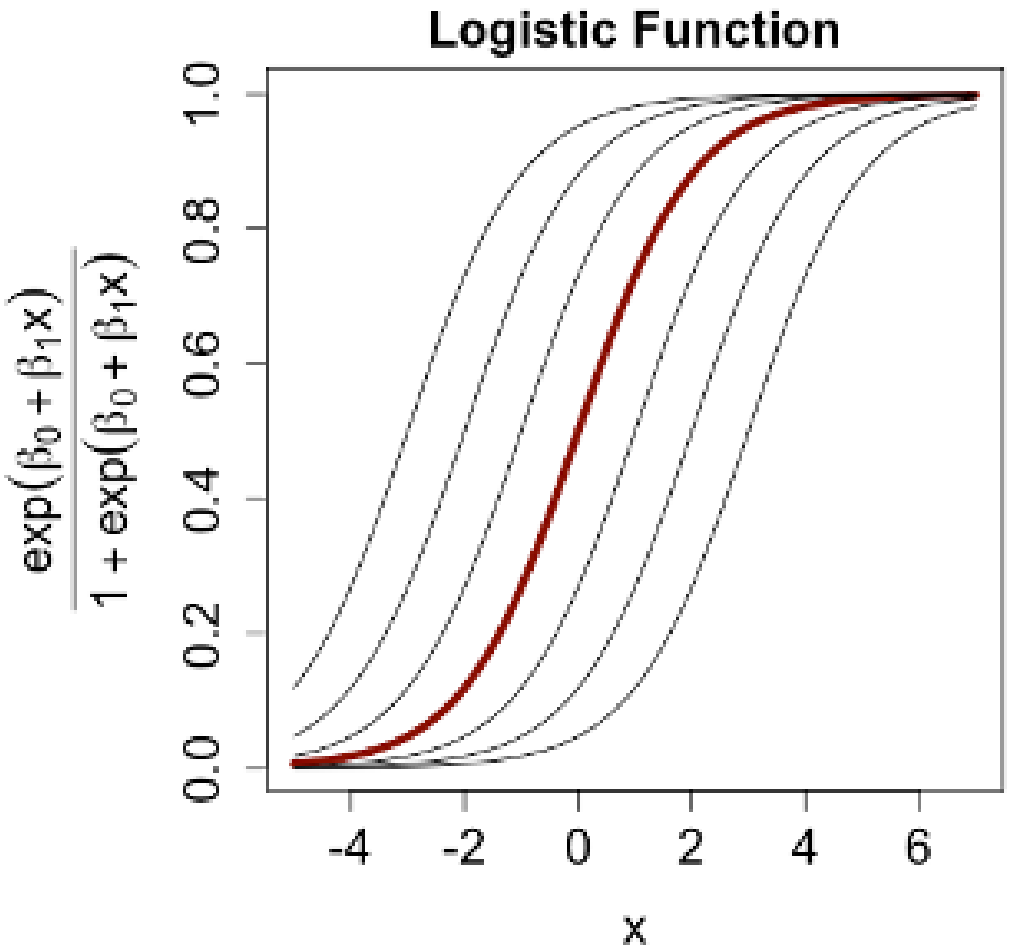
Effect of β_0 on the logistic function



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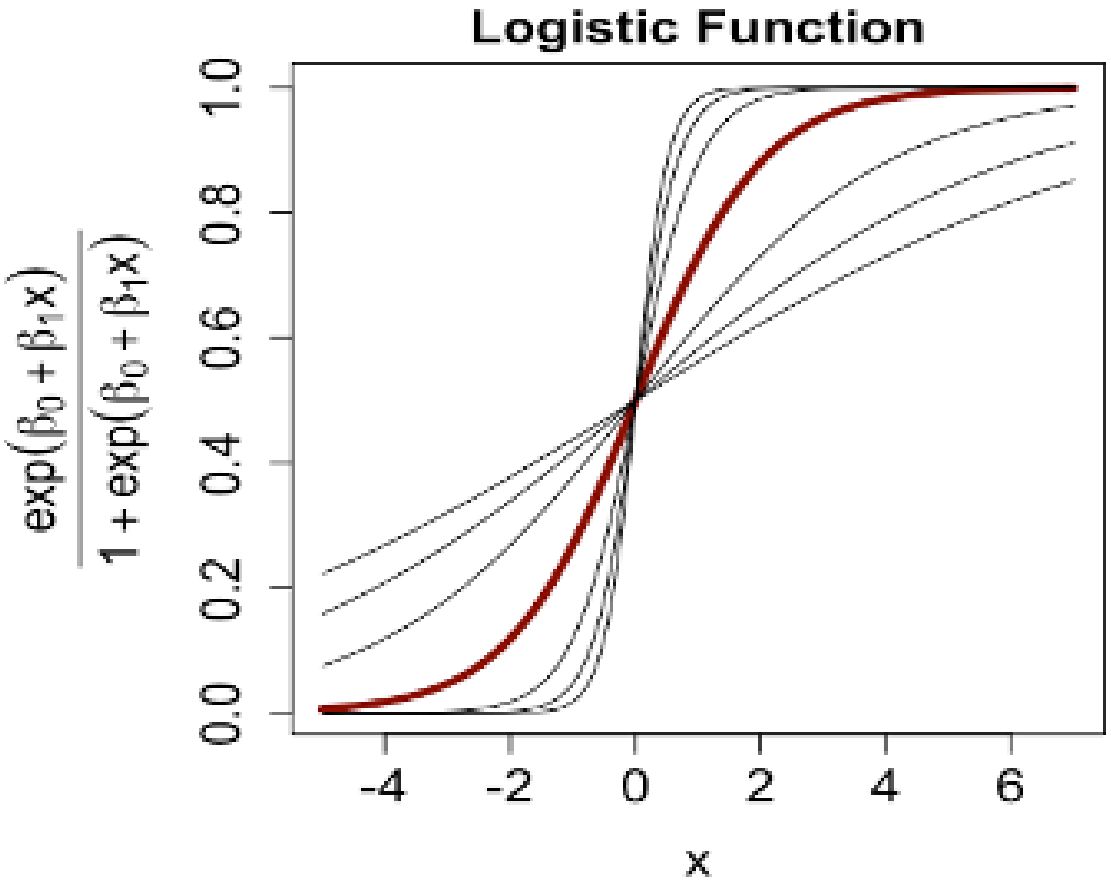
Effect of β_1 on the logistic function



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Interpretation of β_1

- Log odds for $X = x$:

$$\log(\pi(X = x)) = \beta_0 + \beta_1 x$$

- Log odds for $X = x + 1$:

$$\log(\pi(X = x + 1)) = \beta_0 + \beta_1(x + 1) = \beta_0 + \beta_1 x + \beta_1$$

- Note

$$\log\left(\frac{\pi(X = x + 1)}{\pi(X = x)}\right) = \log(\pi(X = x + 1)) - \log(\pi(X = x))$$
$$= (\beta_0 + \beta_1 x + \beta_1) - (\beta_0 + \beta_1 x) = \beta_1$$

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Interpretation of β_1

- Exponentiating both sides:

$$\frac{\pi(X = x + 1)}{\pi(X = x)} = \exp(\beta_1).$$

- The LHS is an odds ratio!
- $\exp(\beta_1)$ corresponds to the odds ratio for a 1-unit increase in X;
- When X is binary, $\exp(\beta_1)$ is the odds ratio of the two groups.

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Interpretation of β_0

- Log odds for $X = 0$:

$$\log(\pi(X = 0)) = \beta_0 + \beta_1 \times 0 = \beta_0$$

- Exponentiating both sides:

$$\pi(X = 0) = \exp(\beta_0).$$

- Binary X: The odds that Y will occur for the reference group
  - If X is biological sex and $X = 0$ codes females, then it's the odds that Y will occur for females.
- Continuous X: The odds that Y will occur when $X = 0$.
  - May not have a meaningful interpretation for continuous X.
  - If X is age, then it's the odds that Y will occur at age 0.

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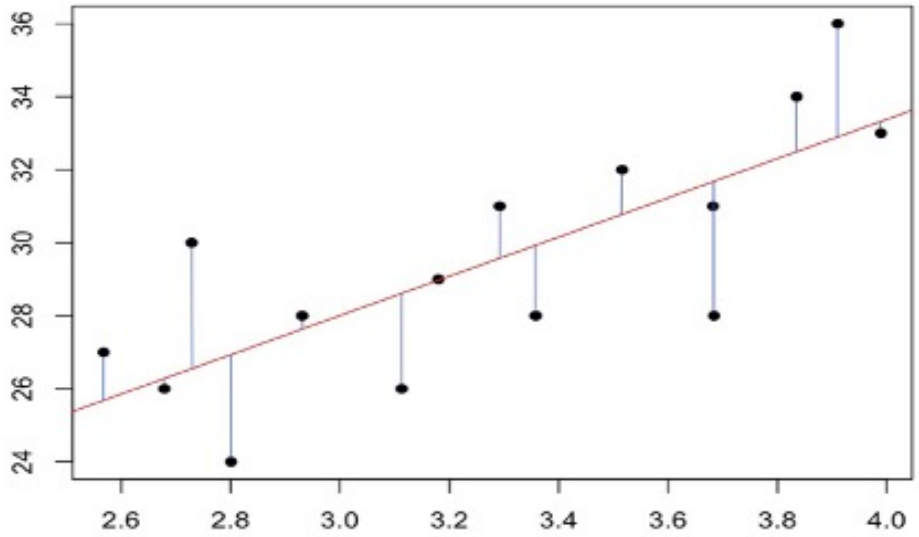
Estimation of β_0, β_1

- In linear regression, the coefficients are estimated by least squares:

$$\arg\min_{\beta_0,\beta_1} \left\{ -\frac{1}{2} \| Y - (\beta_0 + \beta_1 X) \|_2^2 \right\}.$$

- The above formula is equivalent to finding the line that best fits the observed data: Minimizes the sum of the squared vertical distances from the observations to the line.



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Estimation of β_0, β_1

- In logistic regression we estimate β_0 and β_1 (and their corresponding standard errors) by minimizing an alternative measure of distance between the points *to the logistic curve*.
- This method is called *maximum likelihood estimation*.

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Hypothesis testing

- $\beta_1/\exp(\beta_1)$ quantifies the association between X and Y;
- We want to test if this association is statistically significant.
- The null hypothesis $H_0 : OR = 1$ or equivalently $H_0 : \beta_1 = 0$.
- One way to test this hypothesis is to compare the test statistic

$$Z = \frac{\hat{\beta}_1}{\widehat{se}(\hat{\beta}_1)}$$

  against the standard normal distribution $\mathcal{N}(0, 1)$.
- We reject H_0 if Z is large, or equivalently, if the p-value is small.

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Logistic Regression in R

- Logistic regression (logit model) can be fit in R used the `glm()` function.
- glm: Generalized linear model (will discuss later)

```
glm(y ~ x, family = "binomial", data = df)
```

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Binary X

```
lr_sex <- glm(asthma ~ sex, family="binomial", data=chs)
summary(lr_sex)
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -1.4404     0.1118 -12.886   <2e-16 ***
sexM          0.2300     0.1559   1.476     0.14
```

- $\hat{\beta}_1 = \exp(0.23) = 1.258$. p-value $= 0.14$, not statistically significant at the $\alpha = 0.05$ level;
- $\hat{\beta}_0 = \exp(-1.4404) = 0.236$

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CHS Example

From 2×2 table:

X/Y	No	Yes	Total
Female	418	99	517
Male	369	110	479
Totals	787	209	996

- $\text{OR} = ad/bc = (418 \times 110)/(99 \times 369) = 1.258$
- $\hat{\pi}_0 = (99/517)/(418/517) = 99/418 = 0.236$

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CHS Example

From 2×2 table:

X/Y	No	Yes	Total
Female	418	99	517
Male	369	110	479
Totals	787	209	996

- OR $= ad/bc = (418 \times 110)/(99 \times 369) = 1.258$
- $\hat{\pi}_0 = (99/517)/(418/517) = 99/418 = 0.236$
- Same results as the logistic regression model!

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Continuous X

```
lr_age <- glm(asthma ~ age, family = "binomial", data=chs)
summary(lr_age)

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   0.7521     1.9465   0.386    0.699
age          -0.1364     0.1278  -1.067    0.286
```

- $\hat{\beta}_1 = \exp(-0.136) = 0.87$. A 1-year increase in age is associated with a decrease in the odds of having asthma
- $\hat{\beta}_0 = \exp(0.752) = 2.12$

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Multivariable logistic regression

- For multivariable logistic logistic regression:

$$\log(\pi(X)) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_p X_p,$$

  where $X = (X_1, X_2, \ldots, X_p)$.
- $\hat{\beta}_1$: Log-odds ratio for Y associated with a one-unit change in X_1 while keeping all other variables (e.g. $X_2, \ldots, X_p$) fixed.
- $\hat{\beta}_2$: Log-odds ratio for Y associated with a one-unit change in X_2 while keeping all other variables (e.g. $X_1, X_3, \ldots, X_p$) fixed.
- And so on...

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Multivariable logistic regression

```
lr_sex_age = glm(asthma ~ sex + age,
                 family = "binomial", data = chs)
summary(lr_sex_age)
```

```
Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   0.9373     1.9517   0.480    0.631
sexM          0.2491     0.1568   1.589    0.112
age          -0.1567     0.1285  -1.219    0.223
```

- $\hat{\beta}_{age} = \exp(-0.1567) = 0.85$.
- $\hat{\beta}_{age}$ is the estimated log-odds ratio for asthma associated with a change of one year increase in age but keeping biological sex category the same (M or F).

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In summary

- Logistic regression is the most commonly-used regression model for binary outcomes;
- Coefficient estimates are interpreted as log odds-ratios;
- Odds ratios can be estimated in all study designs (case-control, cross sectional, cohort, etc.);
- When the disease is rare in the general population, the odds ratio approximates the relative risk ratio.

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Some food for thought

- Logistic regression (in some form) can be used for polychotomous outcomes (nominal or ordinal).
- Logistic regression is a *generalized linear model* (GLM).
  - GLMs are typically used when trying to model non-normal, non-continuous data.
  - $g(x) = \log(x/(1-x))$ is known as a link function.
  - The log-odds interpretation comes from the use of this specific link function
  - Different outcomes will require different link functions (and different interpretations!)

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Aside: Why use the logit function?

- In "linear" regression,

$$E(Y|X) = \Pr(Y = 1|X) = \beta_0 + \beta_1 X = \eta$$

- We provide no restriction for β_0 and β_1.
- While η can be ANY real value, $E(Y|X) \in [0, 1]$.
- Can lead to nonsensical results (Predicted/estimated probabilities less than 0 or greater than 1).
- **Note: Just because models can run, doesn't mean the results are meaningful.**

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Aside: Why use the logit function?

- We want a function of $g(\cdot)$, so that $g[E(Y|X)] = g[\Pr(Y = 1|X)]$ can take on ANY real value.
- What about $g(x) = \log(\frac{x}{1-x})$?
  - $g(\cdot)$ the log-odds (logit function).

$$\log(\pi(X)) = \log\left(\frac{\Pr(Y = 1|X)}{\Pr(Y = 0|X)}\right) = \beta_0 + \beta_1 X$$

$$\Rightarrow \Pr(Y = 1|X) = \frac{\exp(\beta_0 + \beta_1 X)}{1 + \exp(\beta_0 + \beta_1 X)}.$$

- Other functions for $g(\cdot)$ have been proposed.

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