BST 210 Lab: Week 6
Concluding Linear Regression & Motivating Logistic Regression

Multiple linear regression models allow us to assess the relationship between a continuous outcome Y and a set of predictors $X_1, \ldots, X_p$. One (now very familiar!) way of writing this mathematically is

$$E[Y|X_1, \ldots, X_p] = \beta_0 + \beta_1 \cdot X_1 + \ldots + \beta_p \cdot X_p.$$

For the first a few weeks of class, we've mainly focused on how to construct this model and select the predictors $X_1, \ldots, X_p$.

1 Hypothesis Testing and Linear Models

But we also want to be able to use this model to draw statistical conclusions about our predictors $X_1, \ldots, X_p$ and their relationship with Y! There are several main types of hypotheses that we may want to test:

- $H_0 : \beta_j = 0$ for a specific predictor X_j
- $H_0 : \beta_j = \beta_k$ for two predictors X_j and X_k
- $H_0 : \beta_i = \beta_j = \beta_k = 0$ for a collection of predictors $\{X_i, X_j, X_k\}$
- $H_0 : \beta_1 = \beta_2 = \ldots = \beta_p = 0$ for all predictors $\{X_i, X_j, X_p\}$

$\boxed{H_0 : \beta_j = 0}$

Here, we want to assess whether a statistically significant relationship between X_j and Y exists. In other words, we want to answer the question: is X_j a statistically significant predictor of our outcome, Y?

Formal Hypothesis:	$H_0 : \beta_j = 0$ versus $H_1 : \beta_j \neq 0$
Test Statistic:	$t = \frac{\hat{\beta}_j - 0}{\text{s.e.}(\hat{\beta}_j)} \sim t_{n-(p+1)}$
Confidence Interval:	$\hat{\beta}_j \pm t_{n-(p+1),1-\frac{\alpha}{2}} \cdot \text{s.e.}(\hat{\beta}_j)$

$\boxed{H_0 : \beta_j = \beta_k}$

Here, we want to assess whether a linear combination of the βs is significantly different than zero.

Formal Hypothesis:	$\big(H_0 : \beta_j = \beta_k$ versus $H_1 : \beta_j \neq \beta_k\big)$ or $\big(H_0 : \beta_j - \beta_k = 0$ versus $H_1 : \beta_j - \beta_k \neq 0\big)$
Test Statistic:	$t = \frac{(\hat{\beta}_j - \hat{\beta}_k) - 0}{\text{s.e.}(\hat{\beta}_j - \hat{\beta}_k)} \sim t_{n-(p+1)}$
Confidence Interval:	$(\hat{\beta}_j - \hat{\beta}_k) \pm t_{n-(p+1),1-\frac{\alpha}{2}} \cdot \text{s.e.}(\hat{\beta}_j - \hat{\beta}_k)$

This type of hypothesis test is also particularly useful in the setting where X_k is an interaction term, and where $\beta_j + \beta_k$ is the slope for the association between X_j and Y within a particular level of an effect modifier!

Formal Hypothesis:	$H_0 : \beta_j + \beta_k = 0$ versus $H_1 : \beta_j + \beta_k \neq 0$
Test Statistic:	$t = \frac{(\hat{\beta}_j + \hat{\beta}_k) - 0}{\text{s.e.}(\hat{\beta}_j + \hat{\beta}_k)} \sim t_{n-(p+1)}$
Confidence Interval:	$(\hat{\beta}_j + \hat{\beta}_k) \pm t_{n-(p+1),1-\frac{\alpha}{2}} \cdot \text{s.e.}(\hat{\beta}_j + \hat{\beta}_k)$

$\boxed{H_0 : \beta_i = \beta_j = \beta_k = 0}$

Here, we want to determine whether a particular subset of covariates—here X_i, X_j, and X_k—contributes significantly to our model. So we want to test whether, after accounting for all other covariates, X_i, X_j and X_k collectively explain a significant proportion of the remaining variability in Y.

We can equivalently view the test of the null hypothesis $H_0 : \beta_i = \beta_j = \beta_k = 0$ as comparing the fit of the **reduced model** without the covariates X_i, X_j, and X_k,

$$E[Y|X] = \beta_0 + \beta_1 \cdot X_1 + \ldots + 0 \cdot X_i + \ldots + 0 \cdot X_j + \ldots + 0 \cdot X_k + \ldots + X_p,$$

to the fit of the **full model**

$$E[Y|X] = \beta_0 + \beta_1 \cdot X_1 + \ldots + \beta_p \cdot X_p.$$

So we can summarize this test by:

Formal Hypothesis:	$H_0 : \beta_i = \beta_j = \beta_k = 0$ versus H_1 : at least one of β_i, β_j and β_k is not 0
or	
Formal Hypothesis:	$\big(H_0$: the reduced model is sufficient$\big)$ versus $\big(H_1$: the full model is preferred$\big)$
Test Statistic:	$F = \frac{(SSE_{reduced} - SSE_{full})/3}{SSE_{full}/(n-(p+1))} \sim F_{3,n-p-1}$

where $SSE = \sum_{i=1}^{n}(y_i - \hat{y}_i)^2$ is the error sum of squares, this is also called RSS (residual sum of squares), but is different from SSR (regression sum of squares). In this lab, we will use SSE throughout.

We can fairly easily generalize this to a subset of the covariates of size r. *What would the test statistic and its distribution be in that case?*

In fact, we can use this kind of F-test (also known as an ANOVA) to compare any two **nested** models. *What would the test statistic and its distribution be in that case?*

$\boxed{H_0 : \beta_1 = \ldots = \beta_p = 0}$

Here, we want to determine whether the mean model, $E[Y|X] = \beta_0$, is alone sufficient to explain the variability in our outcome Y.

Formal Hypothesis: $H_0 : \beta_1 = \ldots = \beta_p = 0$ versus H_1 : at least one of $\beta_1, \ldots, \beta_p$ is not 0

Test Statistic: $F = \frac{(SSE_{reduced} - SSE_{full})/p}{SSE_{full}/(n-(p+1))} = \frac{(SST - SSE_{full})/p}{SSE_{full}/(n-(p+1))} \sim F_{p,n-p-1}$

2 Hypothesis Testing: Example

For this example, we'll once again use a subset of the Framingham Heart Study, found in the file `framingham.dta`. A full summary of all the covariates in the dataset is given in Table 1 below. In this example, we'll be using total cholesterol (`totchol`) as our outcome of interest.

Let's suppose that we arrived at the model

$$E[\texttt{totchol}|X] = \beta_0 + \beta_1 \cdot \texttt{sex} + \beta_2 \cdot \texttt{age} + \beta_3 \cdot \texttt{diabp} + \beta_4 \cdot \texttt{cigpday} + \beta_5 \cdot \texttt{bmi}. \quad (1)$$

and would like to now perform inference on it. We'll start by fitting this model in Stata!

```
* Reading in the dataset
cd "your_path_here"
use "framingham.dta", clear

* Removing all missing observations
foreach v of var * {
drop if mi(‘v’)
}

* Fitting the regression model
regress totchol sex age diabp cigpday bmi
```

Table 1: Framingham Heart Study - Relevant Variables

Variable	Description
totchol	Serum Total Cholesterol (mg/dL)
sex	Participant sex - 1 = Men, 2 = Women
age	Age at exam (years)
sysbp	Systolic Blood Pressure (mean of last two of three measurements) (mmHg)
diabp	Diastolic Blood Pressure (mean of last two of three measurements) (mmHg)
cursmoke	Current cigarette smoking - 1 = Yes, 0 = No
cigpday	Number of cigarettes smoked each day
bmi	Body Mass Index, weight in kilograms/height meters squared
diabetes	Diabetic according to criteria of first exam treated or casual glucose of 200 mg/dL or more
prevhyp	Prevalent Hypertensive. Subject was defined as hypertensive if treated or, if second exam at which mean systolic was >=140 mmHg or mean Diastolic >=90 mmHg
prevchd	Prevalent Coronary Heart Disease

Source	SS	df	MS	Number of obs	=	2,223
				F(5, 2217)	=	52.95
Model	471898.722	5	94379.7445	Prob > F	=	0.0000
Residual	3951303.33	2,217	1782.27485	R-squared	=	0.1067
				Adj R-squared	=	0.1047
Total	4423202.06	2,222	1990.63999	Root MSE	=	42.217

totchol	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
age	1.322259	.1075758	12.29	0.000	1.111299	1.533219
sex	8.612305	1.97406	4.36	0.000	4.741105	12.48351
diabp	.381843	.0821498	4.65	0.000	.2207443	.5429417
cigpday	.1805195	.0833422	2.17	0.030	.0170825	.3439565
bmi	.5199803	.2029924	2.56	0.010	.1219052	.9180554
_cons	108.9981	8.579065	12.71	0.000	92.17427	125.822

Let's first test to see whether or not the mean model alone (intercept only) is sufficient to explain the variability in total cholesterol. *What are our null and alternative hypotheses?*

```
* Performing an F-test (testing all betas equal to 0)
test sex age diabp cigpday bmi
```

```
( 1)  sex = 0
( 2)  age = 0
( 3)  diabp = 0
( 4)  cigpday = 0
( 5)  bmi = 0

       F(  5,  2217) =   52.95
            Prob > F =    0.0000
```

Based on the output above, we reject the null hypothesis that the mean model alone is sufficient to explain the observed variability in total cholesterol ($p < 0.0001$). As such, we conclude that at least one of age, sex, diastolic blood pressure, number of cigarettes smoked per day, and BMI is a significant predictor of total cholesterol. [In Stata, the results of this F-test is always provided as part of the regression output!]

Suppose we want to look at one of those covariates, BMI—and its relationship with total cholesterol—a little more closely. *Using the regression output given above, conduct the t-test*

$$H_0 : \beta_5 = 0 \quad vs \quad H_1 : \beta_5 \neq 0.$$

What do you conclude, and how would you report this conclusion? Also report the 95% confidence interval for this effect.

Another way that we might go about testing whether BMI is a significant predictor of total cholesterol is through an F-test (ANOVA) in which we compare the full model including BMI to the reduced model without BMI. More specifically, we say that the full model is the one fit above,

$$E[\texttt{totchol}|X] = \beta_0 + \beta_1 \cdot \texttt{sex} + \beta_2 \cdot \texttt{age} + \beta_3 \cdot \texttt{diabp} + \beta_4 \cdot \texttt{cigpday} + \beta_5 \cdot \texttt{bmi},$$

while the reduced model is the one without BMI,

$$E[\texttt{totchol}|X] = \beta_0 + \beta_1 \cdot \texttt{sex} + \beta_2 \cdot \texttt{age} + \beta_3 \cdot \texttt{diabp} + \beta_4 \cdot \texttt{cigpday}.$$

We can then directly compare these two models in Stata:

```
* Performing an F-test (testing beta_bmi equal to 0)
test bmi
```

```
 ( 1)  bmi = 0

       F(  1,  2217) =    6.56
            Prob > F =    0.0105
```

What do you notice, if anything, about the results of this test as compared to the results of the t-test for $\beta_5 = 0$?

In fact, it will always be the case that, if $T \sim t_{n-p-1}$, then $T^2 \sim F_{1,n-p-1}$. So the t-test for $\beta_j = 0$ will always give exactly the same conclusions as the F-test comparing the (full) model including X_j to the (reduced) model without X_j!

Finally, suppose that we want to determine whether or not we should add a spline of BMI to our model. *How can we test for whether linear BMI alone (without an additional flexible regression term) sufficiently captures the association between BMI and total cholesterol?*

```
* Making a cubic spline of bmi with 4 knots
mkspline bmis=bmi, cubic nknots(5)

* Fitting the full model (including spline term)
regress totchol age sex diabp cigpday bmi bmis1 bmis2 bmis3 bmis4

* Peforming an F-test (testing whether the slopes of the spline terms equal 0)
test bmis1 bmis2 bmis3 bmis4
```

```
 test bmis1 bmis2 bmis3 bmis4

( 1)  o.bmis1 = 0
( 2)  bmis2 = 0
( 3)  bmis3 = 0
( 4)  bmis4 = 0
      Constraint 1 dropped

      F(  3,  2214) =    9.80
           Prob > F =    0.0000
```

What are our conclusions?

An extra note about hypothesis testing: be aware there is no formal statistical test for the existence of confounding, so you have to check the causal definition with subject matter knowledge and the "10% change in coefficients" is just a rule of thumb. We do have formal statistcal tests for effect modification.

3 Relaxing the Assumptions for Linear Regression

In fitting and performing inference with a linear regression model, we make four assumptions:

1. **L**inearity
2. **I**ndependence
3. **N**ormality of the residuals
4. **E**qual variance (homoskedasticity)

However, in practice, it's rare that all four of these assumptions hold. So that leaves us with the question: if these assumptions are violated, what happens to our OLS estimates, and is there anything we can do to "fix" them?

If our assumption of linearity is incorrect, that means that our model is misspecified, and $E[Y|X_1, \ldots, X_p] \neq \beta_0 + \beta_1 \cdot X_1 + \ldots + \beta_2 \cdot X_p$. *In this scenario, what happens to our OLS estimates and standard errors? Is there anything we can do?*

However, all hope is not lost! *Under what conditions is our OLS estimate $\hat{\beta}$ still unbiased for the true coefficient β?*

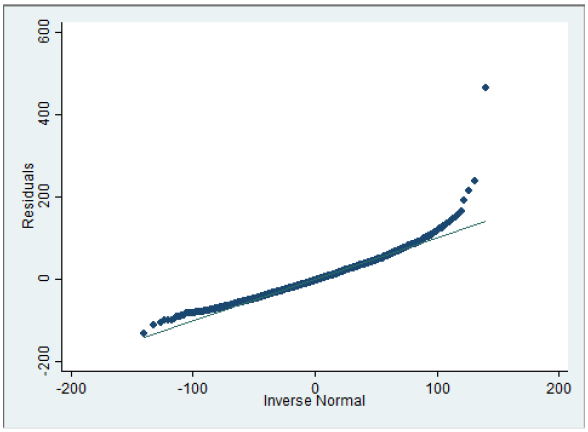
Suppose our model is correctly specified, but that at least one of the other three assumptions is violated. Are our estimates of the standard errors unbiased? If not, what can we do?

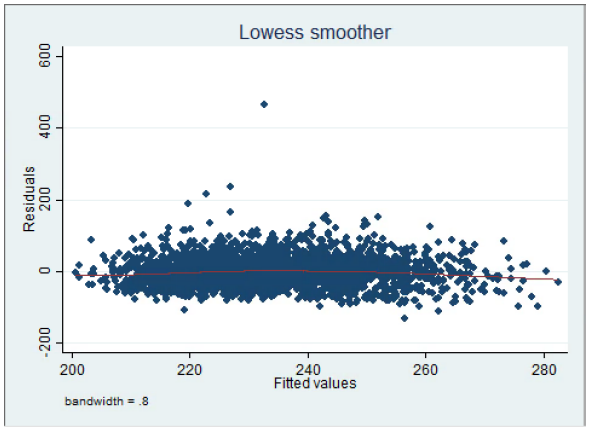
Let's go back to our Framingham Heart data set, and look at some diagnostic plots for regression model (1).

```
* Running Model (1) again
regress totchol age sex diabp cigpday bmi

* Storing the residuals and fitted values
predict lmresid, residuals
predict lmfit

* Creating residual plots for Model (1): qqplot and Lowess curve
qnorm lmresid
lowess lmresid lmfit
```





What do these plots suggest about our LINE assumptions?

Robust standard errors are usually the most helpful when you have unequal variances, but you can use it even when the equal variances assumption holds (it is still valid, but you may lose some efficiency). Let's run a regression with robust standard errors here and compare it to the model using ordinary standard errors.

```
* Running Model (1) again, this time with a robust variance estimator
regress totchol age sex diabp cigpday bmi, vce(robust)
```

```
Linear regression                               Number of obs     =      2,223
                                                F(5, 2217)        =      53.10
                                                Prob > F          =     0.0000
                                                R-squared         =     0.1067
                                                Root MSE          =     42.217
```

totchol	Coef.	Robust Std. Err.	t	P>|t|	[95% Conf.	Interval]
sex	8.612305	2.007778	4.29	0.000	4.674984	12.54963
age	1.322259	.1061529	12.46	0.000	1.11409	1.530429
diabp	.381843	.0810519	4.71	0.000	.2228974	.5407886
cigpday	.1805195	.0793498	2.27	0.023	.0249117	.3361272
bmi	.5199803	.2114899	2.46	0.014	.1052413	.9347193
_cons	108.9981	8.600798	12.67	0.000	92.13165	125.8646

How does this new model with robust standard errors compare to the original fit of Model (1)?

What are some the "trade-offs" of using a more robust variance estimator?

4 Binary Outcomes & Logistic Regression

Often times in public health, we're interested in estimating and modeling some sort of binary ("yes"/"no") outcome, rather than a continuous response. For example, we might be interested in

- Whether a tumor does or does not metastasize
- Whether a patient does or does not have a heart attack
- Whether a child does or does not have asthma

We can think of this binary outcome Y as taking on two distinct values: $Y = 1$ if the event of interest occurs, and $Y = 0$ otherwise. Then we would like to be able to make statements about $E[Y] = P(Y = 1) = p$.

Equivalently, we may also be interested in saying something about the *odds* of Y occurring, where the odds of Y are defined as $P(Y = 1)/P(Y = 0) = p/(1 - p)$.

4.1 Contingency Table Example

Consider the data in the contingency table below, which were collected as part of a study that investigated the effect of parental smoking status (X) on the smoking habits of students in Arizona (Y). The data are taken from the textbook *Categorical Data Analysis*, and can be found on Canvas in the file `smoker.dta` (Agresti 1990).

	At Least One Parent Smokes	Neither Parent Smokes	Total
Student Smokes	816	188	1004
Student Does Not Smoke	3203	1168	4371
Total	4019	1356	5375

What is $p_1 = P(Y = 1|X = 1)$? What about $p_0 = P(Y = 1|X = 0)$?

One measure of effect that we can use to examine the relationship between parental smoking status and student smoking habits is the risk difference: $p_1 - p_0$. Calculate and interpret this quantity.

Another effect measure we discussed in class was the risk ratio. Calculate and interpret the risk ratio for this data.

The last measure of association—and the one that we will use most frequently in this class—is the odds ratio. Calculate and interpret this value.

Construct and report a 95% confidence interval for the odds ratio you found above. Does this confidence interval contain 1? What does that suggest to you?

We can recreate the contingency table found above in Stata by using the following commands:

```
* Reading in the .dta file
use "smoker.dta", clear

* Creating a contingency table for the relationship between student smoking and
* parental smoking
cs ssmoke psmoke [fweight=freq]
```

```
. cs ssmoke psmoke [fweight=freq], or woolf

                |      psmoke
                |   Exposed   Unexposed |      Total
----------------+-----------------------+-----------
          Cases |       816         188 |       1004
       Noncases |      3203        1164 |       4367
----------------+-----------------------+-----------
          Total |      4019        1352 |       5371
                |                       |
           Risk |  .2030356    .1390533 |   .1869298
                |                       |
                |  Point estimate       |  [95% Conf. Interval]
----------------+-----------------------+----------------------
Risk difference |       .0639823        |   .0417378    .0862269
     Risk ratio |       1.460128        |   1.261661    1.689816
Attr. frac. ex. |       .3151286        |    .207394    .4082195
Attr. frac. pop |       .2561205        |
     Odds ratio |       1.577351        |   1.327879    1.873692 (Woolf)
----------------+-----------------------+----------------------
                chi2(1) =    27.25  Pr>chi2 = 0.0000
```

Simple Logistic Regression

In simple logistic regression, we are now interested in modeling a *binary* outcome Y as a function of some predictor variable, X, where X can be either continuous or categorical.

Why is it that we can't use the simple linear regression model $p = E[Y|X] = \beta_0 + \beta_1 \cdot X$ like we did when Y was continuous?

As such, the model we fit for logistic regression is instead in terms of the log odds of Y:

$$\text{logit}(p) = \log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 \cdot X \quad \Longrightarrow \quad p = \frac{\exp\{\beta_0 + \beta_1 \cdot X\}}{1 + \exp\{\beta_0 + \beta_1 \cdot X\}}.$$

What is the intercept term, β_0, estimating? What about e^{β_0}?

For the purposes of this question, let's assume that X is also a binary variable. What is β_1? How do we interpret e^{β_1}?