PM 592 Regression Analysis for Public Health Data Science

Week 6

Confounding & Interaction

1

Confounding & Interaction

Estimating Association

Confounding

Effect Modification

2

Lecture Objectives

- > Describe the two possible goals of regression analysis and how the modeling approach would differ for each.
- > Discern whether a variable could sensibly be a confounder.
- > Assess the extent to which a variable acts as a confounder.
- \succ Specify an interaction term in a linear regression model.
- \succ Interpret continuous-by-categorical and continuous-by-continuous interactions.

1. Review 4	
✓ Shared covariance of independent variables	
✓ The multiple regression model	
✓ Interpretation of multiple regression coefficients	
✓ Interpretation of R ² from a multiple regression model	
✓ Diagnosing collinearity	
✓ Methods for diagnosing outliers and influential points	
4	
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	•
2. Regression: Estimating Association 5	
What is the primary purpose of multiple regression models?	
This depends on your research question!	
1. Estimating Associations.	
 Multiple regression can model the relationship between a dependent variable and a set of independent variables of scientific interest. 	
• The variables are chosen due to hypothesis-driven associations.	
 Covariates are chosen to best capture the true effect of the IV on the outcome. 	
• We include confounding variables (variables that confound the	
relationship between X and Y) and effect modifiers (variables that modify the relationship between X and Y).	
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2. Regression: Estimating Association 6	
When estimating associations:	
The model coefficients reflect the slope adjusting for all other variables in the model.	
The validity of this adjustment is contingent on:	
o The correct covariates being included	
o The covariates being modeled correctly (e.g., correct assumption of	
linearity, interactions modeled correctly)	
With this approach your goal is to model the <u>true</u>	
That and approach your goal is to model the trac	

2. Regression: Estimating Association

What is the primary purpose of multiple regression models?

2. Predicting Outcome

- The main goal isn't to examine a hypothesized association.
- Rather, the main goal is to find the best way to predict outcome.
- Good prediction models use a parsimonious set of independent variables.

With this approach your goal is to find a set of

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2. Regression: Estimating Association

How do we know if an additional variable improves model fit?

1. Extra Sums of Squares Test

ldea: compare the SS of the model with an additional variable vs. the SS of the model without it.

We've already used the this test to determine:

- If a single variable is statistically significant (compared to the null hypothesis)
- If a dummy variable set is statistically significant (i.e., joint significance of all variables)

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2. Regression: Estimating Association

The F-test shown in the output reflects the significant improvement in sum of squares **compared to a model with nothing in it**.

For example, the extra SS (F) test shows that the model below is significantly better than a model with no predictors.

<pre>> m1 <- lm(enjoy_ex1 ~ intervention, data = places) > summary(m1)</pre>
Call: lm(formula = enjoy_ex1 ~ intervention, data = places)
Residuals: Min 1Q Median 3Q Max -3.273 -1.273 -0.079 1.727 3.115
Coefficients: Estimate Std. Error t value Pr(> t)
(Intercept) 3.88507 0.13748 28.259 <2e-16 ***
intervention 0.19396 0.09612 2.018 0.044 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Overall, this model has significant predictive ability.

Residual standard error: 1.854 on 586 degrees of freedom (27 observations deleted due to missingness)
Multiple R. squared: 0.066091, Adjusted R. squared: 0.005207
F-statistic: 4.072 on 1 and 586 DF, p-value: 0.04405

2. Regression: Estimating Association	10
2. Regression: Estimating Association What does a null (unconditional) model lool > m0 <- lm(enjoy_ex1 ~ 1, data = places) > summary(m0) Call: lm(formula = enjoy_ex1 ~ 1, data = places) Residuals: lm(formula = enjoy_ex1 ~ 1, data = places) Residuals: lm(formula = enjoy_ex1 ~ 1, data = places) Residuals: Residuals: Residuals: Residuals: Signif. codes: 0 1157 1.8843 2.8843 Coefficients: Coefficients: Signif. codes: 0 1187 0.8966 53.69 (2e-16 ***) Signif. codes: 0 1187 0.8966 53.69 (2e-16 ***) Signif. codes: 0 1187 0.891 (119 0.89 (119 0.8) (119 0.91 1)	
Residual standard error: 1.859 on 587 degrees of freedom (27 observations deleted due to Bissingness)	no r test.

2. Regression: Estimating Association Recall the Extra Sums of Squares F-test statistic is given by: $\frac{SSE_0 - SSE_1}{F(DFE_0 - DFE_1, DF_1)} = \frac{\frac{SSE_0 - SSE_1}{DFE_0 - DFE_1}}{\frac{SSE_1}{DFE_1}}$ $> \frac{SSE_0 - SSE_1}{DFE_0 - DFE_1}$ $> \frac{SSE_1}{DFE_1}$ $= \frac{SSE_1}{DFE_1}$

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2. Regression: Estimating Association

In this past example we used the ${\sf Extra}\,{\sf SS}$ test to determine how well our model fit, compared to a null model.

We can also use the Extra SS test to determine if the addition of an independent variable – or multiple independent variables – improves our model.

This is especially useful when examining the effect of adding multiple independent variables.

Note: when performing this test, the models must be nested (e.g., the model with intervention is nested within the model with intervention + factor(race))

2. Regression: Estimating Association	13
Suppose we want to test the effect of the ac variables).	ddition of categorical race (4 dummy
> m2 <- lm(enjoy_ex1 ~ intervention + racecat, data = places) > summary(m2)	M1 is the nested model with just intervention.
Call: lm(formula = enjoy_ex1 ~ intervention + racecat, data = places)	M2 is the full model with intervention and
Residuals: Min 10 Median 30 Max -3.483 -1.341 -0.126 1.659 3.416	categorical race.
Coefficients: Estimate Std. Error t value Pr() t)	
(Intercept) 3.91121 0.17624 22.935 (2e-16 intervention 0.21479 0.00991) 2.150 0.8320 0 naccatAsian nac	
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1	
Residual standard ergor: 1,851 on 582 degrees of freedom (27 observations deleted due to missingness) Multiple R-squaped: 0,801726, Adjusted R-squared: 0,008817 F-stalistic: 2,7044 on 5 and 522 DF, p-value: 0,07085	2014 – 1993 21
> anova(mī, mZ) Analysis of Variance Table	$F_{(586-582,58)} = \frac{\frac{2014-193}{586-582}}{1993} = \frac{\frac{21}{4}}{1993} = 1.53$
Model 1: enjoy ext ~ intervention	1995 582 582

		Association

The Extra SS test is quite useful when determining if a set of variables improves the model.

When only one variable is added to the model, this test will mirror the Wald (t) test.

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2. Regression: Estimating Association

Recap

- Models can be created either for 1) estimating associations or 2) prediction.
- The Extra Sums of Squares test can be used to determine if additional variable(s) improve the model.
- This test must be used on nested models (i.e., the parameters in the nested model must also appear in the full model).

۷.	Regression:	Estimating	Association

Recap

- > Explain the difference between an association model and a prediction model
- ➤Compute the Extra Sums of Squares test, including the F-statistic, degrees of freedom, and p-value
- ➤ Explain what the Extra Sums of Squares test is testing

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3. Confounding

Confounding

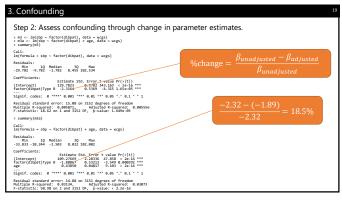
• When the association of interest between the outcome variable (Y) and a specific independent variable (X) is distorted by the influence of a third (or more) variable.

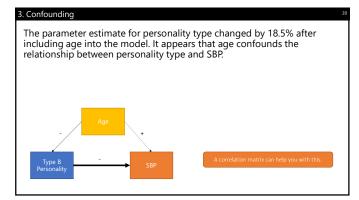
Criteria

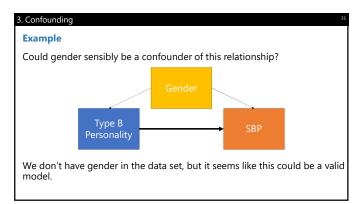
- 1. Change in effect estimate criterion: the adjusted estimate is at least 10-20% different than the unadjusted estimate AND
- 2. The variable must sensibly be able to be a cause of both X and Y

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Example Is the relationship between personality type and SBP confounded by age? Step 1: Can age reasonably be a confounder of this relationship? Age Type B Personality SBP







3. Confounding	•
How do we pick confounders to examine? (Not a simple question!)	
• Philosophically - Sometimes variables are <i>a priori</i> included automatically because they have traditionally been examined as confounders (e.g., age,	
gender, race).	
Demographic variables are most likely to be confounders.	
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3. Confounding 23	
How do we pick confounders to examine? (Not a simple question!)	
• Statistically – We sometimes don't have adequate information to choose all potential confounders.	
• In the CHS study, variables such as pets, carpet type, air conditioning, multivitamin use, etc. can be potential confounders of relationships with	
lung function.	
 Including a large number of "adjustment" variables can pose several problems. 	
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3. Confounding	
Problems with Adding Several Adjustment Variables	
When individuals are missing on certain adjustment variables, those individuals may be eliminated from the analysis, reducing power and	
potentially biasing effect estimates.	

3. Confounding

Problems with Adding Several Adjustment Variables

- Adding several independent variables changes our power to detect effects of interest.
 - **Reduced power**. As the number of predictors in a model increases, the Error DF decreases. This leads to heavier tails in the t-distribution and the observed t-value must be larger to reject H_0 (p<.05).
 - Increased power. The standard error of the slope coefficients are a function of the
 estimated standard deviation of the residuals. If adjustment variables are added
 and they are able to reduce this standard deviation, then the SE will be smaller
 and the t-value will be larger.

$$SE(\hat{\beta}) = \frac{s_{Y|X}}{s_X \sqrt{n-1}}$$

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3. Confounding

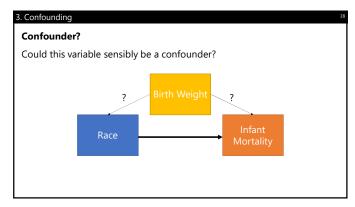
Problems with Adding Several Adjustment Variables

- A large model with many nonsignificant X-variables violates our desire to have a minimal (i.e. "parsimonious") model that does a good job predicting our outcome.
- In model-building, we ultimately want to find the most parsimonious model

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3. Confounding Confounder? Could this variable sensibly be a confounder? ? Cholesterol ? Myocardial Infarction

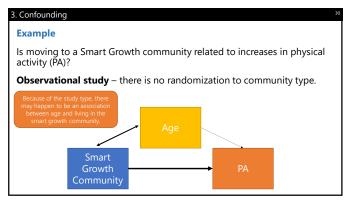
It's not entirely clear whether cholesterol affects BMI or vice versa...



3. Confounding

The potential for confounding is reduced in experimental studies. This is because individuals are randomized into treatment groups, so the treatment/exposure groups are similar in terms of potential confounding variables.

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3. Confounding	
Experimental study – all individuals who want to move to the smart growth community are included into a lottery. Half move and half remain where they had been living.	
Age is less likely to be a confounder here as, by study design, this relationship has been eliminated. Smart Growth Community PA	

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. Confounding

In an observational study there may be several pre-existing associations that we want to control for.

For example, in the CHS:

- Individuals who live in a more polluted community may happen to be of a particular racial/ethnic group (race confounds the association between pollution and lung function).
- Individuals who live in a more polluted community may happen to be of a particular gender (sex confounds the association between pollution and lung function).

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3. Confounding

Mediators

- <u>Confounders</u> are variables that cause a spurious association between an X and Y variable of interest.
- <u>Mediators</u> are variables that are intermediary steps in a causal pathway between X and Y.

3. Confounding	3	
The Theory of Planned Behavior posits that the relationship between an X variable and a behavioral outcome is mediated by intentions.		
In this example, intentions for PA is a mediator in a causal pathway between moving to a smart growth community and physical activity.		
Smart Growth Community		

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3. Confounding

Dealing with Mediators

- \bullet As mediators are within the causal pathway, they do not lead to spurious relationships between X and Y.
- The analysis of mediators is beyond the scope of this course, but their effects can be assessed with path analysis.

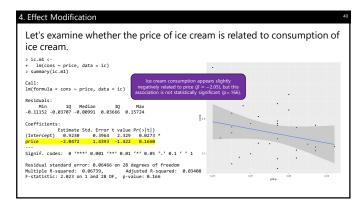
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3. Confounding

Recap

- In order to be a confounder, the variable under consideration must:
 - Change the slope parameter of interest appreciably (>10-20%)
 - Sensibly be a confounder (i.e., not be a causal intermediary)
- By including a confounder in a regression of Y on X, you will be able to calculate the effect of X on Y that is not due to the confounder.

3. Confounding	
Recap	
➤ Determine whether a given variable is a confounder of a relationship between X and Y	
Determine whether a given variable is a causal intermediary of a	
relationship between X and Y	
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A Effect Modification	-
4. Effect Modification 32 Effect Modification	
• When the association of interest between the outcome variable (Y) and a specific independent variable (X) is depends on a third variable (Z).	-
Criteria	
An interaction term will be significant within the model.	
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	4
4. Effect Modification 36	
Example 30 families were asked about their ice cream consumption in the past	
30 families were asked about their ice cream consumption in the past month. The following variables were obtained:	
CONS – ice cream consumption in pints per capita	
INCOME – family income (in \$1,000)	
PRICE – price per ounce of ice cream (\$)	
TEMP – average temperature in the past month	

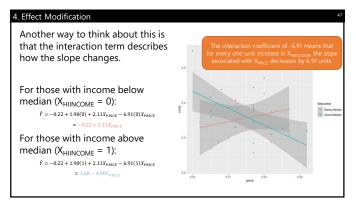


4. Effect Modification What happens when we look at this relationship by income status (high vs. low, dichotomized at the median)? It appears that there are two different effects between price and consumption: 1) For high-income families, higher price is associated with lower consumption. 2) For low-income families, higher price is slightly associated with higher consumption.

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A. Effect Modification If we run the regression separately for those with high income and low income, we come to two separate effects, by the come category: > ic. #2 cc. | ic.

4. Effect Modification 4	
Instead of analyzing these two models separately, we write this as one	
model in the form: $\mu_{Y X1,X2}=\beta_0+\beta_1X_1+\beta_2X_2+\beta_3X_1X_2$	
The variables X1 and X2 are said to interact if $\beta_3 \neq 0$.	
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4. Effect Modification 4	4
Here we want to test:	
$\mu_{Y X1,X2} = \beta_0 + \beta_1 X_{HIINCOME} + \beta_2 X_{PRICE} + \beta_3 X_{HIINCOME} X_{PRICE}$	
44	
44	
	-
4. Effect Modification	
We will arrive at to distinct effects depending on income category:	-
For <u>low income</u> $(X_{HIINCOME}=0)$: $\mu_{Y X1,X2} = \beta_0 + \beta_1(0) + \beta_2 X_{PRICE} + \beta_3(0) X_{PRICE}$	
$\mu_{Y X1,X2} = \mu_0 + \mu_1(0) + \mu_2 \Lambda_{PRICE} + \mu_3(0) \Lambda_{PRICE}$ $= \beta_0 + \beta_2 \chi_{PRICE}$	
For <u>high income</u> (X _{HIINCOME} =1):	
$\mu_{Y X1,X2} = \beta_0 + \beta_1(1) + \beta_2 X_{PRICE} + \beta_3(1) X_{PRICE}$	
$= \beta_0 + \beta_1 + \beta_2 X_{PRICE} + \beta_3 X_{PRICE}$	
$= (\beta_0 + \beta_1) + (\beta_2 + \beta_3) X_{PRICE}$	



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Notes about Interaction Terms

- Main Effects refer to the effects (variables) in the model without modeling any interaction (e.g., the effect of price on consumption regardless of income category).
- If the interaction term is significant then you should retain the effects of all variables included in the interaction term – regardless of significance.
- Detecting an interaction requires **larger sample size** than for main effects; typically 4n, where n is the sample size required to detect a main effect at 80% power. You may want to be more liberal with the α level for interactions (e.g., $\alpha=0.15$).

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4. Effect Modification

Continuous by Continuous Interactions

- We previously examined the interaction of a continuous variable with a dichotomous variable.
- Continuous-by-dichotomous interactions are easier to interpret because we can stratify by the dichotomous variable for interpretation.

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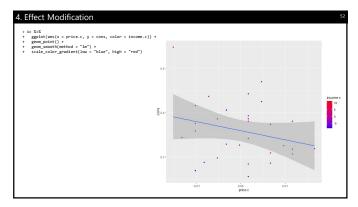
4 Effect Modification

Suppose we want to examine the same interaction as before, but we will leave income in as a continuous variable.

Let's fit the following model:

 $\hat{Y} = \beta_0 + \beta_1 X_{INCOME.C} + \beta_2 X_{PRICE.C} + \beta_3 X_{INCOME.C} X_{PRICE.C}$

Note: it's a good idea to center variables in general, but especially when performing a continuous-by-continuous nteraction. Here the "C" in the variable name is my notation for saying that variable is mean-centered.



4. Effect Modification We see that the interaction between price and income is statistically significant (p=.006): 5. Significant (p=.006): 5. Significant (p=.006): 5. Significant (p=.006): 5. Significant (p=.006): 6. Si

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4. Effect Modification And our model-fit equation becomes: $\hat{Y} = 0.356 - 0.002 X_{INCOME.C} - 1.285 X_{PRICE.C} - 0.696 X_{INCOME.C} X_{PRICE.C}$ What does this tell us? Two ways to interpret main effects:

- 1. At the mean value of income ($X_{\text{INCOME.C}}$ =0), a one-unit increase in X_{PRICEC} is associated with a predicted decrease ice cream consumption of 1.285 units (p=0.34).
- 2. At the mean value of price ($X_{PRICE,C}$ =0), a one-unit increase in $X_{INCOME,C}$ is associated with a predicted decrease in ice cream consumption of 0.002 units (p=0.25).

4. Effect Modification

And our model-fit equation becomes:

 $\hat{Y} = 0.356 - 0.002X_{INCOME.C} - 1.285X_{PRICE.C} = 0.696X_{INCOME.C}X_{PRICE.C}$

What does this tell us?

Two ways to interpret the interaction term:

- 1. For every one-unit increase in $X_{\text{INCOME.C}\prime}$ the slope associated with $X_{\text{PRICE.C}}$ decreases by 0.696.
- 2. For every one-unit increase in $X_{\text{PRICE}.C'}$ the slope associated with X_{INCOMEC} decreases by 0.696.

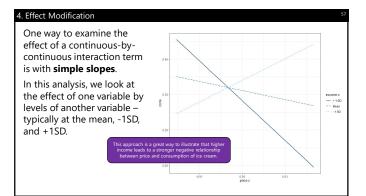
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4. Effect Modification

One way to examine the effect of a continuous-by-continuous interaction term is ${\bf simple\ slopes}.$

In this analysis, we look at the effect of one variable by levels of another variable – typically at the mean, -1SD, and +1SD.

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4. Effect Modification	58	
The calculation of \$\textit{BPRICE.C}\$ at the meastraightforward, but the significance of tricky. I recommend using a package of the state of the significance of tricky. I recommend using a package of the state of the significance of the state of the significance of	of the slope at these values is a bit that will calculate these for you.	
SIMPLE SLOPES ANALYSIS	,	
Slope of price.c when income.c = -6.25 (- 1 SD):		
3.06 2.14 1.43 0.16	643	
Slope of price.c when income.c = 0.00 (Mean):		
Est. S.E. t val. p	000 income	
-1.29 1.32 -0.97 0.34	5 - Mail	
Slope of price.c when income.c = 6.25 (+ 1 SD):		
Est. S.E. t val. p	639	
-5.63 1.77 -3.19 0.00		
This tells us that price is related to consumption only for high levels of income (+1SD and greater).		

4. Effect Modification

Recap

- To determine if the effect of X on Y changes based on the value of another variable Z, you can include an interaction term in the model.
- The significance of the beta coefficient for the interaction term (X*Z) determines whether there is a significant interaction.
- \bullet Compared to main effects, interactions require larger sample size to detect significant effects.

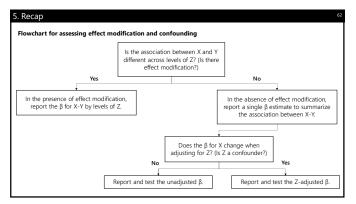
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4. Effect Modification

Recap

- > Determine the presence of an interaction through adding an interaction term in a regression model
- ➤ Explain the effect of X on Y based on:
 - ➤ Levels of Z (if Z is categorical)
 - \succ The value of Z (if Z is continuous)

	als of Data Analysis and Recommendations			
	Model of Association	Prediction Model		
Goal	Explain the true relationship between an X (or set of X) variable and an outcome.	Use a set of X variables to find the model that can best predict the outcome.		
Variables	Choose based on theoretically meaningfulness of associations (e.g., which variables may be distorting the relationship between X and Y).	Choose based on what might be associated with the outcome.		
Method	Control for confounding. Examine effect modification. Keep variables that explain the "true" relationship between X and Y.	Confounding is not important. Examine effect modification. Keep variables that improve model fit.		
Metrics	R ² , parsimony, ensuring you have considered all possible confounders.	R ² , parsimony, validation with an external		



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- Keep variables continuous when possible. In this lecture we categorized income to examine its interaction with price and ice cream consumption categorizing a variable results in a loss of information, but with added interpretability. Because income is continuous, it may be more desirable to keep a continuous-by-continuous interaction with price.
- Keep all lower-order terms for significant interactions. When an interaction is included in the model, keep all variables included in the interaction term (regardless of significance).

5. Recap	
Check interactions first. Because interactions reflect strata-specific effects, check for interaction variables before assessing confounding.	
Don't get overwhelmed. With several independent variables it may be tempting to examine many possible interactions. Stick to a priori hypothesized interactions, or interactions that make the most sense. This will reduce the amount of possible variables you have to look at.	
Stick to parsimony. A good model attempts to simplify reality while retaining accuracy. A parsimonious model explains as much of the relationship of interest as possible with as few variables as possible.	
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5. Recap 65	
Additional Reading Explanatory vs. Prediction Modeling	
https://www.stat.berkeley.edu/~aldous/157/Papers/shmueli.pdf	
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5. Recap	1
Packages and Functions interactions: interact_plot()	
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