Warnings
Remember that most of the inference we have discussed, e.g., for linear regression, requires certain assumptions to hold:

- The population model is linear.
- The errors are normally distributed.
- The errors are i.i.d., with mean zero.

These assumptions are easily violated; as discussed earlier in the course, many of these kinds of violations can be checked by examining the residuals, as well as by considering transformations of the variables.
Hypothesis testing has similar warnings attached.

- “Rejecting the null hypothesis” means: the data suggests the null is not true.

- We might fail to reject because the null is true; OR because we don’t have enough data (low power).

- So failure to reject does not mean the null is true!

- Always be precise about your null hypothesis, and what sampling distribution it implies for your estimator.

  E.g., in linear regression, to get the sampling distribution of $\hat{\beta}_j$ assuming $\beta_j = 0$, we still assume the linear normal model with i.i.d. errors.
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Modeling assumptions: Hypothesis testing

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E.g., in linear regression, to get the sampling distribution of $\hat{\beta}_j$ assuming $\beta_j = 0$, we *still* assume the linear normal model with i.i.d. errors.
Even in a correct regression model, significant relationships between covariate(s) and the outcome are evidence of association (i.e., correlation in the population model), not causation.

Suppose we fit a regression with $p$ covariates $X_1, \ldots, X_j$, and outcome $Y$.

A causal interpretation of $\hat{\beta}_j$ says that if we change $X_j$ by 1 unit, then (holding other covariates constant) the outcome $Y$ will change by $\hat{\beta}_j$ units.
Association vs. causation

For us to interpret $\hat{\beta}_j$ causally, we typically want changes in $X_j$ in our data to be (essentially) independent of other variables (this is closely related to a concept in statistics called exogeneity). What might go wrong?
Association vs. causation

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- **Collinearity.** If $X_j$ is collinear (correlated with) other covariates in our data, then when $X_j$ varies in our data, the reason for variation in $Y$ might actually be associated variation in the correlated covariates. This can make it difficult to accurately estimate the specific impact of $X_j$ on $Y$. 
Association vs. causation

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► **Omitted variable bias.** If a covariate $Z$ is left out of our model that is correlated with $X_j$ and $Y$, then when $X_j$ varies in our data, the reason for variation in $Y$ might actually be the associated (unobserved) variation in $Z$. 
How do we enforce exogeneity? Run an experiment where we (the experimenters) vary $X_j$ exogenously at random, and observe the effect on $Y$.

This is why randomized experiments are the benchmark of causal inference.
More warnings

In the next two sections we look at two additional pitfalls:

- Multiple hypothesis testing
- Post-selection inference
Multiple hypothesis testing
An example: Multiple linear regression

Suppose that I have \( n \) rows of data with outcomes \( Y \) and corresponding covariates \( X \). Suppose \( p = 100 \).

I run a linear regression with all the covariates and check statistical significance. I order the resulting covariates in descending order of p-value:

<table>
<thead>
<tr>
<th>Covariate index</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>0.0070</td>
</tr>
<tr>
<td>58</td>
<td>0.018</td>
</tr>
<tr>
<td>93</td>
<td>0.034</td>
</tr>
<tr>
<td>69</td>
<td>0.040</td>
</tr>
<tr>
<td>57</td>
<td>0.042</td>
</tr>
<tr>
<td>10</td>
<td>0.047</td>
</tr>
</tbody>
</table>

You walk away excited: these six coefficients are all significant at the 95% level, and you now have a starting point for building your model.
In fact: *There is no relationship in this data between $X$ and $Y$!*

I used synthetic data to generate this example, with:

- $Y_i \sim \mathcal{N}(0, 1)$ for each $i$, i.i.d.
- $X_{ij} \sim \mathcal{N}(0, 1)$ for each $i, j$, i.i.d.

So what happened?
What happened?

Recall the p-value is the answer to the following question:

*What is the chance I would see an estimated coefficient (from the data) as extreme as what I found, if the true coefficient was actually zero?*
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*What is the chance I would see an estimated coefficient (from the data) as extreme as what I found, if the true coefficient was actually zero?*

If we use a cutoff of 0.05 to determine whether a coefficient is “statistically significant”, then we are willing to accept a 5% rate of *false positives*: coefficients that look large due to random chance, despite the fact that there is really no underlying relationship.

This means with 100 covariates, we should expect 5 of the coefficients to be significant due to random chance alone — even if there is no effect there! (In our case we get slightly more than this.)
Multiple hypothesis testing

This is a systematic issue with statistical significance based on p-values from individual hypothesis tests:

If you use a cutoff of 0.05 (or 0.01, etc.), you should expect 5% (or 1%, etc.) of your discoveries (rejections) to be false positives.

This applies across all hypothesis tests you do: so for example, if you use a 5% cutoff every day at your job on every test you ever run, you will generate false positives in 5% of your hypothesis tests.
Multiple hypothesis testing

Is this a problem? Perhaps not: if you understand that false positives are generated in this way, you can be wary of overinterpreting significance with many hypothesis tests.

The problem is that interpretation of the results becomes much harder: which results are “trustworthy”, and which are “spurious”? 
Multiple testing corrections provide a systematic approach to identifying “meaningful” effects when dealing with many simultaneous hypothesis tests.

This has been an active area of work in the last two decades in statistics, as the range of applications where many hypothesis tests are possible has increased.
Example: The Optimizely results page

Optimizely runs an “A/B testing” platform, a way to test different versions of a website’s design against each other. Here is a typical results page for an experiment:

Real dashboards can have many more simultaneous hypothesis tests present.
Example: Bonferroni correction

The simplest example of a multiple testing correction is the *Bonferroni* correction.

This approach tries to ensure that the probability of declaring even one false positive (also called the *familywise error rate*, FWER) is no more than, e.g., 5%.
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The Bonferroni correction declares as significant (rejects the null) any hypothesis where the p-value is $\leq 0.05/p$, where $p$ is the number of hypothesis tests being carried out.

In our example, $p = 100$, so only coefficients with p-values $\leq 0.0005$ are declared significant — *none* in the example I showed!
Example: Bonferroni correction

Why does the Bonferroni correction work?

- For a collection of events $A_1, \ldots, A_p$, we have the following bound:

$$\mathbb{P}(A_1 \text{ or } A_2 \text{ or } \cdots A_p) \leq \sum_{j=1}^{p} \mathbb{P}(A_j).$$
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- So now let $A_j$ be the event that the $j$'th coefficient is declared significant, with a cutoff of $0.05/p$ on the p-value. Then:

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P(A_j|\beta_j = 0) \leq \frac{0.05}{p}.$$
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▶ Finally, suppose that all the $\beta_j$’s are in fact zero. Then the probability even one of the $A_j$’s true is $\leq p \times 0.05/p = 0.05$. 
Example: Benjamini-Hochberg

The Bonferroni correction works by essentially forcing your attention only on the smallest p-values (most significant results).

In practice, though, it can be too conservative, especially as the number of hypotheses (e.g., coefficients) increases.

Other methods have emerged to deal with this issue, to allow valid inference while being somewhat less conservative. We consider one, the *Benjamini-Hochberg (BH)* procedure.
Example: Benjamini-Hochberg

Suppose we run $p$ hypothesis tests. Of these, suppose that for hypotheses in $S_0$ the null is in fact true, and on the remainder, the null is false. Suppose that under a given decision procedure, you reject the null for the set of hypotheses in $R$.

The *false discovery proportion* (FDP) is the fraction of your rejections that were also in the null set:

$$FDP = \frac{|S_0 \cap R|}{|R|}.$$

The *false discovery rate* (FDR) is the expected value of this fraction over all the randomness in the data:

$$FDR = \mathbb{E}[FDP].$$

The BH procedure aims to ensure FDR is less than or equal to $\alpha$.

\[1\]FDP is defined to be zero if you make no rejections.
Consider the Optimizely results page again.

Suppose we use BH with $\alpha = 0.05$. This ensures that on average, of those cells that are declared significant, we will have made mistakes on at most 5% of them.

The criterion is stronger than just controlling each individual test at $\alpha = 0.5$, but weaker than controlling the familywise error rate at $\alpha = 0.05$.  

Example: Benjamini-Hochberg

The BH procedure at level $\alpha$ is simple to implement:

1. Compute p-values for each of your hypothesis tests, and order them in *increasing* order. Denote these by $q(1), q(2), \ldots, q(p)$.

2. Find the largest $j$ such that:

$$q(j) \leq \frac{\alpha j}{p}.$$  \hfill (1)

3. Reject all hypotheses $1, \ldots, j$.

As long as all hypothesis tests are independent of each other, this procedure ensures $\text{FDR} \leq \alpha$.\(^2\)

\(^2\)If the hypotheses are not independent, the same result can be guaranteed by changing the right hand side of (1) to $\frac{\alpha j}{p \log p}$.\(^2\)
Example: Benjamini-Hochberg

A picture:
Example: Benjamini-Hochberg

As a numerical example, suppose that we run BH at level $\alpha = 0.05$ with 5 hypothesis tests, where we assume the tests are independent, and we receive p-values 0.001, 0.045, 0.0004, 0.025, 0.15.

We first order the p-values from lowest to highest: 0.0004, 0.001, 0.025, 0.045, 0.15.

Since $\alpha/5 = 0.01$, we look for the largest $j$ such that the $j$'th p-value in the ordered list is $\leq 0.01j$. This is 0.025, so we reject the three hypotheses with p-values 0.0004, 0.001, and 0.025.
Example: Benjamini-Hochberg

The BH procedure is desirable because:

- It is easy to implement.
- It is less conservative than the Bonferroni correction, while still providing useful inference when many hypothesis tests are run.

You should have the habit of always using a procedure like BH when you run many hypothesis tests, to validate that your findings are actually meaningful.
Post-selection inference
Selecting a model

Let’s suppose we are building a model using linear regression.

We have $n = 100$ observations $Y$, two covariates in the design matrix $X$, and two models we consider:

- In the first model: $Y \sim 0 + X_1$.
- In the second model: $Y \sim 0 + X_1 + X_2$.

(Ignore the intercept for simplicity.)

Suppose that the design matrix $X$ is such that the two columns each have norm 1, and their sample correlation is $\approx \frac{2}{3}$.

Also suppose $Y_i \sim 1.5X_{i2} + \varepsilon_i$, where $\varepsilon_i \sim \mathcal{N}(0, 1)$ (i.i.d.).
Selecting a model

Example plot of $X_2$ vs. $X_1$: 

![Example plot of $X_2$ vs. $X_1$]
Selecting a model

Example plot of $Y$ vs. $X2$:
Selecting a model

We follow this procedure:

1. We check for significance of $\hat{\beta}_2$ in the complete model. If it is significant, we keep it in the model; if it is not, we drop it.
2. We use the resulting fit to estimate $\hat{\beta}_1$, as well as its standard error $\hat{SE}_1$.
3. When done we check if $\hat{\beta}_1$ is statistically significant at the 5% level.
Selecting a model

We do this in 10,000 “parallel universes”, with $n = 100$ in each universe.

In what fraction of our universes should $\hat{\beta}_1$ be significant?
Selecting a model

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In what fraction of our universes should $\hat{\beta}_1$ be significant?

We find that $\hat{\beta}_1$ is significant in 12.8% of the universes — even though by using a 5% threshold, we should have controlled our false positive rate at 5%!
Selecting a model

What went wrong?

Note that $X_1$ is highly collinear with $X_2$. So when we fit the full model, there is a good chance that $\hat{\beta}_2$ might not be significant.
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But the universes in which this happens are also more likely to be those universes where $X_1$ does a good job of explaining the variation in $Y$!

As a result, our selection process makes us more likely to choose models in which $\hat{\beta}_1$ is significant, even if the true $\beta_1$ is zero; but when we do our hypothesis test, we don’t account for this fact.

(Formally, we are doing the hypothesis test assuming that under the null $\hat{\beta}_1$ is $\mathcal{N}(0, \widehat{SE}_1^2)$, when in fact under the null together with our selection process, $\hat{\beta}_1$ is actually more likely to be positive.)
Selecting a model: A picture

The black density plot is the sampling distribution of $\hat{\beta}_1 / \hat{SE}_1$ under our selection process (over 10,000 parallel universes), while the red curve is the $N(0,1)$ density:
This is an example of post-selection inference:

- You apply lots of procedures to your data to find a model you “like”.
- *Then* you report your regression table, with p-values, etc.
- But by doing so, you have *favorably biased* your selection of p-values!

(A less generous term for this type of exercise is “p-value hacking”.)
Post-selection inference

How can we deal with this?

▶ We can take into account our selection procedure when we determine the distribution of \( \hat{\beta}_1 \) under the null hypothesis, and use this “corrected” sampling distribution for significance testing.

Progress is being made on this approach, but it remains less common in most practical settings.
Post-selection inference

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▶ We can validate our findings on new data: Fit the same model on a completely new data set, and compute the p-values and significance levels there.

These are correctly interpretable, because now the model selection is not based on the data we are using to check significance.
Concluding thoughts
So now what?

Inference seems loaded with warnings: it is easy to read too much into a statistical analysis, and see “phantom” effects that are not real.

So: how are we meant to build meaningful inferences in practice?
Inference for linear regression

If we’ve built a meaningful linear regression model, then:

The relationships we declare to be present in our estimated model should be exactly those that are present in the population model.

(*Recall*: Here we are only talking about association, not causation. Additional steps need to be taken to make sure we can interpret a relationship causally.)
External validity

The best evidence that we have a meaningful population model is that it delivers meaningful insight even *outside* of the data on which it was built.

This is the strategy suggested to deal with issues like post-selection inference. Note the similarity to evaluation of predictive models!
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What it means in practice is that inference does not stop at just one dataset and one modeling approach; often we should ask for corroborating evidence (from other studies, other datasets, other experiments, common sense, etc.) to strengthen the case for a particular relationship.
Principles to live by

▶ Be inquisitive.
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- Be inquisitive.
- Be precise.
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▶ Be precise.
▶ Be skeptical.
Principles to live by

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▶ Be skeptical.
▶ Be bold.