BST 210 Lab: Week 8
Model Building & Goodness of Fit for Logistic Regression

Over the past two weeks, we've used logistic regression as our primary tool for estimating associations between and make predictions about a binary outcome Y and a set of predictors $X_1, \dots X_p$:

$$\text{logit}\big(P(Y=1)\big) = \beta_0 + \beta_1 \cdot X_1 + \ldots + \beta_p \cdot X_p.$$

But there are many possible ways of modeling our outcome of interest—how and why did we settle on this one? As was the case for linear regression, we'd like to be able to formally compare different logistic regression models, and to decide which of our potential predictors are most appropriate/important to include in our model.

Our general process for going about model building is exactly the same as before! We:

1. Determine our objective for building the model
2. Select some metric that we'll use to assess which models are "best" (ex: AIC, BIC, covariate p-values)
3. Use subject matter knowledge and/or an automated procedure (such as forward selection, backward selection, stepwise selection, or best subsets selection) to arrive at a potential model
4. Validate the appropriateness/fit of our final model

We also want to keep the same guiding principles of parsimony and hierarchical well-formulation in mind.

However, as we saw in class this week, there are several additional wrinkles when it comes to logistic regression...

Maximum Likelihood Estimation

In linear regression, we fit our models by selecting the coefficient values that minimize the squared residual terms. In other words, we choose the parameter estimates that give us the smallest

$$SSE = \sum \epsilon_i^2 = \sum (y_i - \beta_0 - \beta_1 X_1 - \ldots - \beta_p X_p)^2.$$

This is why we are able to calculate/interpret:

- The sum of squares decomposition
- The Adjusted R^2
- The (root) MSE
- The F test statistic

In logistic regression, we instead estimate our coefficients so that we maximize the likelihood of our observed data—this approach is called **maximum likelihood estimation**.

Suppose that we have a data set with n individuals, and that for each of these individuals we observe a single binary outcome Y_i, and a single predictor X_i. The logistic regression relating X_i and Y_i is

$$\text{logit}\big(P(Y_i = 1)\big) = \beta_0 + \beta_1 X_i \quad \Longrightarrow \quad P(Y_i = 1) = \frac{e^{\beta_0+\beta_1 X_i}}{1 + e^{\beta_0+\beta_1 X_i}}.$$

Given this particular form of the model, the likelihood of the observed data is given by

$$\begin{aligned}
\mathcal{L}(\beta_0, \beta_1) &= \prod_{i=1}^{n} P(Y_i = 1)^{y_i} \big(1 - P(Y_i = 1)\big)^{1-y_i} \\
&= \prod_{i=1}^{n} \left(\frac{e^{\beta_0+\beta_1 X_i}}{1 + e^{\beta_0+\beta_1 X_i}}\right)^{y_i} \left(1 - \frac{e^{\beta_0+\beta_1 X_i}}{1 + e^{\beta_0+\beta_1 X_i}}\right)^{1-y_i} \\
&= \prod_{i=1}^{n} \left(\frac{e^{\beta_0+\beta_1 X_i}}{1 + e^{\beta_0+\beta_1 X_i}}\right)^{y_i} \left(\frac{1}{1 + e^{\beta_0+\beta_1 X_i}}\right)^{1-y_i}.
\end{aligned}$$

When estimating β_0 and β_1, we choose the estimates $\widehat{\beta}_0$ and $\widehat{\beta}_1$ that make this likelihood—or equivalently the log likelihood, $\log(\mathcal{L})$—the largest.

Can we still use an F test to compare nested logistic regression models? If not, what other test(s) can we use instead?

No. Constructing and computing the F test statistic requires the sum of squares decomposition, which we only have in linear regression. If we want to compare nested logistic regression models, we can use (a) Wald tests (which we've seen for testing whether a single predictor is significant/needed) or (b) Likelihood Ratio tests (which we've seen for testing a group of coefficients for significance.

Can we still use the Adjusted R^2 and MSE to compare non-nested models? If not, what metric(s) can we use instead?

No. The Adjusted R^2 and MSE also rely on the sum of squares decomposition. However, we can still use the AIC and the BIC to compare non-nested logistic regression models!

An Example: Model Building in the GLOW Dataset

Let's return to the same data set that we saw last week: the Global Longitudinal Study of Osteoporosis in Women (GLOW). The data set is available on Canvas in the file `glow.csv`. Once again, our outcome of interest will be whether or not a study participant has a fracture within the first year of follow-up. Let's suppose that our objective is to build a prediction model for this probability of fracture, and that we have all of the variables in Table 1 at our disposal!

We'll start by reading the data set into SAS:

```
* Reading in the GLOW dataset;
proc import file='glow.csv' out=glow dbms=csv replace;
        getnames=yes;
run;
```

Table 1: Global Longitudinal Study of Osteoporosis in Women - Relevant Variables

Variable	Description
SUB_ID	Subject identification code (numbered 1 through 500)
SITE_ID	Study site
PHY_ID	Physician ID code
PRIORFRAC	Indicator of history of prior fracture
AGE	Age at enrollment in the study
WEIGHT	Weight at enrollment in the study
HEIGHT	Height at enrollment in the study
BMI	BMI at enrollment in the study
PREMENO	Whether menopause occurred before age 45 (= 1) or after (= 0)
MOMFRAC	Whether the subject's mother had a hip fracture (= 1) or did not (= 0)
ARMASSIST	Whether arms are needed to stand from a chair (= 1) or not (= 0)
SMOKE	Whether a subject is a former or current smoker (= 1) or not (= 0)
RATERISK	Self-reported risk of fracture, recorded as 1 (less than others of the same age), 2 (same as others of the same age), or 3 (greater than others of the same age)
FRACSCORE	Composite fracture risk score
FRACTURE	Indicator for whether any fracture occurred in the first year of follow-up

While we could select and implement any of the automatic model building procedures we've talked about, let's focus on forward selection and backward elimination using a p-value criterion of 0.15. *How do these two model selection procedures work again?*

Forward selection starts with a (logistic) regression model including only the intercept. At each step of the algorithm, we add the most significant of our remaining potential predictors into the model. Once a covariate is added to our (logistic) regression model, it cannot be removed. We stop the process when all of the remaining covariates not in our model have p-values that are greater than our entry level (here, the entry level $\alpha = 0.15$). Backward elimination parallels forward selection, but in that case we start with the full model and continue to remove the predictors with the least significant p-values until all the remaining covariates are significant at $\alpha = 0.15$.

```
* Running a forward selection procedure;
proc logistic data=glow descending;
        model fracture = fracscore raterisk smoke armassist momfrac premeno
                bmi height age priorfrac / selection=forward slentry=0.15;
run;
```

After four steps, no remaining variables are significant at the $\alpha = 0.15$ entry level, and the the forward selection process stops:

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	3.3045	2.8588	1.3361	0.2477
FRACSCORE	1	0.1871	0.0496	14.2564	0.0002
RATERISK	1	0.3706	0.1411	6.8989	0.0086
HEIGHT	1	-0.0375	0.0176	4.5724	0.0325
PRIORFRAC	1	0.4301	0.2634	2.6663	0.1025

So our final fitted model from forward selection is

$$\text{logit}(p) \;=\; 3.30 + 0.187 \cdot \texttt{fracscore} + 0.371 \cdot \texttt{raterisk} - 0.038 \cdot \texttt{height} + 0.430 \cdot \texttt{priorfrac}.$$

We can alternatively run a backward elimination procedure in SAS using the following code:

```
* Running a backward elimination procedure;
proc logistic data=glow descending;
        model fracture = fracscore raterisk smoke armassist momfrac premeno
                bmi height age priorfrac / selection=backward slstay=0.15;
run;
```

Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	2.4497	3.2323	0.5744	0.4485
RATERISK	1	0.3503	0.1455	5.7994	0.0160
ARMASSIST	1	0.4463	0.2328	3.6756	0.0552
MOMFRAC	1	0.6237	0.3070	4.1266	0.0422
HEIGHT	1	-0.0442	0.0182	5.9113	0.0150
AGE	1	0.0344	0.0130	6.9775	0.0083
PRIORFRAC	1	0.6412	0.2457	6.8104	0.0091

What is our final fitted logistic regression model from the backward elimination procedure?

Our final logistic regression model from backward elimination is

$$\text{logit}(p) \;=\; 2.45 + 0.350 \cdot \texttt{raterisk} + 0.446 \cdot \texttt{armassist} + 0.624 \cdot \texttt{momfrac} - 0.044 \cdot \texttt{height}.$$

Note that we arrived at two different "best" models for the probability of developing a fracture over the course of the study! *Are these two final models nested? If so, which is the full model and which is the reduced model?*

No. Recall that a "reduced" model is nested within a "full" model if we can place restrictions on the coefficients of the full model to end up back at the reduced model; the most common type of restriction is setting a coefficient to zero (i.e. removing a predictor from the model). In other words, our full model must include all of the information in the reduced model, and then some. Here, the backward elimination model is the larger model, but it fails to include the covariate `fracscore`, which **is** in the smaller forward selection model.

If they are not nested, how might we decide between them?

We can still use metrics such as the AIC and BIC (as discussed above), and may also want to use subject matter knowledge and the principle of parsimony to help us decide between the two models. But we might want to first make sure that the two models we're comparing are actually good, well-fitting models. To that end, we want to ask ourselves: (1) Do both of these models fit the data well? (2) Does one of these models do a better job of classifying cases/predicting our outcome than the other?

Assessing Goodness-of-Fit via Calibration

One possible goodness-of-fit metric that we discussed in lecture this past week is **calibration**. A logistic regression model is well-calibrated if the predicted probabilities we get from our regression model are reasonably close to the true probabilities in our observed data—in other words, that our model is a reasonable approximation of reality.

There are several key terms and ideas to keep in mind when we talk about calibration:

- **Covariate pattern:** a particular combination of covariate values
  - When we talk about calibration, we are typically concerned with the total number of covariate patterns in our observed data *for the covariates included in our model*
- **Saturated model:** a model that includes as many parameters as there are possible covariate patterns

Suppose that—when modeling the probability of a study participant having a fracture within the first year of follow-up—we had only included one predictor: the prior fracture indicator.

$$\text{logit}(p) = \beta_0 + \beta_1 \cdot \texttt{priorfrac}.$$

How many covariate patterns are there? Is this model saturated? And if not, what would the saturated model be?

There are two covariate patterns: individuals may either have a history of prior fracture, or not have a history of prior fracture. Since we have two covariate patterns and two parameters in our model (β_0 and β_1), our model is saturated.

Now suppose that we also add in the self-reported risk of fracture, represented as a categorical variable:

$$\text{logit}(p) = \beta_0 + \beta_1 \cdot \texttt{priorfrac} + \beta_2 \cdot I(\texttt{raterisk} = 1) + \beta_3 \cdot I(\texttt{raterisk} = 2).$$

How many covariate patterns are there now? Is this model saturated? And if not, what would the saturated model be?

We're now considering two different covariates: history of prior fracture and categorical risk score. There are two possible values for `priorfrac` (yes/no) and three possible values for `riskscore` (low/medium/high), so that there are $2 \times 3 = 6$ covariate patterns. Our model only includes four parameters, so it is not saturated. The saturated model includes six parameters:

$$\begin{aligned}\text{logit}(p) \;=\; & \beta_0 + \beta_1 \cdot \texttt{priorfrac} + \beta_2 \cdot I(\texttt{raterisk} = 1) + \beta_3 \cdot I(\texttt{raterisk} = 2) \\ & + \beta_4 \cdot \texttt{priorfrac} \cdot I(\texttt{raterisk} = 1 + \beta_5 \cdot \texttt{priorfrac} \cdot I(\texttt{raterisk} = 2).\end{aligned}$$

Finally, suppose that we also included information on a participant's BMI at study entry. Then:

$$\text{logit}(p) = \beta_0 + \beta_1 \cdot \texttt{priorfrac} + \beta_2 \cdot I(\texttt{raterisk} = 1) + \beta_3 \cdot I(\texttt{raterisk} = 2) + \beta_4 \cdot \texttt{BMI}.$$

How many covariate patterns are there now? Is this model saturated? And if not, what would the saturated model be?

Since each individual in our data set has a unique set of covariate values, there are as many covariate patterns as there are individuals in our dataset. So the above model is not saturated, and generally speaking it's a little difficult to conceptualize a saturated model that includes continuous covariates. If we fit a logistic regression model that includes an indicator variable for each observation in the data set (i.e. that has n parameters), that model would be saturated.

Generally speaking, what—if anything—can we say about the predicted probabilities/calibration of a saturated model?

The predicted probabilities from our saturated model will always *exactly* match the observed probability of the outcome in each of our covariate patterns. In that sense, a saturated model is always perfectly calibrated. When assessing a particular logistic regression model's goodness-of-fit, we always implicitly refer back to this saturated model, and try to measure to what extent our model differs from/arrives at different fitted probabilities than the saturated model.

Note that just because a particular model is saturated or well-calibrated, that does not necessarily mean that it includes all important predictors, or that it does a good job of describing variation in our outcome due to other covariates not in our model![1]

The Pearson Chi-Square Test

Suppose that we fit a logistic regression model with p predictors, and that in our data set there are J covariate patterns involving those predictors. For the j^{th} of those patterns, suppose that we have n_j individuals, O_j observed events, and $E_j = n_j \cdot \widehat{p}_j$ expected events (based on our model), and that we estimate the variability in the observed event counts by $V_j = n_j \cdot \widehat{p}_j(1 - \widehat{p}_j)$. Then as long as the total number of covariate patterns J is small relative to our sample size, we can use the Pearson Chi-Square Test to assess the calibration of our model!

Hypothesis:	(H_0: the model has an acceptable fit) versus (H_1: the model does not fit well)
Test Statistic:	$\sum_{j=1}^{J} \frac{(O_j - E_j)^2}{V_j} \sim \chi^2_{J-(p+1)}$
Intuition:	How similar are our predicted probabilities/number of events to the truth?

Recall the two models that we arrived at using forward selection and backward elimination:

$$\text{logit}(p) = 3.30 + 0.187 \cdot \texttt{fracscore} + 0.371 \cdot \texttt{raterisk} - 0.038 \cdot \texttt{height} + 0.430 \cdot \texttt{priorfrac}$$

$$\begin{aligned}\text{logit}(p) = {} & 2.45 + 0.350 \cdot \texttt{raterisk} + 0.446 \cdot \texttt{armassist} + 0.624 \cdot \texttt{momfrac} - 0.044 \cdot \texttt{height} \\ & + 0.0334 \cdot \texttt{age} + 0.641 \cdot \texttt{priorfrac}\end{aligned}$$

Can we use the Pearson Chi-Square Test to assess either of their calibration? If so, what distribution will we compare the test statistic to? If not, why are we unable to perform the test?

No. We can only use the Pearson Chi-Square test to assess the calibration of models for which there are a **small number of covariate patterns** relative to the size of our data set. If we look at the forward selection and backward elimination models above, we can see that they both include the `height` covariate, which is continuous. So in both cases, we have 500 covariate patterns—each person in our GLOW dataset has a different/unique combination of `fracscore`, `raterisk`, `height` and `priorfrac` values (and similarly for the backward elimination model. So we have too many covariate patterns to use the Pearson Chi-Square test.

[1] To address this issue, some individuals define covariate patterns and saturated models differently. They consider all possible covariate patterns in the *entire* observed data set, including covariates that are not included in the model. SAS, Stata, and R assess calibration using our definition of covariate patterns/saturation, and in any sort of exam setting the two approaches will likely coincide.

For the purposes of seeing this test in action, let's consider a model that just includes `priorfrac` and `armassist`:

```
* Performing the Pearson Chi-Square test;
proc logistic data=glow descending;
        model fracture = priorfrac armassist / aggregate scale=none;
run;
```

Deviance and Pearson Goodness-of-Fit Statistics				
Criterion	Value	DF	Value/DF	Pr > ChiSq
Deviance	0.1355	1	0.1355	0.7128
Pearson	0.1351	1	0.1351	0.7132

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-1.6134	0.1566	106.1030	<.0001
PRIORFRAC	1	0.9567	0.2279	17.6259	<.0001
ARMASSIST	1	0.5503	0.2170	6.4330	0.0112

What are our conclusions about the goodness-of-fit of the above model?

Our p-value $p = 0.7132$ is well above 0.05. As such, we fail to reject our null hypothesis, and so conclude that the model including both `priorfrac` and `armassist` fits our data adequately.

The Hosmer-Lemeshow Test

If we have a large number of covariate patterns—and in particular if we have a continuous covariate in our logistic regression model—we can't use the Pearson Chi-Square Test to assess goodness-of-fit. So we instead rely on a second test: the Hosmer-Lemeshow Test.

- Creates pseudo-covariate patterns by ranking the predicted probability for each individual, and then grouping observations into G groups of approximately equal sizes on the basis of these predicted probabilities
- Usually choose $G = 10$, corresponding to splitting the fitted probabilities into deciles

Hypothesis:	(H_0: the model has an acceptable fit) versus (H_1: the model does not fit well)
Test Statistic:	$\sum_{j=1}^{G} \frac{(O_j - E_j)^2}{n_j \overline{p}_j (1-\overline{p}_j)} \sim \chi^2_{G-2}$
Intuition:	Similar to the Pearson Chi-Square Test with user-defined groups of observations

We can use the Hosmer-Lemeshow test to formally assess whether our forward selection and backward elimination models are well-calibrated:

```
* Performing the H-L Test for the forward selection model;
proc logistic data=glow descending;
        model fracture = fracscore raterisk height priorfrac /lackfit;
run;

* Performing the H-L Test for the backward elimination model;
proc logistic data=glow descending;
        model fracture = raterisk armassist momfrac height age priorfrac /lackfit;
run;
```

Partition for the Hosmer and Lemeshow Test					
		FRACTURE = 1		FRACTURE = 0	
Group	Total	Observed	Expected	Observed	Expected
1	51	3	4.50	48	46.50
2	51	6	6.18	45	44.82
3	51	7	7.53	44	43.47
4	51	8	8.51	43	42.49
5	50	12	9.68	38	40.32
6	50	11	11.26	39	38.74
7	50	12	13.63	38	36.37
8	50	23	16.79	27	33.21
9	50	20	21.12	30	28.88
10	46	23	25.80	23	20.20

Hosmer and Lemeshow Goodness-of-Fit Test		
Chi-Square	DF	Pr > ChiSq
5.8511	8	0.6639

(a) Hosmer-Lemeshow results from the forward selection model.

Partition for the Hosmer and Lemeshow Test					
		FRACTURE = 0		FRACTURE = 1	
Group	Total	Observed	Expected	Observed	Expected
1	50	23	21.44	27	28.56
2	50	28	29.26	22	20.74
3	50	33	33.45	17	16.55
4	50	36	36.93	14	13.07
5	50	38	39.02	12	10.98
6	50	39	40.44	11	9.56
7	50	39	41.75	11	8.25
8	50	47	42.81	3	7.19
9	50	45	44.11	5	5.89
10	50	47	45.78	3	4.22

Hosmer and Lemeshow Goodness-of-Fit Test		
Chi-Square	DF	Pr > ChiSq
5.3162	8	0.7233

(b) Hosmer-Lemeshow results from the backward elimination model.

What conclusions do we reach regarding the goodness-of-fit of the forward selected model? What about regarding the backward elimination model?

Both the forward selection model and backward elimination model provide adequate fits to the observed data ($p = 0.66$ and $p = 0.723$, respectively). Note that we cannot compare the p-values between the two model/say anything about which of the two of them provides a better fit relative to the other.

How useful is assessing goodness-of-fit via calibration when we want to compare and decide between models?

Honestly, not very. If one of the models we're comparing does not fit the data well (i.e., has a significant Pearson Chi-Square or Hosmer-Lemeshow test result), then that gives us a strong reason to not select it as our final model. But if both models provide an adequate fit—and most models we consider will meet this threshold—calibration can't help us differentiate between them.

A note: usually we think of smaller p-values as being "better", as they typically denote that some effect or relationship of interest is significant. However, in the case of goodness-of-fit, we *want* our p-values to be non-significant!

Assessing Goodness-of-Fit via Discrimination

Alternatively, we can assess a model's goodness-of-fit by looking at its **discrimination**—its ability to correctly separate out those individuals who actually had the event (i.e., those individuals with $Y = 1$) from those individuals who did not ($Y = 0$).

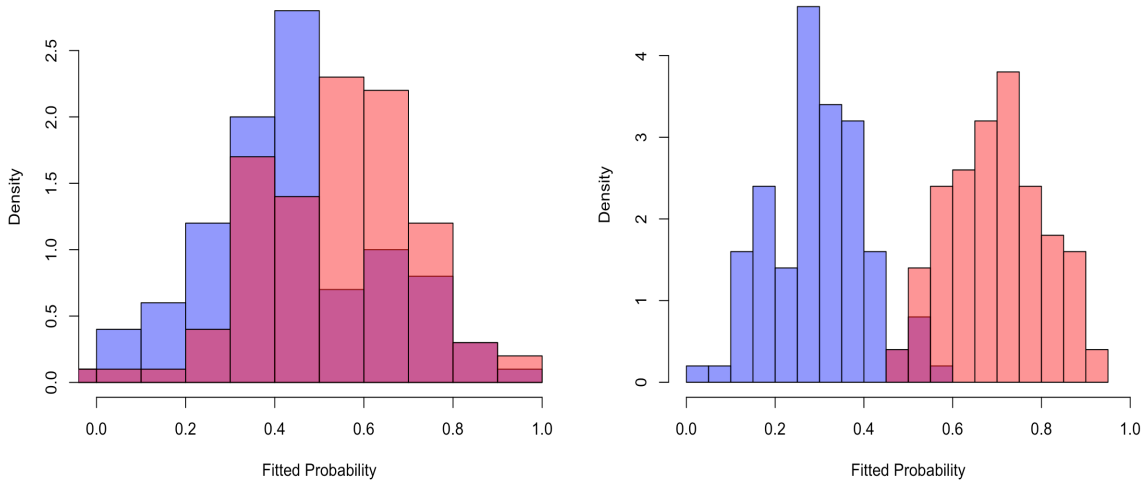


Figure 2: Fitted probabilities among those who are known to be cases (red) and known to be controls (blue). The model on the left has low discrimination, while the model on the right has high discrimination.

We often (eventually) want to use our fitted probabilities to actually predict whether or not a particular individual is a case (i.e. has $Y = 1$). To do this, we first need to choose some cut-off value, p_c, to use when classifying observations! We'll classify an individual as a case if their fitted probability of having an event, $\widehat{p}_i \geq p_c$, and we'll classify an individual as a non-case if their fitted probability of having an event, $\widehat{p}_i \leq p_c$.

- **Sensitivity:** the probability that we correctly classify someone as being a case, given that they truly are a case ($Y = 1$)

$$P\big(\ \widehat{p}_i \geq p_c \mid \text{the individual is a case}\big)$$

- **Specificity:** the probability that we correctly classify someone as a non-case, given that they truly are a non-case ($Y = 0$)

$$P\big(\ \widehat{p}_i < p_c \mid \text{the individual is a non-case}\big)$$

Note that—for any choice of p_c—there is a trade-off between the resulting sensitivity and specificity. *For example, what happens to our sensitivity and specificity if we choose $p_c = 0$?*

If we choose $p_c = 0$, then we will classify every single individual in our dataset as a case, regardless of their actual fitted/predicted probability of being a case (i.e. having $Y = 1$). This means we'll have a sensitivity of 1 (as we'll always classify cases correctly) and a specificity of 0 (as we'll always incorrectly classify non-cases as cases).

What happens if we choose $p_c = 1$?

The exact opposite happens. If we use $p_c = 0$, then every single person in our dataset will be classified as a non-case, meaning we will a sensitivity of 0 and a specificity of 1.

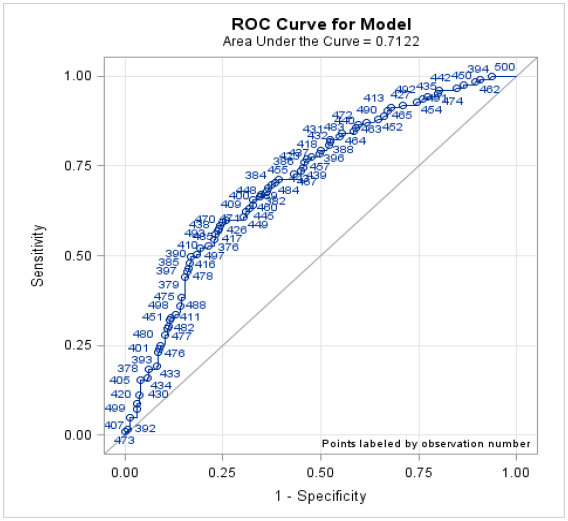
Models with higher discrimination make it easier for us to find a cut-point p_c that produces good results!

The ROC Curve

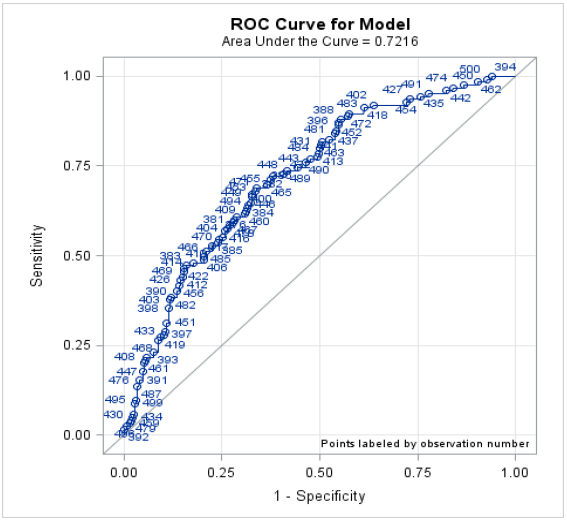
The ROC Curve (receiver-operator curve) helps us to visualize the trade-off between sensitivity and specificity, and to determine how well our logistic regression model discriminates between cases and controls. It plots our model's corresponding sensitivity and specificity for every possible choice of p_c.

Let's return to the GLOW data set, and plot the ROC curves for our two possible fracture models!

```
ods graphics on;

* Forward selection model;
proc logistic data=glow descending plots(only)=roc(id=obs);
        model fracture = fracscore raterisk height priorfrac
run;

* Backward elimination model;
proc logistic data=glow descending plots(only)=roc(id=obs);
        model fracture = raterisk armassist momfrac height age priorfrac;
run;

ods graphics off;
```



(a) ROC for forward selection model.



(b) ROC for backward elimination model.

Note that the area under the curve (**AUC**) is also sometimes known as the **c statistic**: it corresponds to the probability that a case (an individual with $Y = 1$) has a higher fitted probability than a non-case (an individual with $Y = 0$). *Do we prefer larger or smaller values of the AUC?*

We prefer larger AUC values, since this indicates that our model has both high specificity and high sensitivity.

Comparing the two ROC curves above, what do you notice? In particular, which model appears to provide a better fit to the data?

The two models have nearly identical AUCs—the forward selection model has an AUC of 0.71, while the backward elimination model has an AUC of 0.72. So the backward elimination model has ever-so-slightly better discrimination, but both models fit the data reasonably well.

What would it mean if the ROC curve fell exactly on the y=x line? What if it fell below the y=x line?

If the ROC curve fell exactly on the $y = x$ line, that would indicate that our model was no better at determining which observations were cases and which observations were non-cases than if we had simply flipped a coin and assigned $Y = 1/Y = 0$ at random. In other words, our model isn't at all useful for classifying cases and non-cases! If the ROC curve fell below the $y = x$ line, this would mean that we're classifying almost everyone who has $Y = 1$ incorrectly as a non-case, and almost everyone who has $Y = 0$ incorrectly as a case. If this happens, this is likely an indication that you accidentally switched the $Y = 0/Y = 1$ coding when fitting the logistic regression model!

Finally, based on all of the goodness-of-fit results above—as well as subject matter knowledge and the general principles of model building—which of the two fracture models do you prefer?

I would tend to prefer the smaller forward selection model. Both models fit the data reasonably well (i.e. they were both well-calibrated and had reasonable discrimination), but the forward selection model is more parsimonious. If we also had information on the AIC or BIC for these models, we could additionally use that information to guide our decision.

Midterm Exam Review

An Overview of Linear and Logistic Regression

Suppose that we have information on a continuous outcome Y_1 (say, systolic blood pressure), a binary outcome Y_2 (say, hypertension), and two predictors X_1 (stress levels) and X_2 (genetic background). We fit the following two models:

$$E[Y_1|X_1, X_2] = \beta_0 + \beta_1 X_1 + \beta_2 X_2 \quad (1)$$

$$\text{logit}\big(P(Y_2 = 1)\big) = \beta_0 + \beta_1 X_1 + \beta_2 X_2. \quad (2)$$

Compare and contrast the linear and logistic regression models on each of the following points:

What assumptions do we make in fitting these models?

Linear: We make four key assumptions, namely (1) **L**inearity—that the model we write down is the correct model relating our predictors X_1 and X_2 to the outcome Y_1, (2) **I**ndependence—that the observations in our data set are providing us completely separate pieces of information, (3) **N**ormality of the residuals, and (4) **E**qual variance—that we are equally as precise at predicting/estimating individuals' outcomes when we have small fitted values as when we have large fitted values.

Logistic: We don't require/make as many assumptions as in the linear regression case, but we still assume (1) that we have written down the model correctly, i.e. that the model we fit accurately reflects the true relationships between X_1, X_2, and Y, and (2) that the observations in our data set are independent.

How do we assess the appropriateness/goodness-of-fit of these models?

Linear: We've seen a number of ways of going about this. In order to assess the **L**, **N**, and **E** assumptions above, we've relied on residual analyses (specifically histograms, qq-plots, and scatter plots) using either the raw residuals or some sort of standardized/studentized residuals. We've also examined how well our model fits the data by looking at metrics such as the Adjusted R^2 and the MSE. Finally, we've performed outlier analyses and examine our data set for points with high leverage (which we assess using values from the "hat" matrix) and/or high influence (which we can assess using, for example, DFBETAS).

Linear: We've seen two main ways of thinking about goodness-of-fit: calibration (which we assess using either the Pearson Chi-Square Test or the Hosmer-Lemeshow Test) and discrimination (which we assess using the AUC).

How can we incorporate possible non-linear effects into these models?

In both types of models, we can incorporate non-linear effects by including quadratic/higher order terms (while making sure to keep our models hierarchically well-formulated!) or by modeling a continuous covariate using GAMs or splines.

How do we get predicted values from these models?

Linear: We can get a fitted/predicted value for a particular individual or subpopulation by taking the observed covariate values and plugging them into our fitted regression model:

$$\widehat{Y} = \widehat{\beta}_0 + \widehat{\beta}_1 X_1 + \widehat{\beta}_2 X_2.$$

Logistic: We're usually interested in getting a fitted/predicted *probability*, but our logistic regression model models the log odds of the outcome as a linear function of the predictors. So to get the fitted probabilities, we need to use the following formula, again plugging in our particular covariate values in for X_1 and X_2:

$$\widehat{p} = \frac{e^{\widehat{\beta}_0 + \widehat{\beta}_1 X_1 + \widehat{\beta}_2 X_2}}{1 + e^{\widehat{\beta}_0 + \widehat{\beta}_1 X_1 + \widehat{\beta}_2 X_2}}.$$

Remember to include units when you find the fitted value from a linear regression model!

How would we interpret the intercept β_0?

Linear: β_0 is the mean value of Y_1 in the population of individuals for whom both X_1 and X_2 are 0.

Logistic: e^{β_0} corresponds to the odds of the outcome ($Y_2 = 1$) among the population of individuals for whom both X_1 and X_2 are 0.

How would we interpret the slope for X_1, β_1?

Linear: A one unit increase in X_1 is associated with a β_1 unit increase in the mean value of Y_1, holding X_2 constant.

Logistic: A one unit increase in X_1 is associated with an e^{β_1} times increase in the odds of $Y_2 = 1$, holding X_2 constant.

How might we use these models to assess whether X_2 is a meaningful confounder of the association between X_1 and Y_1/Y_2? What additional models, if any, would we need to build to make this assessment?

For both linear and logistic models, we first want to determine whether X_2 meets our causal definition of a confounder: is it (1) associated with X_1, (2) associated with Y_1/Y_2 and (3) not a downstream consequence of X_1? If not, we do not need to go any further. However, if X_2 meets this definition, we then need to decide whether it causes meaningful or substantial bias. To do this, we compare the estimated slope for X_1 from an unadjusted model (that doesn't include X_2) to the estimated slope for X_1 from an adjusted model (that does include X_2), and use our 10% rule-of-thumb.

Note that for both linear and logisitic regression, we are looking/assessing the 10% rule of thumb on the raw beta values (and not on, say, the odds/odds ratio scale)!

How might we use these models to test whether X_1 is a significant predictor of Y_1/Y_2? What additional models, if any, would we need to build to make this assessment?

Linear: Since we are just testing whether a single predictor is significant (for testing multiple predictors/interaction terms, see the problems in the next section), we can use a **t-test**; the information needed to carry out a t-test/the p-value associated with that t-test are included in the model output.

Logistic: In order to test whether X_1 is a significant predictor in a logistic regression context, we use a **Wald** test; the information needed to carry out this test is included in the model output.

How would we use these models to test whether X_1 is an effect modifier of the association between X_2 and Y_1/Y_2? What additional models, if any, would we need to build to make this assessment?

In order to test for the presence of effect modification, we will need to include an interaction term between X_1 and X_2:

$$E[Y_1|X_1, X_2] = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 \cdot X_2$$
$$\text{logit}\big(P(Y_2 = 1)\big) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_1 \cdot X_2.$$

We can then test whether this interaction is significant (i.e. whether $\beta_3 = 0$) by using either a t-test (for a linear regression model) or a Wald test (for a logistic regression model).

A Deep Dive into Testing

Consider the following results from the linear regression of systolic blood pressure (measured in mmHg) on current smoking status, age, and categorical BMI (< 18.5, $18.5-25$, $25-30$, > 30), using 4434 observations:

$$E[\texttt{sysbp}|X] = \beta_0 + \beta_1 \texttt{cursmoke} + \beta_2 \texttt{age} + \beta_3 \texttt{sex} + \beta_4 \texttt{age} \cdot \texttt{sex} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}.$$

The output is below:

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	7	524088	74870	194.41	<.0001
Error	4426	1704506	385.11199		
Corrected Total	4433	2228593			

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	129.22893	5.77431	22.38	<.0001
cursmoke	Current Cig Smoker Y/N	1	-0.04100	0.62482	-0.07	0.9477
age	Age (years) at examination	1	-0.10906	0.11229	-0.97	0.3315
sex	SEX	1	-31.23358	3.50522	-8.91	<.0001
agesex		1	0.68148	0.06907	9.87	<.0001
underweight		1	-2.95686	2.29682	-1.29	0.1980
overweight		1	6.95257	0.66034	10.53	<.0001
obese		1	14.62625	0.95135	15.37	<.0001

Is age significantly associated with systolic blood pressure among individuals with $sex = 0$? How about among individuals with $sex = 1$? Construct and interpret a 95% Confidence Interval for each of these effects. Note that the covariance between $\widehat{\beta}_2$ and $\widehat{\beta}_4$ is -0.00736.

Sex = 0:

For individuals with $sex = 0$, the fitted regression line can be written as

$$E[\texttt{sysbp}|X, \texttt{sex} = 0] = \beta_0 + \beta_1 \texttt{cursmoke} + \beta_2 \texttt{age} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}.$$

So we can see that the association between age and systolic blood pressure in individuals with $sex = 0$ is represented by β_2. Based on the SAS output above, we can conclude that age is not a significant predictor

of systolic blood pressure among individuals with $sex = 0$, and after adjusting for information regarding current smoking status and BMI ($p = 0.33$). Note that our 95% confidence interval can be calculated as follows:

$$\begin{aligned} 95\%\ CI:\ \widehat{\beta}_2\ \pm\ t_{n-(p+1),\ 0.975} \cdot s.e.(\widehat{\beta}_2) &= -0.109\ \pm\ t_{4434-(7+1),\ 0.975} \cdot 0.112 \\ &= -0.109\ \pm\ 1.96 \cdot 0.112 \\ &= (-0.329,\ 0.111). \end{aligned}$$

So with 95% confidence a one year increase in age is associated with between a 0.329 mmHG decrease and a 0.111 mmHG increase in mean systolic blood pressure, holding current smoking status and BMI category constant.

<u>$Sex = 1$</u>:

For individuals with $sex = 1$, the fitted regression line can be written as

$$E[\texttt{sysbp}|X, \texttt{sex} = 1] = (\beta_0 + \beta_3) + \beta_1 \texttt{cursmoke} + (\beta_2 + \beta_4)\texttt{age} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}.$$

So in individuals with $sex = 1$, the association between age and systolic blood pressure is now given by $\beta_2 + \beta_4$. From the SAS output, we can see that this association is estimated to be $-0.109 + 0.681 = 0.572$. Note that we don't have a standard error or p-value for this quantity in the above output... But we can calculate it ourselves! We first need to find $Var(\widehat{\beta}_2 + \widehat{\beta}_4)$:

$$\begin{aligned} Var(\widehat{\beta}_2 + \widehat{\beta}_4) &= Var(\widehat{\beta}_2) + Var(\widehat{\beta}_4) + 2 \cdot Cov(\widehat{\beta}_2, \widehat{\beta}_4) \\ &= (0.112)^2 + (0.069)^2 + 2 \cdot (-0.00736) \\ &= 0.00259. \end{aligned}$$

We can then calculate our test statistic and perform a t-test:

$$T\ =\ \frac{\widehat{\beta}_2 + \widehat{\beta}_4 - 0}{\sqrt{Var(\widehat{\beta}_2 + \widehat{\beta}_4)}}\ =\ \frac{-0.109 + 0.681 - 0}{\sqrt{0.00259}}\ =\ \frac{0.572}{0.0509}\ =\ 11.2 \sim t_{4434-(7+1)}.$$

[Note that we can find the corresponding p-value using an online calculator or a t-table.] So we conclude that age is a significant independent predictor of systolic blood pressure among individuals with $sex = 1$ ($p < 0.0001$). Our 95% confidence interval can be calculated as follows:

$$95\%\ CI:\ 0.572\ \pm\ 1.96 \cdot 0.0509\ =\ (0.472, 0.672).$$

With 95% confidence, a one year increase in age is associated with between a 0.472 mmHG and a 0.672 mmHG increase in mean systolic blood pressure, holding current smoking status and BMI category constant.

<u>Note</u>: I had originally forgotten to provide you the covariance between the main effect of age and the age by sex interaction. If you did not have that information, you would *not* be able to conduct the hypothesis test or construct a 95% confidence interval for the effect of age on systolic blood pressure among those with $sex = 1$.

Suppose that we wish to test whether overweight individuals have mean systolic blood pressures that are 10 mmHg higher than individuals with BMI between 18.5 and 25. What are our null and alternative hypothesis? What is our test statistic, and what distribution do we compare it to?

We want to compare individuals who are considered overweight (who have BMI values between 25 and 30) to individuals with BMI values between 18.5 and 25; note that this second group of individuals corresponds to our reference level. So in this case, our null and alternative hypotheses are:

$$H_0:\ \beta_6\ =\ 10\quad vs.\quad H_1:\ \beta_6 \neq 10.$$

We can use a t-test in order to formally decide between these hypotheses:

$$T = \frac{\widehat{\beta}_6 - 10}{s.e.(\widehat{\beta}_6)} = \frac{6.95 - 10}{0.66} = \frac{-4.95}{0.66} = -7.52 \sim t_{4434-(7+1)},$$

where our reference distribution is a t-distribution with $\big(n - (p+1)\big)$ degrees of freedom ($n = 4434$, $p = 7$). If we calculate the corresponding p-value, we find that it is $p < 0.0001$.

Based just on the output above, do we have enough information to tell whether categorical BMI is a significant predictor of systolic blood pressure?

No. Since BMI is being treated as a categorical variable, we need to test whether at least one of these categories contributes something meaningful to our model/explains something meaningful about an individual's systolic blood pressure. With that in mind, we want to test

$$H_0 : \beta_5 = \beta_6 = \beta_7 = 0 \quad vs. \quad H_1 : \text{at least one of } \beta_5, \beta_6 \text{ or } \beta_7 \text{ is non-zero}$$

or, equivalently,

H_0 : the reduced model (without categorical BMI) is sufficient $\quad vs. \quad$ H_1 : the full model (with BMI) is preferred.

In order to conduct this test, we will need information on the sum of squares decomposition for both the reduced and the full model—which means that we will need output from both the model with and the model without BMI.

Suppose that we also fit the linear regression model that omits all categorical BMI terms:

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

The output is below:

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	418221	104555	255.79	<.0001
Error	4429	1810373	408.75426		
Corrected Total	4433	2228593			

Parameter Estimates

Variable	Label	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	Intercept	1	145.35344	5.85572	24.82	<.0001
cursmoke	Current Cig Smoker Y/N	1	-1.67146	0.63502	-2.63	0.0085
age	Age (years) at examination	1	-0.28151	0.11519	-2.44	0.0146
sex	SEX	1	-39.82493	3.56925	-11.16	<.0001
agesex		1	0.82822	0.07057	11.74	<.0001

Using this additional information, conduct the formal hypothesis test for assessing whether or not categorical BMI is a significant predictor of systolic blood pressure.

As mentioned above, our null/alternative hypotheses of interest are

$$H_0 : \beta_5 = \beta_6 = \beta_7 = 0 \quad vs. \quad H_1 : \text{at least one of } \beta_5, \beta_6 \text{ or } \beta_7 \text{ is non-zero.}$$

We can formally test this hypothesis using an F test. The test statistic is given by:

$$\begin{aligned} F &= \frac{(SSE_{reduced} - SSE_{full})/3}{SSE_{full}/(n-p-1)} \\ &= \frac{(1,810,373 - 1,704,506)/3}{1,704,506/4,426} \\ &= \frac{35,289}{385.112} \\ &= 91.63, \end{aligned}$$

which we then compare to a $F(3, 4426)$ distribution. The resulting p-value is $p < 0.0001$. So we reject the null hypothesis, and conclude that BMI is a significant predictor of systolic blood pressure ($p < 0.0001$).

Suppose that we now fit the same two models, but that this time we take hypertension (dichotomized as "yes"/"no") as our outcome of interest:

$$\text{logit}(p) = \beta_0 + \beta_1 \texttt{cursmoke} + \beta_2 \texttt{age} + \beta_3 \texttt{sex} + \beta_4 \texttt{age} \cdot \texttt{sex} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}$$

and

$$\text{logit}(p) = \beta_0 + \beta_1 \texttt{cursmoke} + \beta_2 \texttt{age} + \beta_3 \texttt{sex} + \beta_4 \texttt{age} \cdot \texttt{sex}.$$

The output is on the next page.

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	5577.714	4804.564
SC	5584.111	4855.741
-2 Log L	5575.714	4788.564

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	-0.3219	0.7037	0.2093	0.6473
cursmoke	1	-0.0154	0.0749	0.0425	0.8366
age	1	-0.0178	0.0133	1.7762	0.1826
sex	1	-3.3955	0.4530	56.1932	<.0001
agesex	1	0.0658	0.00862	58.2917	<.0001
underweight	1	-0.2996	0.3334	0.8078	0.3688
overweight	1	0.6846	0.0796	73.9428	<.0001
obese	1	1.5745	0.1095	206.7097	<.0001

(a) Output from the full model

Model Fit Statistics		
Criterion	Intercept Only	Intercept and Covariates
AIC	5577.714	5028.470
SC	5584.111	5060.455
-2 Log L	5575.714	5018.470

Analysis of Maximum Likelihood Estimates					
Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	1	1.2986	0.6742	3.7108	0.0541
cursmoke	1	-0.1832	0.0719	6.4955	0.0108
age	1	-0.0344	0.0129	7.1058	0.0077
sex	1	-4.0538	0.4388	85.3591	<.0001
agesex	1	0.0767	0.00836	84.1258	<.0001

(b) Output from the reduced model

In the full model (on the right), is age significantly associated with hypertensive status among individuals with sex = 0? How about among individuals with sex = 1? Construct and interpret a 95% Confidence Interval for each of these effects. Note that the covariance between $\widehat{\beta}_2$ and $\widehat{\beta}_4$ is -0.000109.

Our strategy for approaching this question is similar to the strategy we used for linear regression, but with some minor modifications! In particular, we'll assess significance using Wald tests, and then construct our 95% confidence intervals using the 97.5^{th} percentile of a standard normal distribution and the standard error of our effect estimates. Also note that we want to put our final effect estimates back on the odds/odds ratio scale!

Sex = 0:

Note that the fitted logistic regression line for individuals with $sex = 0$ is given by

$$\text{logit}(p) = \beta_0 + \beta_1 \texttt{cursmoke} + \beta_2 \texttt{age} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}.$$

So the association between age and hypertension is captured by β_2.

(1) In order to assess whether age is a significant predictor of hypertension among those with $sex = 0$, we want to perform a Wald test of the hypotheses: $H_0 : \beta_2 = 0$ vs. $H_1 : \beta_2 \neq 0$. The results of this test are reported in the SAS output. In particular, we find that—after adjusting for current smoking status and BMI category—age is not a significant predictor of hypertension among those with $sex = 0$ ($p = 0.183$).

(2) We can construct a 95% confidence interval for this quantity as follows:

$$\begin{aligned} 95\%\ CI \text{ for } \beta_2 : \widehat{\beta}_6 \pm z_{0.975} \cdot s.e.(\widehat{\beta}_6) &= -0.0178 \pm 1.96 \cdot 0.0133 \\ &= (-0.044,\ 0.008) \\ \implies 95\%\ CI \text{ for } e^{\beta_2} : e^{(-0.044,\ 0.008)} &= (0.957,\ 1.008) \end{aligned}$$

With 95% confidence, a one year increase in age is associated with between a $(1 - 0.957) \times 100 = 4.3\%$ decrease and a $(1.008 - 1) \times 100 = 0.8\%$ increase in the odds of developing hypertension among individuals with $sex = 0$, holding current smoking status and BMI category constant ($p = 0.183$).

Sex = 1

The fitted regression line for individuals with $sex = 1$ is given by

$$\text{logit}(p) = (\beta_0 + \beta_3) + \beta_1 \texttt{cursmoke} + (\beta_2 + \beta_4)\texttt{age} + \beta_5 \texttt{underweight} + \beta_6 \texttt{overweight} + \beta_7 \texttt{obese}.$$

So the association between age and hypertension is captured by $\beta_2 + \beta_4$.

(1) We now want to conduct a Wald test of the hypotheses $H_0 : (\beta_2 + \beta_4) = 0$ vs. $H_1 : (\beta_2 + \beta_4) \neq 0$. Unlike in the $sex = 0$ case, we do not have the results of the hypothesis test directly in the SAS output, but we can still conduct the test by hand! In particular:

$$\begin{aligned} Z &= \frac{\widehat{\beta}_2 + \widehat{\beta}_4 - 0}{\sqrt{Var(\widehat{\beta}_2 + \widehat{\beta}_4)}} \\ &= \frac{\widehat{\beta}_2 + \widehat{\beta}_4 - 0}{\sqrt{Var(\widehat{\beta}_2) + Var(\widehat{\beta}_4) + 2 \cdot Cov(\widehat{\beta}_2, \widehat{\beta}_4)}} \\ &= \frac{-0.0178 + 0.0658 - 0}{\sqrt{0.0133^2 + 0.0086^2 - 2 \cdot 0.0001}} \\ &= \frac{0.048}{\sqrt{0.00005}} \\ &= 6.73. \end{aligned}$$

We compare this test statistic to a standard $N(0,1)$ distribution (you can do this using a normal table, an online calculator, or your statistical package), and find that the associated p-value is $p < 0.0001$. So we reject the null hypothesis, and conclude that age is a significant predictor of hypertension among individuals with $sex = 1$ ($p < 0.0001$).

(2) To construct a 95% confidence interval for the association between age and the odds of hypertension among individuals with $sex = 1$, we first construct a confidence interval for the quantity $\beta_2 + \beta_4$:

$$95\%\ CI : \widehat{\beta}_2 + \widehat{\beta}_4 \pm 1.96\sqrt{Var(\widehat{\beta}_2 + \widehat{\beta}_4)} = 0.048 \pm 1.96 \cdot \sqrt{0.00005} = (0.034, 0.062).$$

We then transform this confidence interval back onto the odds/odds ratio scale by exponentiating both the lower and upper bounds:

$$95\%\ CI \text{ for } e^{\beta_2+\beta_4} : (e^{0.034},\ e^{0.062}) = (1.03,\ 1.06).$$

With 95% confidence, a one year increase in age is associated with between a 3% and a 6% increase in the odds of hypertension among individuals with $sex = 1$, holding current smoking status and BMI category constant.

Assess whether categorical BMI is a significant predictor of hypertensive status.

Our hypotheses of interest are

$$H_0 : \beta_5 = \beta_6 = \beta_7 = 0 \quad vs. \quad H_1 : \text{ at least one of } \beta_5, \beta_6, \beta_7 \text{ is non-zero.}$$

Because we're in a logistic regression setting, we'll use a likelihood ratio test to formally decide between these hypotheses. Then our test statistic is given by:

$$X = -2 \cdot \log \mathcal{L}(reduced) + -2 \cdot \log \mathcal{L}(full) = Deviance_{reduced} - Deviance_{full} = 5018.470 - 4788.564 = 230.$$

We compare this test statistic to a χ^2_3 distribution (using a table, an online calculator, or a statistical package), and find that the p-value is $p < 0.0001$. So we reject the null hypothesis, and conclude that categorical BMI is a significant predictor of hypertensive status ($p < 0.0001$).