

Logistic Regression (continued)

- Recall that logistic regression provides a way of relating predictor variables X to binary (0,1) outcome variable Y. This outcome variable is an indicator for "yes/no", "event/non-event", etc
- The model actually predicts Pr(Y = 1|X). This equals the expected value (mean) of Y, as in linear regression. How?
 - Note that for a binary variable, the mean of Y and covariate X , $\sum_{j=1}^{N_i} Y_i/N_i = p_i$, or the proportion that equal 1.
 - For a binomial random variable (independent draws, probability p of success for each draw), this proportion equaling 1 is the same as $\Pr(Y=1)$

Logistic Regression

- The model for $\Pr(Y=1|X)$ is nonlinear. We model linearly via the logit transform:

$$\log\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots \beta_q X_q$$

- β_j in the model is the difference in log odds for a one unit increment in X_j . This is same as the **log odds ratio**. Exponentiating gives the **odds ratio**, reflecting the relative odds of event (being a '1') for a one-unit increment in X. Note that this is a multiplicative difference (rather than additive as in difference of means)
- Ex: $\beta_{age}=0.336$. Then $\exp(0.336)=1.4$. For a one-year increase in age, relative odds of event goes up by 1.4, or 40%

Logistic Regression

- The model can produce a probability of event for each case in the dataset, based on the predictors X, via the equation

$$\Pr(Y = 1|X) = \frac{\exp(\beta_0 + \beta_1 X_1 + \dots + \beta_q X_q)}{1 + \exp(\beta_0 + \beta_1 X_1 + \dots + \beta_q X_q)}$$

• With these values, one can assess how well individual cases may be classified with respect to outcome (will discuss shortly)

Logistic Regression - another example model coefficient interpretation

- **Glioblastoma (GBM):** A randomized clinical trial was conducted comparing standard treatment (radiation + chemotherapy) to this treatment plus bevacizumab (Avastin) with the goal of improving two endpoints:
 - progression-free survival (time remaining alive and free of disease progression) and
 - survival time
- Here, we analyze PFS at 18 months from study entry
- While prognosis is generally unfavorable, important new tumor molecular markers are strongly associated w/outcomes and possibly treatment response. O(6)-methylguanine-DNA methyltransferase (MGMT) inactivation via methylation is also examined

Logistic Regression model coefficient interpretation

Examining effects individually via tables:

. cc fail_18mo trt

| | | | | | | Proportion | |
|------------|--------|---------|-----------|---------|------------|------------|-----|
| | 1 | Exposed | Unexposed | | Total | exposed | |
| Cases | ·+ | 225 | 235 | -+- | 460 | 0.4891 | |
| Controls | • | 87 | 74 | İ | 161 | 0.5404 | |
| Total | | 312 | 309 | + | 621 | 0.5024 | - |
| | | | estimate | | [95% Conf. | Interval] | |
| Odds ratio | | | 81438 | | .5587526 | 1.185748 | (ex |

Modest treatment effect - 19% lower odds of failure

. cc fail_18mo mgmt_grp

| | roportion | Pr | | | |
|---------|-------------------------------|--------------------------|---------------------------------|--------------------|------------|
| | exposed | Total | Unexposed | Exposed | |
| | 0.7696 | 460 | 106 | 354 | Cases |
| | 0.5714 | 161 | 69 | | Controls |
| | 0.7182 | 621 | 175 | | Total |
| | Interval] | | estimate | | |
| (exact) | 3.724206 | 1.678978 | 504717 | | Odds ratio |
| (e | 0.5714 0.7182 Interval] | 161 621 [95% Conf. | 69 +- 175 estimate | 92 446 Point | Controls |

MGMT unmethylated have 2.5 times greater odds of failure

Logistic Regression model coefficient interpretation

The model run:

```
. logit fail_18mo trt mgmt_grp

Iteration 0: log likelihood = -355.38631
. . .
```

Iteration 3: $\log likelihood = -343.79561$

| Logistic regre | ession | | | Number | of obs | = | 621 |
|----------------|---------------|-----------|-------|---------|--------|------|-----------|
| | | | | LR chi2 | (2) | = | 23.18 |
| | | | | Prob > | chi2 | = | 0.0000 |
| Log likelihood | l = -343.7956 | 1 | | Pseudo | R2 | = | 0.0326 |
| fail_18mo | Coef. | Std. Err. | z | P> z | | | Interval] |
| trt | | .1870863 | -1.07 | 0.286 | 5663 | | .1670335 |
| mgmt_grp | .9167454 | .1941661 | 4.72 | 0.000 | .5361 | .868 | 1.297304 |
| _cons | .5330665 | .1833776 | 2.91 | 0.004 | .1736 | 5529 | .8924801 |

Adjusted ORs: trt OR: $e^{-.19964} = 0.819$. MGMT OR: $e^{.91674} = 2.50$

Logistic Regression model coefficient interpretation

We can generate 3 odds ratios <u>relative to the reference group</u> [no bev, MGMT methylate]d:

Treatment

| MGMT Status | Placebo | Bevac |
|--------------|---------|-------|
| methylated | 1.00 | 0.82 |
| unmethylated | 2.51 | 2.04 |

Note that $2.51 \times 0.82 = 2.04$, i.e., the treatment effect is the same in both MGMT groups according to this model

Logistic Regression - another model

We can add a treatment by MGMT interaction term to the model, permitting different trt effects in each MGMT group:

```
. logit fail_18mo trt mgmt_grp trt_by_mgmt
Iteration 0: log likelihood = -355.38631
I . .
Iteration 3: log likelihood = -342.3045
Logistic regression
                                       Number of obs =
                                                            621
                                      LR chi2(3) =
                                                           26.16
                                       Prob > chi2 =
                                                          0.0000
Log likelihood = -342.3045
                                      Pseudo R2
                                                          0.0368
  fail_18mo | Coef. Std. Err. z P>|z| [95% Conf. Interval]
       trt | -.6310748 .3145175 -2.01 0.045 -1.247518 -.0146317
   mgmt_grp | .561396 .2849644 1.97 0.049
                                              .002876 1.119916
trt_by_mgmt | .6745599 .3920708 1.72 0.085 -.0938848 1.443005
                                            .3079791 1.221233
      _cons | .7646061 .2329773 3.28
                                       0.001
```

There is a suggestion of interaction between treatment and MGMT status

Logistic Regression - another model

We again generate 3 odds ratios <u>relative to</u> [no bev, MGMT methylated]:

Treatment

| MGMT Status | Placebo | Bevac |
|--------------|---------|-------|
| methylated | 1.00 | 0.53 |
| unmethylated | 1.75 | 1.83 |

Now note that

- Bev effect in methylated is larger, 47% reduction in odds of failure
- No Bevt effect in unmethylated, which we can see by computing 1.83/1.75 equals OR = 1.045. Another way to obtain is $e^{-.6311+.6745}=1.045$. We can check these effects by estimating treatment effects separately by MGMT status.

Logistic Regression - Stratified Treatment Effect

. cc fail_18mo trt if mgmt_grp==0

| | | | | • | Proportion |
|------------|---------|-----------|-----|---------|------------|
| <u> </u> | Exposed | Unexposed | • | otal | exposed |
| Cases | 48 | 58 | | 106 | 0.4528 |
| Controls | 42 | 27 | | 69 | 0.6087 |
| Total | 90 | 85 | | 175 | 0.5143 |
| 1 | Point | estimate | [95 | % Conf. | Interval] |
| Odds ratio | . 53 | 320197 | .27 | 36227 | 1.029957 |

. cc fail_18mo trt if mgmt_grp==1

| | | | | Proportion |
|------------|---------|------------|-----------------|----------------------|
| | Exposed | Unexposed | Total + | exposed |
| Cases | 177 | 177 | 354 | 0.5000 |
| Controls | 45 | 47 | 92 | 0.4891 |
| Total | • | 224 | + 446 | 0.4978 |
| | 1 | estimate | [95% Conf. | <pre>Interval]</pre> |
| Odds ratio | |)44444 | + .6430068 | 1.697515 |

Logistic Regression - Model Significance & Goodness of Fit

- As we discussed, a *likelihood ratio* test can be defined contrasting the model in question with a null model containing no predictors. This is analogous to the global F-test in SLR/MLR
- The test statistic:

$$D_{global} = -2(\mathsf{log\text{-}likelihood}_{null} - \mathsf{log\text{-}likelihood}_{full})$$

is χ^2_{df} where degrees of freedom df = number of predictors

- This same type of test is used for contrasting two nested models, say, dropping out 3 predictors out of 7 candidates

$$D_{nested} = -2(\text{log-likelihood}_{smaller\ model} - \text{log-likelihood}_{bigger\ model})$$

is χ^2_3 (3 df) and tests whether the three parameters considered for dropping simultaneously have $\beta_j=0$

Logistic Regression - Quantifying Fit

- The global LR test evaluates whether there is a worthwhile model relative to no model at all. What about a test against 'the best model available', or a perfect fit?
- In the case of discrete predictors (where tables can be formed), such as test is available and can give a sense of what is the model that predicts best with the least number of predictors.

- Model Goodness of Fit - Deviance: notation and definition

The quantity D above is known as the deviance and can be used to assess model fit: define

- 1. \hat{L}_c : the maximized likelihood (likelihood given the MLE) under the current model of interest
- 2. \hat{L}_f : the maximized likelihood under the model fits the data perfectly, which is termed the *full* or *saturated model*

Then the Deviance: $D = -2\log(\hat{L}_c/\hat{L}_f) = -2\{\log\hat{L}_c - \log\hat{L}_f\}$

- D measures the extent to which the current model deviates from the full model:
- ullet Large D when \hat{L}_c is small relative to \hat{L}_f , indicating the current model fit is poor.
- ullet Small D when \hat{L}_c is similar to \hat{L}_f , indicating 'good' current model fit.

- Model Goodness of Fit - Deviance: notation and definition Deviance: formula

• Recall: the likelihood function based on observations y_i/n_i , for i=1,2,...,n groups defined by unique covariate combinations, with unknown p_i is

$$L = \prod_{i=1}^{n} \binom{n_i}{y_i} p_i^{y_i} (1 - p_i)^{n_i - y_i}$$

$$\log L = \sum_{i=1}^{n} \{ \log \binom{n_i}{y_i} + y_i \log p_i + (n_i - y_i) \log(1 - p_i) \}$$
 (1)

ullet Let $\hat{p}_i,\ i=1,...,n$ be the fitted values under *current model*, then

$$\log \hat{L}_c = \sum_{i=1}^n \{ \log \binom{n_i}{y_i} + y_i \log \hat{p}_i + (n_i - y_i) \log(1 - \hat{p}_i) \}$$
 (2)

• Define $\tilde{p}_i = y_i/n_i, \ i=1,...,n$ which are the actual probabilities in

these table cells. We define this as the full model:

$$\log \hat{L}_f = \sum_{i=1}^n \{ \log \binom{n_i}{y_i} + y_i \log \tilde{p}_i + (n_i - y_i) \log(1 - \tilde{p}_i) \}$$
 (3)

• The *Deviance* is then given by

$$D = -2\{\log \hat{L}_c - \log \hat{L}_f\}$$

$$= 2\sum_{i=1}^n \{y_i \log(\frac{\tilde{p}_i}{\hat{p}_i}) + (n_i - y_i) \log(\frac{1 - \tilde{p}_i}{1 - \hat{p}_i})\}$$
(4)

- Model Goodness of Fit - Deviance Statistic

- To use the deviance statistic, we have to have the following circumstances for the covariate set **X**:
 - We assume there is a model that reproduces the probability of event at a given X combination perfectly (from a table of response by X category, the \tilde{p} from eqn. 4 above), and ...
 - there are model(s) with fewer parameters (for example, main effects only for \mathbf{X} , or a given X represented as a numeric index or on a continuous scale).
- ullet Then, we can contrast models via estimated \hat{p} and $ilde{p}$

Logistic Regression - D as Goodness of Fit Measure

Deviance: distribution of the deviance statistic D

- We use D to evaluate the current model, and so we need to know it's distribution. Under H_0 that the current model requires no additional parameters to fit well, as the groups size $n_i \longrightarrow \infty$, D converges to χ^2_{n-p} , where $p=\sharp$ parameters fit, $n=\sharp$ of groups.
- ullet Thus, for reasonably large groups, the deviance provides a goodness of fit test for the model, and $D\sim\chi^2_{n-p}$ approximately. In this case,
 - The value of deviance statistic, D, can be compared to tables of percentage points of the χ^2_{n-p} distribution. Note here we expect a large statistic (small p-value) under bad fit.
 - Since mean of a χ^2_{n-p} r.v. is n-p, a useful rule of thumb is the D does not exceed n-p, the model may be satisfactory.

Logistic Regression - D as Goodness of Fit Measure Deviance: distribution (continued): Case of 'continuous' X values:

- For the case where X is (in practical terms) on a continuous scale, so that for each X value there is only one response (0/1) for Y (and thus no natural way to form a table), $\log \hat{L}_f = 0$, and D depends only on the fitted success \hat{p}_i :
 - $D = -2\sum_{i=1}^{n} {\{\hat{p}_i \text{logit}(\hat{p}_i) + \log(1 \hat{p}_i)\}}$. In this case, the deviance is uninformative about the goodness of fit of a model.
- ullet In this case where $n_i=1$, for all i, D is not even approximately χ^2 .
- Even when the n_i all exceed unity (i.e, we have 'tables'), the χ^2 approximation may not be particularly good when the data are sparse, i.e., some of the binomial denominators n_i are very small.

We will look at an alternative test for this case a bit later . . .

Logistic Regression - D as Goodness of Fit Measure

Example: Donner Party: In 1846 the Donner and Reed families left Springfield, Illinois, for California by covered wagon. In July, the Donner Party, as it became known, reached Fort Bridger, Wyoming. There, 87 people and 20 wagons crossed the Wasatch Range and the desert west of the Great Salt Lake and entering the eastern Sierra Nevada mountains in late October (later than planned). Heavy snows stranded the group in the mountains, and by the time of complete rescue in April, 1847, 40 of the 87 members had died from famine and exposure.

What factors were related to survival?

Example - D as Goodness of Fit Measure Listing of part of the data for 45 individuals

list AGE SEX STATUS in 5/20, noobs clean

| STATUS | SEX | AGE |
|----------|--------|-----|
| DIED | MALE | 15 |
| SURVIVED | MALE | 25 |
| DIED | MALE | 25 |
| SURVIVED | FEMALE | 22 |
| SURVIVED | MALE | 20 |
| SURVIVED | FEMALE | 24 |
| DIED | MALE | 25 |
| DIED | FEMALE | 25 |
| SURVIVED | FEMALE | 15 |
| SURVIVED | MALE | 18 |
| SURVIVED | FEMALE | 25 |
| SURVIVED | FEMALE | 23 |
| SURVIVED | MALE | 28 |
| SURVIVED | MALE | 28 |
| SURVIVED | FEMALE | 21 |
| DIED | MALE | 28 |

We form a discrete age categorical variable for illustrative purposes, classifying individuals as under 25 years or 25 and over.

The model:

. logistic died sex age25plus

| Logistic regre | ssion | | | Number | of obs | = | 45 |
|----------------|--------------|-----------|-------|---------|--------|----------|-----------|
| | | | | LR chi2 | (2) | = | 8.09 |
| | | | | Prob > | chi2 | = | 0.0175 |
| Log likelihood | = -26.868228 | 3 | | Pseudo | R2 | = | 0.1309 |
| died | Odds Ratio | Std. Err. | z | P> z | | Conf. | Interval] |
| sex | 3.597994 | 2.515823 | 1.83 | 0.067 | .9138 | 3505 | 14.16595 |
| age25plus | 3.84985 | 2.832213 | 1.83 | 0.067 | .9104 | 196 | 16.27968 |
| _cons | .2056279 | .1604821 | -2.03 | 0.043 | .0445 | 5413 | .9492959 |

Note: _cons estimates baseline odds.

We have two predictors of mortality: males and those over 25 have over 3-fold greater odds of death.

A full or saturated model here would include the sex by age group interaction, which will reproduce exactly the probabilities for the sex by age group by died/survived 3-way table:

```
. logit died sex age25plus agebysex
```

. . .

Iteration 10: log likelihood = -25.096587

| Logistic regre | ession | | | Number LR chi Prob > | | = = | 45 11.63 0.0088 |
|----------------|--------------|-----------|-------|----------------------------|-------|-------|-----------------------|
| Log likelihood | d = -25.0965 | 587 | | Pseudo | R2 | = | 0.1882 |
| died | Coef. | Std. Err. | | P> z | | Conf. | Interval] |
| sex | 17.63652 | 2388.794 | 0.01 | 0.994 | -4664 | .313 | 4699.586 |
| age25plus | 17.57199 | 2388.794 | 0.01 | 0.994 | -4664 | .378 | 4699.522 |
| agebysex | -17.03307 | 2388.794 | -0.01 | 0.994 | -4698 | .983 | 4664.917 |
| _cons | -17.34885 | 2388.794 | -0.01 | 0.994 | -4699 | . 298 | 4664.6 |

This coefficient estimates 'go crazy' since the (female, under 25) group has zero deaths, but the model accurately reproduces the observed probabilities of death in the 4 unique groups. The log likelihood statistic (the part we need (-25.096587)) is provided.

The Deviance statistic $D = -2\{\log \hat{L}_{current} - \log \hat{L}_{full}\}$ is then

$$D = -2\{-26.868228 - (-25.096587)\} = 3.5432$$

The associated p-value for a χ^2_1 distribution is 0.06. So, the model with two predictors passes as a possibly suitable model relative to the 'perfect' model

To do this in Stata, need to install a module called *ldev* and run after the model of interest (here, the main effects model)

. ldev

Logistic model deviance goodness-of-fit test

```
number of observations = 45
number of covariate patterns = 4
deviance goodness-of-fit = 3.54
degrees of freedom = 1
Prob > chi2 = 0.0598
```

Goodness of Fit Measures - continuous covariates

- What if we have continuous predictors (no tables or very sparse tables)?
- the Hosmer-Lemeshow test goodness of fit measure in logistic regression groups the n observations into groups (according to their estimated probability of event) and calculates the corresponding generalized Pearson χ^2 statistic. Usually deciles (10 groups) are used.

$$H = \sum_{g=1}^{G} \frac{(O_g - E_g)^2}{n_g(\hat{p}_g(1 - \hat{p}_g))}$$

Where O_g is the number of events in group g and $E_g = n_g * \hat{p}_g$ is the expected number of events

- In this type of test, a *large* p-value (> 0.05) indicates good correspondence between observed and predicted outcomes.

Goodness of Fit Measures - HL Test

The test can also be run on discrete data - Donner party data

```
. estat gof
```

Logistic model for died, goodness-of-fit test

```
number of observations = 45

number of covariate patterns = 28

Pearson chi2(25) = 24.35

Prob > chi2 = 0.4991
```

Logistic Regression - Model Significance and Goodness of Fit Measures

. logit sta typ age

```
Iteration 0: \log \text{ likelihood} = -100.08048
Iteration 1: \log \text{ likelihood} = -87.895217
```

. . .

Iteration 5: log likelihood = -86.537821

| Logistic regre | ssion | | | Number LR chi2 Prob > | 2(2) | = = | 200 27.09 0.0000 |
|-------------------------|-----------------------------------|--------------------------------|-----------------------|-----------------------------|----------------------------|-------|-----------------------------------|
| Log likelihood | = -86.53782 | 1 | | Pseudo | R2 | = | 0.1353 |
| sta | Coef. | Std. Err. | z | P> z | | Conf. | Interval] |
| typ age _cons | 2.453535 .0340162 -5.508762 | .75257 .0106944 1.033511 | 3.26 3.18 -5.33 | 0.001 0.001 0.000 | .9785 .01305 -7.5344 | 556 | 3.928545 .0549767 -3.483118 |

[.] estat gof, group(10) table

Logistic model for sta, goodness-of-fit test

(Table collapsed on quantiles of estimated probabilities)

| Prob + | | | | - | | | | Exp_0 | | Total |
|-----------|--|--|--|--|--|--|---|-----------------------|--|---|
| • | • | | | | | | | | İ | 20 |
| 0.0478 | | 1 | ١ | 0.9 | 1 | 20 | | 20.1 | 1 | 21 |
| 0.0812 | | 1 | | 1.2 | 1 | 18 | 1 | 17.8 | ١ | 19 |
| 0.1209 | | 2 | 1 | 1.8 | | 18 | | 18.2 | 1 | 20 l |
| 0.1916 | | 2 | | 3.1 | | 18 | | 16.9 | | 20 l |
| + | -+- | | +- | | + | | +- | | +- | |
| 0.2531 | - | 7 | | 4.6 | | 14 | | 16.4 | | 21 |
| 0.2936 | | 6 | | 6.1 | | 16 | | 15.9 | | 22 |
| 0.3376 | | 5 | 1 | 5.8 | 1 | 13 | | 12.2 | 1 | 18 |
| 0.3846 | | 8 | 1 | 7.3 | 1 | 12 | | 12.7 | 1 | 20 l |
| 0.5186 | I | 8 | ١ | 8.7 | ١ | 11 | | 10.3 | ١ | 19 |
| | 0.0362 0.0478 0.0812 0.1209 0.1916 0.2531 0.2936 0.3376 0.3846 | 0.0362 0.0478 0.0812 0.1209 0.1916 0.2531 0.2936 0.3376 0.3846 | 0.0362 0 0.0478 1 0.0812 1 0.1209 2 0.1916 2 0.2531 7 0.2936 6 0.3376 5 0.3846 8 | 0.0362 0 0.0478 1 0.0812 1 0.1209 2 0.1916 2 0.2531 7 0.2936 6 0.3376 5 0.3846 8 | 0.0362 0 0.5 0.0478 1 0.9 0.0812 1 1.2 0.1209 2 1.8 0.1916 2 3.1 0.2531 7 4.6 0.2936 6 6.1 0.3376 5 5.8 0.3846 8 7.3 | 0.0362 0 0.5 0.0478 1 0.9 0.0812 1 1.2 0.1209 2 1.8 0.1916 2 3.1 0.2531 7 4.6 0.2936 6 6.1 0.3376 5 5.8 0.3846 8 7.3 | 0.0362 0 0.5 20 0.0478 1 0.9 20 0.0812 1 1.2 18 18 0.1209 2 1.8 18 18 0.1916 2 3.1 18 18 18 18 18 18 18 | 0.0362 0 0.5 20 | 0.0362 0 0.5 20 19.5 0.0478 1 0.9 20 20.1 17.8 18 17.8 18 18.2 18 18.2 18 16.9 19.5 19 | 0.0362 0 0.5 20 19.5 0.0478 1 0.9 20 20.1 |

number of observations = 200
number of groups = 10
Hosmer-Lemeshow chi2(8) = 2.95
Prob > chi2 = 0.9372

Logistic Regression - Goodness of Fit Measures

This result looks very positive - good fit. However, Pseudo- $R^2=13\%$, so not that much variation explained.

Pseudo- R^2 measures proportion reduction in log-likelihood over null model. This is a useful measure, but more like another F-test than a measure of model explanatory power.

The Hosmer-Lemeshow g.o.f. test is more valuable as a means to identify major systematic variation that is not explained. Large p-value does not assure that prediction will be highly accurate, etc.

Logistic Regression - Goodness of Fit for the Donner Data

With continuous age predictor and sex:

. logistic died sex $\ensuremath{\mathsf{AGE}}$

| Logistic regre | | Number | of obs = | | 45 | | |
|----------------|----------------|-----------|----------|---------|-------|-------|-----------|
| | | | | LR chi2 | 2(2) | = | 10.57 |
| | | | | Prob > | chi2 | = | 0.0051 |
| Log likelihood | 1 = -25.628142 | 2 | | Pseudo | R2 | = | 0.1710 |
| died | Odds Ratio | Std. Err. | z | P> z | | Conf. | Interval] |
| sex | | 3.731909 | 2.11 | 0.034 | | 1236 | 21.71599 |
| AGE | 1.081343 | .0403206 | 2.10 | 0.036 | 1.005 | 5135 | 1.16333 |
| _cons | .0395411 | .0548425 | -2.33 | 0.020 | .0026 | 8089 | .5992974 |

Note: _cons estimates baseline odds.

. estat gof, group(10) table

Logistic model for died, goodness-of-fit test

(Table collapsed on quantiles of estimated probabilities)

| Gro | up | Prob | -1 | | - | - | | Obs_0 | | Exp_0 | Total |
|-----|----|--------|--------------|---|-------------|-----|---|-------|---|-------|-------|
| | 1 | 0.1928 | | 0 | | 0.8 | | 5 | | 4.2 | 5 |
| 1 | 2 | 0.3257 | | 1 | 1 | 1.3 | 1 | 4 | 1 | 3.7 | 5 |
| 1 | 3 | 0.4827 | | 1 | 1 | 1.8 | 1 | 3 | 1 | 2.2 | 4 |
| 1 | 4 | 0.5662 | | 3 | ١ | 2.2 | 1 | 1 | 1 | 1.8 | 4 |
| 1 | 5 | 0.5798 | | 7 | ١ | 4.6 | 1 | 1 | 1 | 3.4 | 8 |
| | + | | -+- | | + | | + | | + | + | |
| | 6 | 0.6226 | 1 | 1 | 1 | 0.6 | 1 | 0 | | 0.4 | 1 |
| | 7 | 0.6637 | 1 | 3 | 1 | 3.2 | | 2 | | 1.8 | 5 |
| | 8 | 0.6878 | 1 | 3 | 1 | 2.7 | | 1 | | 1.3 | 4 |
| | 9 | 0.8770 | | 2 | 1 | 4.0 | 1 | 3 | | 1.0 | 5 |
| 1 | 10 | 0.9692 | 1 | 4 | | 3.8 | | 0 | | 0.2 | 4 |

number of observations = 45
number of groups = 10
Hosmer-Lemeshow chi2(8) = 10.94
Prob > chi2 = 0.2049

Logistic Regression - Predictive Ability

Since the model generates $\Pr(Y=1)$ for all cases, we can assess how well we might predict failure or success with the model. Specifically:

- We can simply assess how many correct and incorrect for a given $\Pr(Y=1)$ criterion, such as 0.5. Ordinary sensitivity/specificity type calculations can be used to assess the result
- We can try to select a probability value that optimizes the above parameters. Note that as in sensitivity/specificity problems, there is a trade-off between predicting cases and non-cases correctly

Logistic Regression - Example of Predictive Ability

Glioblastoma (GBM) randomized clinical trial comparing standard treatment (radiation + chemotherapy) to same plus bevacizumab (Avastin), Analysis of survival

We will additionally include MGMT and composite prognostic indicator known as *RPA class*, as predictors

(Gilbert et al NEJM 2014)

Logistic Regression - Predictive Ability

- GBM data:

.* TRT effect = exposed here is trt = 1 (bev), use cohort with MGMT
. cc survival trt if cohort==1

| | - | • | Total | - | |
|-------------------|------------------|----------------|----------------|-------------|---------|
| Cases Controls | 210 | 193 108 | 403 | 0.5211 | |
| Total | 307 | 301 | 608 | 0.5049 | |
| | ' Point | Point estimate | | . Interval] | |
| Odds ratio | 1.2 | 1.211474 | | 1.721077 | (exact) |
| Attr. frac. ex. | .17 | . 1745591 | | .4189684 | (exact) |
| Attr. frac. pop | .09 | 09613 | I | | |
| • | + | chi2(1) = | 1.25 Pr>ch | i2 = 0.2639 | |

- .* MGMT effect exposed here is bad marker value (=1)
- . cc survival mgmt_grp if cohort==1

| | | | | Proportion | |
|-----------------|----------------|-----------|-----------------|------------|---------|
| | - | - | Total + | - | |
| Cases | | 82 | | | |
| Controls | • | 90 | | 0.5610 | |
| Total | + 436 | 172 | | 0.7171 | |
| | • | estimate | [95% Conf. + | Interval] | |
| Odds ratio | 3.0 | 63627 | 2.085235 | 4.496513 | (exact) |
| Attr. frac. ex. | .6735895 | | .5204378 | .7776055 | (exact) |
| • | + | chi2(1) = | 37.16 Pr>chi | 2 = 0.0000 | |

- No treatment benefit for survival (trt/control OR = 1.21, indicating 21% greater odds of failure on Avastin, although not significantly different from 1.0). MGMT- unmethylated patients have 3-fold greater risk of death. In GBM, this marker represents significant heterogeneity in prognosis

Logistic Regression - Predictive Ability

Examine treatment, MGMT, and RPA class (a baseline prognostic class indicator) together via logistic regression

```
. logit survival trt mgmt_grp rpa_class, or
Iteration 0:
              log likelihood = -388.59785
              log likelihood = -361.36406
Iteration 1:
              log\ likelihood = -361.10958
Iteration 4:
Logistic regression
                                                Number of obs
                                                                        608
                                               LR chi2(3)
                                                                      54.98
                                                Prob > chi2
                                                                     0.0000
Log likelihood = -361.10958
                                                Pseudo R2
                                                                     0.0707
    survival | Odds Ratio Std. Err.
                                              P>|z|
                                                       [95% Conf. Interval]
                1.253899 .2259569
                                      1.26
                                              0.209
                                                       .8807916
                                                                   1.785057
        trt |
    mgmt_grp |
                                       6.27
                                                       2.298569
                3.354802 .6471911
                                              0.000
                                                                   4.896394
  rpa_class | 1.967377
                          .3278095
                                     4.06
                                                                   2.727201
                                              0.000
                                                       1.419248
```

.0358217

_cons |

.0507661

-4.22

0.000

.0127335

.2023957

- Predict probabilities and assess

- . predict phat
- . list trt mgmt_grp rpa_class survival phat in 20/40, clean

| | trt | ${\tt mgmt_grp}$ | rpa_cl~s | survival | phat |
|-----|-----|-------------------|----------|----------|----------|
| 20. | 1 | 1 | 3 | 1 | .6192176 |
| 21. | 1 | 1 | 5 | 1 | .8629051 |
| 22. | 1 | 1 | 4 | 0 | .7618647 |
| 23. | 1 | 1 | 4 | 0 | .7618647 |
| 24. | 0 | 1 | 5 | 1 | .8338792 |
| 25. | 1 | 1 | 3 | 0 | .6192176 |
| | • | | | | |
| 34. | 1 | 1 | 4 | 0 | .7618647 |
| 35. | 1 | 0 | 4 | 0 | .4881366 |
| 36. | 1 | 1 | 3 | 1 | .6192176 |
| 37. | 1 | 1 | 4 | 1 | .7618647 |
| 38. | 0 | 1 | 3 | 1 | .5646291 |
| 39. | 1 | 0 | 3 | 0 | .3264767 |
| 40. | 1 | 1 | 4 | 1 | .7618647 |

One can 'assign' all those with, say, phat > .5, to failure, and compare to actual failure outcome

- A summary function to do this is provided in Stata

. estat classification
Logistic model for survival

| Classified | | ~D | • | Total |
|------------|-------------|-----------|------|------------|
| + | 340 63 | 131 74 | | 471 137 |
| Total | 403 | 205 | | 608 |

----- True -----

Classified + if predicted Pr(D) >= .5True D defined as survival != 0

Sensitivity Pr(+| D) = 84.37%Specificity $Pr(-| ^{\sim}D) = 36.10\%$ Positive predictive value Pr(D| +) = 72.19%Negative predictive value $Pr(^{\sim}D| -) = 54.01\%$ Correctly classified = 68.09% - The above rule uses 0.5 as a classification probability. What about other values? List the predicted probabilities.

. tab phat

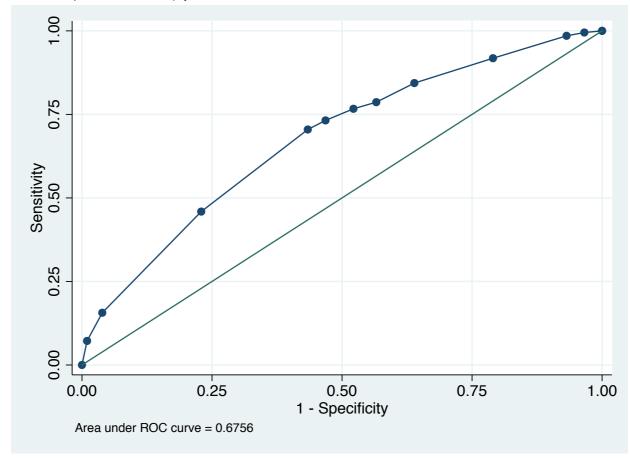
| Pr(survival) | 1 | Freq. | Percent | Cumul. |
|--------------|-------|-------|---------|--------|
| .2788 | + | 9 | 1.48 | 1.48 |
| .3264767 | | 11 | 1.81 | 3.29 |
| .4319939 | 1 | 56 | 9.21 | 12.50 |
| .4881366 | | 61 | 10.03 | 22.53 |
| .5646291 | 1 | 38 | 6.25 | 28.78 |
| .5994036 | 1 | 17 | 2.80 | 31.58 |
| .6192176 | 1 | 25 | 4.11 | 35.69 |
| .6523169 | | 18 | 2.96 | 38.65 |
| .718427 | 1 | 141 | 23.19 | 61.84 |
| .7618647 | 1 | 161 | 26.48 | 88.32 |
| .8338792 | 1 | 40 | 6.58 | 94.90 |
| .8629051 | + | 31 | 5.10 | 100.00 |
| Total | | 608 | 100.00 | |

Re-run the classification with all those with predicted probability greater than 0.66 declared failures

| | ification, cuto l for survival True | | | | |
|---|---|-----|-------|--|--|
| Classified | D | ~D | Total | | |
| · | 284 | 89 | | | |
| - | 119 | 116 | | | |
| Total | 403 | 205 | 608 | | |
| Classified + if predicted Pr(D) >= .667 True D defined as survival != 0 | | | | | |
| Sensitivity Pr(+ D) | | | | | |
| Specificity Pr(- ~D) | | | | | |
| Positive predictive value Pr(D +) | | | | | |
| Negative predictive value Pr(~D -) | | | | | |
| Correctly classified 65. | | | | | |

- This rule is better on some measures, worse on others. To look at all probability cutoff values at once, use ROC curve (command *lroc*

Logistic Regression - ROC Curve for Prediction



Logistic Regression - ROC Curve for Prediction

- Area under curve is the metric of interest. Perfect prediction has area = 1.0. Area under 'Guessing' line = 0.50. Area can be thought of as equalling, if given two cases (event and non-event), the probability of correctly classifying one as event and other and non-event
- Point closest to upper left corner is the best classifier (best trade-off between sensitivity and specificity)
- This model has area = 0.68, best probability cutpoint near specificity = 75%, specificity = 50%. Can examine ordered list of predicted probabilities to find (1roc in Stata will not list plot values (?)

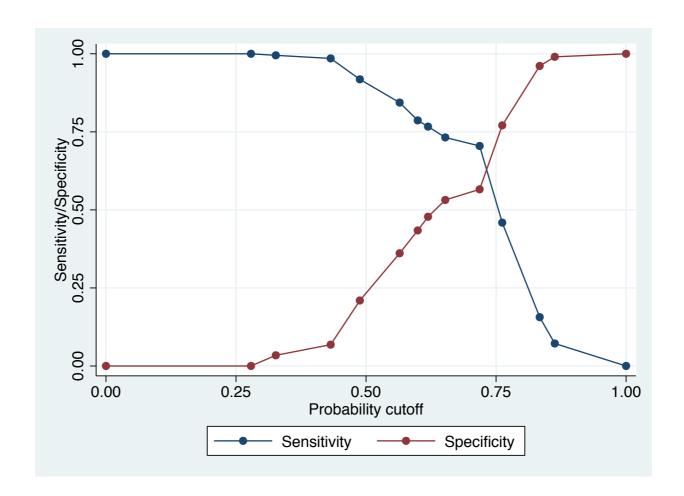
A related option lsens in Stata will provide the sensitivity/specificity values at each model predicted probability.

Logistic Regression - ROC Curve for Prediction

- . lsens, gense(sensval) gensp(specval)
- . list p sensval specval in 1/12, clean

```
specval
                   sensval
             p
      .8629051
                 0.000000
                             1.000000
 1.
 2.
      .8338792
                 0.071960
                             0.990244
 3.
      .7618647
                 0.156328
                             0.960976
      .718427
                 0.459057
                             0.770732
 4.
 5.
      .6523169
                 0.704715
                             0.565854
                 0.732010
 6.
      .6192176
                             0.531707
      .5994036
                             0.478049
                 0.766749
 7.
 8.
      .5646291
                 0.786600
                             0.434146
 9.
      .4881366
                 0.843672
                             0.360976
      .4319939
                 0.918114
                             0.209756
10.
11.
      .3264767
                 0.985112
                             0.068293
12.
         .2788
                 0.995037
                             0.034146
```

- These are the points on the ROC curve. A plot is also produced



- IMPORTANT NOTE: Optimizing cut point on a given dataset does not establish that classifier will work on novel data - requires validation in an independent sample (not used to build the predictor model)

Classification - Donner Party Data

. estat classification Logistic model for died

| | | True | |
|------------|-----------|---------|----|
| Classified | D | ~D | |
| + - | 23 2 | 8 12 | |
| Total | + 25 | 20 | -+ |

Classified + if predicted Pr(D) >= .5. True D defined as died != 0 Sensitivity Pr(+| D) 92.00% Specificity Pr(-|~D) 60.00% Positive predictive value Pr(D| +) 74.19% Negative predictive value Pr(~D| -) 85.71% Pr(+|~D) 40.00% False + rate for true ~D Pr(-| D) 8.00% False - rate for true D False + rate for classified + Pr(~D| +) 25.81%

False - rate for classified -

Correctly classified 77.78%

14.29%

Pr(D| -)

Classification - Donner Party Data

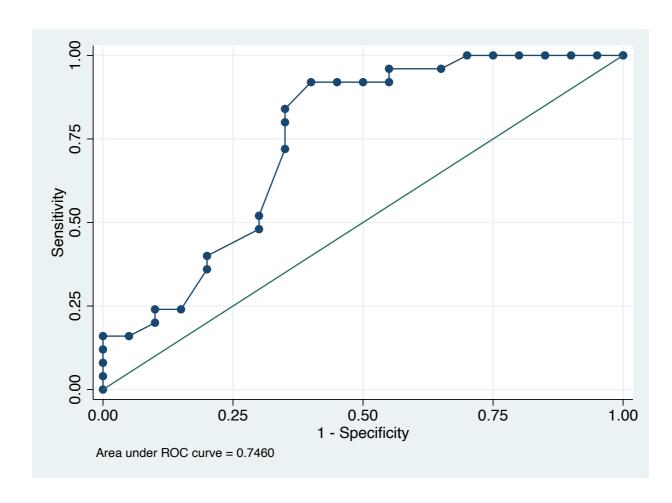
All possible cutpoints (except the extremes):

```
. predict phat
. list phat sensual specual, clean
10.
       .6636918
                  0.360000
                             0.800000
11.
        .635664
                             0.800000
                  0.400000
12.
       .6094921
                  0.480000
                             0.700000
13.
      .5798071
                  0.520000
                             0.700000
14.
      .5716949
                  0.720000
                             0.650000
15.
      .5606443
                             0.650000
                  0.800000
16.
       .541299
                  0.840000
                             0.650000
17.
      .4827471
                  0.920000
                             0.600000
18.
      .4744595
                  0.920000
                             0.550000
19.
      .4438758
                             0.500000
                  0.920000
20.
      .3869718
                  0.920000
                             0.450000
21.
      .3256594
                  0.960000
                             0.450000
 . . .
```

probability cutpoint around 0.54 is best, as also shown in the ROC curve

Classification - Donner Party Data

- .* get ROC curve
- . lroc



Summary: Logistic Regression Models

• Several diagnostic quantities, aiming to detect outliers and influential points, are defined (C&H 12.5, not covered in SPRM). These borrow concepts from linear regression, discussed next . . .