

Lab #11 Discussion

Question 1. What do the results from `tabodds` indicate about the associations between these three variables and esophageal cancer?

. tabodds case alcgp, or

alcgp	Odds Ratio	chi2	P>chi2	[95% Conf. Interval]	
0-39 gm~y	1.000000	.	.	.	.
40-79	3.556034	32.55	0.0000	2.232193	5.665003
80-119	7.693966	73.98	0.0000	4.439351	13.334630
120+	27.155172	159.99	0.0000	12.476332	59.104180

Test of homogeneity (equal odds): chi2(3) = 157.99

Pr>chi2 = 0.0000

Score test for trend of odds: chi2(1) = 151.98

Pr>chi2 = 0.0000

. tabodds case tobgp, or

tobgp	Odds Ratio	chi2	P>chi2	[95% Conf. Interval]	
0-9 gm/~y	1.000000	.	.	.	.
10-19	1.871507	10.54	0.0012	1.274043	2.749151
20-29	1.934066	8.01	0.0047	1.214629	3.079632
30+	3.491202	25.41	0.0000	2.078915	5.862908

Test of homogeneity (equal odds): chi2(3) = 29.58

Pr>chi2 = 0.0000

Score test for trend of odds: chi2(1) = 27.30

Pr>chi2 = 0.0000

. tabodds case agegp, or

agegp	Odds Ratio	chi2	P>chi2	[95% Conf. Interval]	
25-34	1.000000	.	.	.	.
35-44	5.447368	3.18	0.0743	0.671840	44.167984
45-54	31.676647	26.29	0.0000	3.943092	254.472873
55-64	52.650602	43.21	0.0000	6.304213	439.719592
65-74	59.669811	46.18	0.0000	6.674741	533.426917
75+	48.225806	32.67	0.0000	4.682406	496.695189

Test of homogeneity (equal odds): chi2(5) = 96.94

Pr>chi2 = 0.0000

Score test for trend of odds: chi2(1) = 83.37

Pr>chi2 = 0.0000

The results show increasing esophageal cancer risk with increasing levels of the categories of each of the three categorized predictors. Lower confidence bounds for each estimated OR (for all three) indicate significantly elevated disease odds (above the baseline category) for all levels except for the age group 35-44. Further, the global test of homogeneity and trend are significant for all three predictors. The former test evaluates the hypothesis that odds ratios are constant across predictor levels. (Note that the interpretation of this test differs from the analogous test used to investigate differences in odds ratios for one predictor compared across levels of a second predictor.) Rejection indicates unspecified differences across levels. The trend test is based on the more specific alternative that the log odds increase linearly with increasing levels of the

predictors (assuming the levels are equally spaced). We can conclude that we have fairly strong evidence for increased risk (as measured by the odds) associated with increasing levels of all three predictors.

Question 2. *Do the above results indicate that age has a confounding influence on the measured associations between tobacco and/or alcohol consumption and the outcome?*

. tabodds case tobgp, or adjust(agegp)

Mantel-Haenszel odds ratios adjusted for agegp

tobgp	Odds Ratio	chi2	P>chi2	[95% Conf. Interval]	
0-9 gm/~y	1.000000	.	.	.	.
10-19	1.830268	8.92	0.0028	1.223417	2.738134
20-29	1.980508	7.50	0.0062	1.202969	3.260607
30+	6.528439	39.26	0.0000	3.318106	12.844832

Score test for trend of odds: chi2(1) = 34.17
Pr>chi2 = 0.0000

. tabodds case alcgp, or adjust(agegp)

Mantel-Haenszel odds ratios adjusted for agegp

alcgp	Odds Ratio	chi2	P>chi2	[95% Conf. Interval]	
0-39 gm~y	1.000000	.	.	.	.
40-79	4.286018	37.49	0.0000	2.578709	7.123699
80-119	7.829443	58.20	0.0000	4.182181	14.657465
120+	28.533878	139.50	0.0000	12.130672	67.117648

Score test for trend of odds: chi2(1) = 134.09
Pr>chi2 = 0.0000

The odds ratios estimated in the above `tabodds` commands are adjusted for the presence of age (as measured by the categorical predictor `agegp`). This means that the estimates are obtained by separately estimating the odds ratios for each level of the exposure variables (`alcgp` and `tobgp`) in each of the six strata defined by `agegp`, and combining the estimates into a single weighted estimate using the Mantel-Haenszel (M-H) procedure. These age-adjusted estimates correspond very closely to those obtained in a logistic regression model including both predictors. For example, the following model for `tobgp` and `agegp` yields age-adjusted odds ratio estimates for tobacco consumption:

. logistic case i.tobgp i.agegp

Logistic regression

Number of obs	=	975
LR chi2(8)	=	157.69
Prob > chi2	=	0.0000
Pseudo R2	=	0.1594

Log likelihood = -415.89796

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
_Itobgp_2	1.835637	.3782121	2.95	0.003	1.225763	2.748952
_Itobgp_3	1.946139	.4880221	2.66	0.008	1.190482	3.181447
_Itobgp_4	5.706004	1.725556	5.76	0.000	3.154422	10.32154
_Iagegp_2	6.009024	6.405328	1.68	0.093	.743814	48.54489
_Iagegp_3	36.04627	36.94488	3.50	0.000	4.83547	268.7088
_Iagegp_4	61.51665	62.82635	4.03	0.000	8.3113	455.3197
_Iagegp_5	83.19723	85.4861	4.30	0.000	11.10426	623.3445
_Iagegp_6	60.18631	64.24026	3.84	0.000	7.429544	487.5659

The differences between the adjusted and unadjusted estimates (obtained in Question #1) are not large, but the adjusted results yield larger estimated odds ratios for the highest levels of tobacco and alcohol consumption, indicating some confounding influence. You may have noticed that we haven't ruled out the possibility of interaction between age and these two exposures in their influence on cancer risk. Evaluation using frequency table methods would be awkward given the large number of categories. Logistic regression (possibly using appropriately modeled continuous versions of these predictors) would be simpler and more interpretable.

Question 3. *Interpret the results of the likelihood ratio tests. Which risk factor results in the biggest change in log-likelihood?*

```
. quietly logistic case i.tobgp i.alcgp i.agegp
. estimates store M0
. quietly xi:logistic case i.tobgp i.agegp
. lrtest M0
likelihood-ratio test                                LR chi2(3)  =    127.52
(Assumption: . nested in M0)                        Prob > chi2 =    0.0000
. quietly logistic case i.alcgp i.agegp
. lrtest M0
likelihood-ratio test                                LR chi2(3)  =     23.69
(Assumption: . nested in M0)                        Prob > chi2 =    0.0000
```

Clearly alcohol makes a bigger likelihood contribution than tobacco in a model including all three predictors. This would be more difficult to evaluate using the individual coefficients, associated Z statistics and Wald test results.

Question 4. *Create a dichotomous indicator of heavy alcohol use with the statements below, and evaluate it as a predictor in the model including tobgp and agegp. Use the likelihood ratio test to compare this model to the model including the four-level categorical predictor tobgp (fitted above). Do we lose anything from modeling alcohol consumption as a binary predictor?*

```
. quietly logistic case alc2 i.agegp i.tobgp
. lrtest M0
likelihood-ratio test                                LR chi2(2)  =     57.59
(Assumption: . nested in M0)                        Prob > chi2 =    0.0000
```

The two-level version of alcohol is derived from the four-level version by collapsing categories of, so the model requested is nested within the full model fitted above. The LR test results indicate a significant change from the model incorporating four levels of alcohol consumption. We conclude that the model based on the reduced variable fits less well than the full model, and that some information is lost in the simplification. Based on these results, we would prefer to retain more categories of alcohol consumption (or use the continuous version) in further analyses. Of course, this doesn't preclude investigating specific hypothesis about heavy drinkers if this category of individuals is of interest.

Question 5. *Compare the results of this model to the model fitted above including only the indicator est of estrogen use and comment on the apparent effects of including the additional risk factors on the association between the outcome and estrogen use.*

Assuming that estrogen use is the predictor of primary interest, comparison of the two regression models (see below) indicates potential confounding influence of the other predictors on the association between `est` and the outcome.

```
. clogit case est hyp non gall obes, group(set) or
Conditional (fixed-effects) logistic regression    Number of obs    =        315
                                                    LR chi2(5)        =        49.05
                                                    Prob > chi2       =        0.0000
Log likelihood = -76.868906                      Pseudo R2        =        0.2419
```

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
est	6.782407	3.086647	4.21	0.000	2.779747 16.54864
hyp	.8248199	.2903746	-0.55	0.584	.413711 1.644452
non	1.951244	.9958351	1.31	0.190	.717618 5.305545
gall	3.633828	1.503164	3.12	0.002	1.615316 8.174687
obes	1.610575	.5871015	1.31	0.191	.7883029 3.290552

```
. clogit case est, group(set) or
Conditional (fixed-effects) logistic regression    Number of obs    =        315
                                                    LR chi2(1)        =        35.35
                                                    Prob > chi2       =        0.0000
Log likelihood = -83.72159                      Pseudo R2        =        0.1743
```

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
est	7.954681	3.347525	4.93	0.000	3.486714 18.14802

```
. gen galest = gall*est
. clogit case est hyp non gall obes galest, group(set) or
Conditional (fixed-effects) logistic regression    Number of obs    =        315
                                                    LR chi2(6)        =        53.38
                                                    Prob > chi2       =        0.0000
Log likelihood = -74.704446                      Pseudo R2        =        0.2632
```

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
est	12.26034	7.651924	4.02	0.000	3.607865 41.66338
hyp	.8183825	.2849189	-0.58	0.565	.4136296 1.619202
non	2.104605	1.125999	1.39	0.164	.7375024 6.005895
gall	18.75607	16.72336	3.29	0.001	3.267312 107.6696
obes	1.564086	.5779477	1.21	0.226	.7581096 3.226929
galest	.1254424	.1255502	-2.07	0.038	.0176405 .8920255

However, further analysis reveals a significant negative interaction between the indicator of gall bladder disease (`gall`) estrogen use (`est`) (shown below). Note the use of `lincom` (below) giving the estimated odds ratios for the association between `est` and case status for women with and without gall bladder disease. Note the large standard error and upper 95% confidence bound for the coefficients for `gall` and `est` in the model above. The two tables below show the reason for the uncertainty: the relatively small number of cases (7) reporting no estrogen use.

```
. lincom est, or
( 1) est = 0
```

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
(1)	12.26034	7.651924	4.02	0.000	3.607865	41.66338

```
. lincom est + galest, or
( 1) est + galest = 0
```

case	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
(1)	1.537967	1.243321	0.53	0.594	.3153693	7.500227

```
. tab case gall if est==0
```

Case status (1=case, 0=control)	Gallbladder disease		Total
	No	Yes	
0	117	8	125
1	3	4	7
Total	120	12	132

```
. tab case gall if est==1
```

Case status (1=case, 0=control)	Gallbladder disease		Total
	No	Yes	
0	111	16	127
1	43	13	56
Total	154	29	183