

Logistic Regression

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Objectives

By the end of this session you should be able to:

- Use a logistic regression model
- Interpret the results of logistic regression
- Compare models using the likelihood ratio test
- Use interaction terms in logistic regression



Dependent variable

- It is a dichotomous variable
- It takes only two values, which usually represent the occurrence or non-occurrence of some outcome event (coded as 0 or 1)
- For example
 - CVD (0 "No" 1 "Yes")
 - Mortality (0 "Alive" 1 "Dead")
 - HIV (0 "Uninfected" 1 "Infected")



Logistic regression

- It is a variation of ordinary (linear) regression
- The logistic regression model is used to explain the effects of the explanatory variable(s) on the binary response.
- The dependent variable (Y) is a dichotomous or binary variable
- The independent/explanatory variable(s) (X) can be continuous or binary/categorical



Logistic Regression

 Logistic regression models the log odds of having the event of interest

$$\ln(odds) = \ln\left\{\frac{\hat{p}}{1-\hat{p}}\right\} = \beta_0 + x\beta_1,$$

where

- \hat{p} is the observed probability of having the event
- β_0 is the intercept
- β_1 is the slope parameter



Logistic Regression

- We fit a regression model for the log odds of disease as the outcome measure
- The log odds can take any value, pos or neg, whereas risks (and probabilities) are constrained to lie between 0 and 1
- The model is fitted using the method of "Maximum likelihood" which is an iterative procedure



An example: a model with one independent variable

```
. logit cvddef1 sex
Iteration 0:
               log likelihood = -6106.9672
Iteration 1: \log \text{ likelihood} = -6103.9477
Iteration 2: \log \text{ likelihood} = -6103.9464
Iteration 3:
               log likelihood = -6103.9464
Logistic regression
                                                   Number of obs
                                                                            14,836
                                                   LR chi2(1)
                                                                               6.04
                                                   Prob > chi2
                                                                             0.0140
Log likelihood = -6103.9464
                                                   Pseudo R2
                                                                             0.0005
     cvddef1
                             Std. Err.
                                                              [95% Conf. Interval]
                     Coef.
                                              Z
                                                   P>|z|
                                                   0.014
                 -.1154694
                              .0469308
                                          -2.46
                                                              -.207452
                                                                         -.0234867
         sex
                 -1.721946
                              .0343153
                                         -50.18
                                                   0.000
                                                            -1.789202
                                                                         -1.654689
       cons
```

- Women compared to men are less likely to have CVD
- The constant is the log odds of CVD when sex=0, i.e. for men



Odds ratio

- If the OR = 1 there is no association
- 0 ≤ OR < 1 means lower risk of disease
- OR > 1 means higher risk of disease



How to obtain the odds ratio

STATA COMMAND: logistic cvd sex

.1787181

. logistic cvddef1 sex

cons

Logistic regression				Number o	f obs	=	14,836
				LR chi2(1)	=	6.04
				Prob > cl	ni2	=	0.0140
Log likelihood	d = -6103.9464	1		Pseudo R	2	=	0.0005
cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95%	Conf.	<pre>Interval]</pre>
sex	.8909479	.0418129	-2.46	0.014	.8126	522	.976787

.0061328

 Women compared to men are less likely to have CVD, exp(-0.115) = 0.89

-50.18

0.000

.1670934

.1911515



How to interpret the results

- Among women the odds of having CVD is 0.89 times lower than men
- The p-value < 0.05
- The confidence interval tells us that there is a 95% chance that the interval [0.81, 0.97] captures the true OR



Testing for association

- We use the Wald test to test the null hypothesis that the true parameter value is 0 (i.e., in this case OR = 1, meaning that there is no association)
- z statistic is calculated as

z = coefficient / SE

z = In(OR) / SE (InOR)

we compare z with a Normal distribution

For our example

$$z = -0.15 / 0.046 = -2.46$$

p < 0.05 we reject the null hypothesis of no association



Another example

Dependent variable: CVD

Independent variable: diabetes

Variables in the Equation

								95% C.I.fo	or EXP(B)
		В	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1 ^a	diabetes	1.356	0.087	242.309	1	0.000	3.882	3.272	4.604
	Constant	-1.868	0.025	5751.755	1	0.000	0.154		

a. Variable(s) entered on step 1: diabetes.

How do we interpret the results?



A model with more than one independent variable

Dependent variable: CVD

Independent variables: sex and diabetes

Variables in the Equation

								95% C.I.fo	or EXP(B)
		В	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1 ^a	diabetes	1.350	0.087	239.566	1	0.000	3.856	3.250	4.575
	sex	-0.094	0.047	3.917	1	0.048	0.910	0.830	0.999
	Constant	-1.816	0.036	2608.265	1	0.000	0.163		

a. Variable(s) entered on step 1: diabetes, sex.

How do we interpret the results?



Interpretation

- The logistic regression has produced simultaneously a summary estimate of the effect of diabetes adjusted for sex, and a summary estimate of the effect of sex adjusted for diabetes.
- 3.8=exp(1.35) represents the (summary) odds ratio of having CVD among those who have diabetes compared to those who don't, adjusted for any confounding effect of sex



An example with a continuous independent variable

m1 <- glm(cvddef1 ~ diabetes + sex + age, data = logit, family = binomial(link = "logit"))

```
Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) -4.243353 0.090688 -46.791 < 2e-16
          0.832845 0.091848 9.068 < 2e-16
diabetes
           -0.161172   0.049628   -3.248   0.00116
sex
          0.046396 0.001451 31.972 < 2e-16
age
Signif. codes: 0 (***, 0.001 (**, 0.01 (*, 0.05 (., 0.1 (), 1
                            2.5 %
(Intercept) 0.01435937 0.01200256 0.01712679
diabetes
            2.29985246 1.91897256 2.75103357
            0.85114554 0.77227223 0.93813868
sex
            1.04748865 1.04452898 1.05048824
age
```

- Note: Age is continuous
- The odds of having CVD is increasing by 1.05 times per each year increase in age (adjusted for sex and diabetes)



We can also add a categorical independent variable, cigarette smoking

m1 <- glm(cvddef1 ~ diabetes + sex + age + factor(cigst1), data = logit, family = binomial(link = "logit"))

```
Coefficients:

Estimate Std. Error z value Pr(>|z|)

(Intercept) -4.294709 0.098359 -43.663 < 2e-16 ***
diabetes 0.818697 0.092065 8.893 < 2e-16 ***
sex -0.111087 0.050659 -2.193 0.0283 *
age 0.045027 0.001512 29.771 < 2e-16 ***
factor(cigst1)2 -0.019517 0.110426 -0.177 0.8597
factor(cigst1)3 0.268925 0.059305 4.535 5.77e-06 ***
factor(cigst1)4 0.082462 0.068856 1.198 0.2311
---
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
odds 2.5 % 97.5 %
(Intercept) 0.01364054 0.01122987 0.01651344
diabetes 2.26754279 1.89121064 2.71353762
sex 0.89486092 0.81031304 0.98833822
age 1.04605566 1.04297419 1.04917671
factor(cigst1)2 0.98067184 0.78691380 1.21353669
factor(cigst1)3 1.30855733 1.16486777 1.46977530
factor(cigst1)4 1.08595749 0.94828028 1.24218780
```



Likelihood ratio test (LRT)

- LRT = $2(L_1 L_0)$
- L₁ is the log likelihood of the model with variable that you want to test
- L₀ is the log likelihood of the model without that variable
- Under the null hypothesis LRT is distributed as a Chi-square with 1 d.f. (because there is only one predictor)



Hypothesis testing

Suppose we want to test the null hypothesis:
 H₀: after taking into account the effect of sex diabetes and age, there is no association between smoking and CVD

We can use the LR test



In Stata...

- Obtain L₁ by fitting the model with smoking logistic cvd diabetes sex age i.cist1
- Save L₁
 estimates store a
- Obtain the value L₀ by fitting the model without smoking logistic cvd diabetes sex age
- Save L₀
 estimates store b
- Compare L₁ and L₀
 lrtest a b



LRT result

1rtest a b

BUT!

The number of observations differs between models a (with smoking) and b (without smoking):

14764 vs. 14836



We need to re-run the model without smoking by excluding the people that have not answered to the question on smoking

. xi:logistic cvd diabetes sex age if cigst!=.

Logistic regression

Log likelihood = -5407.2266

Number of obs = 14,764LR chi2(3) = 1362.84

Prob > chi2 = 0.0000

Pseudo R2 = 0.1119

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
diabetes	2.298955	.2111569	9.06 -3.16	0.000	1.920209	2.752406
sex age	1.047421	.0424689	31.83	0.002	1.044438	1.050413
_cons	.014396	.0013095	-46.62	0.000	.0120452	.0172056

. est store x

. 1rtest a x

Likelihood-ratio test
(Assumption: x nested in a)

LR chi2(3) = 22.32Prob > chi2 = 0.0001



Results

- p < 0.05 so we reject H_0
- After taking into account the effect of sex diabetes and age, there is an association between smoking and CVD



INTERACTIONS (EFFECT MODIFICATION)



Analysis with two independent variables: CVD vs diabetes (yes/no) and age (old/young)

(d) had cardiovasc ular condition (excluding			
diabetes/h	ageg	gr	
igh bp)	<=50	51+	Total
no	7,706	4,998	12,704
	93.39	75.90	85.63
yes	545	1,587	2,132
	6.61	24.10	14.37
Total	8,251	6,585	14,836
	100.00	100.00	100.00

. (d) had						
cardiovasc						
ular						
condition	(d) doctor (diagnosed				
(excluding	diabetes (excluding				
diabetes/h	pregna	pregnant)				
igh bp)	no	yes	Total			
no	12,322	382	12,704			
	86.62	62.52	85.63			
yes	1,903	229	2,132			
	13.38	37.48	14.37			
Total	14,225	611	14,836			
	100.00	100.00	100.00			

Pearson chi2(1) = 910.9149

Pr = 0.000

Pearson chi2(1) = 276.5524 Pr = 0.000



Analysis with two independent variables: CVD vs diabetes (yes/no) and age (old/young)

Note: **agegr** is coded **0** for age \leq 50 and **1** for age > 50

. logistic cvd diabetes agegr

Logistic regression

Number of obs = 14836LR chi2(2) = 1027.46

Log likelihood = -5593.237

Prob > chi2 = 0.0000Pseudo R2 = 0.0841

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
diabetes	2.568399	.2314766	10.47	0.000	2.152524	3.064622
agegr	4.208948	.22483	26.91		3.790572	4.673501
_cons	.0693111	.0030804	-60.06		.0635291	.0756193



Interaction term

- In the previous model we estimated the joint effects of diabetes and age, assuming constant odds ratios across strata.
- If the odds ratios differ across strata then there is interaction between the two variables and the odds of the exposure should be reported separately for different levels of the effect modifying/interacting variable.



We can check by stratifying the analysis

•	xi:logist	cic cvd i	.diabet	es if	agegi	r==0	
	cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
	Idiabetes_1		.7698466			1.945352	
•	_cons xi:logist	.0688658 cic cvd i	.0031103 .diabet	-59.24 ces if	o.ooo agegi	.0630318 r==1	.0752398
	cvddef1	Odds Ratio	Std. Err.	Z			Interval]
	Idiabetes_1	2.494317				2.065708	3.011858
•	_cons xi:logist						.31069
	_	Odds Ratio					Interval]
		4.248769	.2318272	26.51	0.000	3.817848	4.728328
•	xi:logist	.0688658 ic cvd i	.0031103 .aqeqr	-59.24 if dia	o.ooo abetes	.0630318 5==1	.0752398
	_	Odds Ratio			P> z	[95% Conf	. Interval]
	 _Iagegr_1	3.371091	.8676534	4.72	0.000	2.035578	5.582815
	_cons	.216495	.0521067	-6.36	0.000	.135076	.3469906



Interaction in logistic regression (logit)

STATA COMMAND: xi:logit cvd i.diabetes*i.agegrp

Log likelihood = -5592.8637

Pseudo R2

0.0842

cvddef1	Coef.	Std. Err.	Z	P> z	[95% Conf.	Interval]
Idiabetes_1 Iagegr_1 IdiaXage 1 1	1.145407 1.446629 2313918	.2448839 .0545634 .2631007	4.68 26.51 -0.88	0.000 0.000 0.379	.6654431 1.339687 7470596	1.62537 1.553572 .284276
cons	-2.675595	.0451644	-59.24	0.000	-2.764116	-2.587075

$$\ln(odds) = -2.7 + 1.1 * (diabetes = 1) + 1.4 * (agegrp = 1) + (-0.2) * (diabetes = 1) * (agegrp = 1)$$

Interaction between diabetes and agegrp



Interaction in logistic regression (logistic)

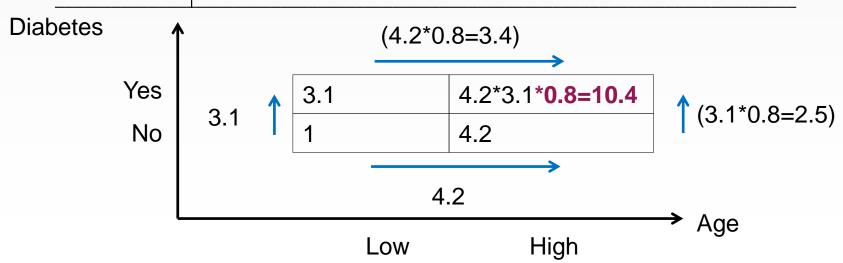
STATA COMMAND: xi:logistic cvd i.diabetes*i.agegr

Logistic regression

Log likelihood = -5592.8637

Number of obs = 14836 LR chi2(3) = 1028.21 Prob > chi2 = 0.0000 Pseudo R2 = 0.0842

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
_Idiabetes_1	3.14372	.7698465	4.68	0.000	1.945352	5.080301
_Iagegr_1	4.248769	.2318272	26.51		3.817848	4.728327
_IdiaXage_1_1	.7934285	.2087516	-0.88	0.379	.4737575	1.3288
_cons	.0688658	.0031103	-59.24		.0630318	.0752398





Interpretation

- The interaction term between diabetes and age has odds ratio 0.8
 - The odds ratio of age is different in people with and without diabetes
 - The odds ratio of diabetes is different between younger and older
- Among those aged ≤ 50 (the baseline of age) the odds ratio for diabetes vs no-diabetes is 3.1
- Among those aged 51+ (not at the baseline) the odds ratio for diabetes vs no-diabetes is 3.1 multiplied by the interaction parameter 0.8 = 2.5
- Among no-diabetes (the baseline of diabetes), the odds ratio for high age (51+ vs ≤50) is 4.2
- Among diabetes, the odds ratio for high age (51+ vs ≤ 50) is 4.2 multiplied by 0.8 = 3.4



Important

In the model **without** interaction between diabetes and age, the parameter

OR for diabetes = 2.6

is interpreted as the summary odds ratio for diabetes adjusted for the effect of age

In the model **with** interaction term between diabetes and age, the parameters

OR for diabetes = 3.1 in the agegr = 0 stratum

OR for diabetes = 2.5 in the agegr = 1 stratum

are interpreted as a stratum specific odds ratios: the odds ratios for diabetes in each stratum of age



Another example with physical activity (low=0, high=1)

(d) had cardiovasc ular condition (excluding			•
diabetes/h	pact	_	
igh bp)	0	1	Total
no	8,746 83.14	3,915 91.64	12,661 85.60
yes	1,773 16.86	357 8.36	2,130 14.40
Total	10,519	4,272 100.00	14,791

(d) had cardiovasc ular condition (excluding diabetes/h	Sé	⊇x	
igh bp)	men	women	Total
no	5,601	7,103	12,704
	84.84	86.26	85.63
yes	1,001	1,131	2,132
	15.16	13.74	14.37
Total	6,602	8,234	14,836
	100.00	100.00	100.00

Logistic regression

Number of obs = 14,791LR chi2(2) = 211.85

Log likelihood = -5990.484

Prob > chi2 = 0.0000Pseudo R2 = 0.0174

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
sex	.8215553	.0390729	-4.13	0.000	.7484346	.9018196
pact	.4378771	.0269326	-13.43	0.000	.3881479	.4939777
_cons	.2270913	.0084758	-39.72	0.000	.2110721	.2443263



logistic cvd sex if pact==0

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
sex _cons		.0402843			.693363 .2183931	.8515525 .2543825

logistic cvd sex if pact==1

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
sex _cons		.1227473			.8930298 .0746909	1.377971

logistic cvd pact if sex==0

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
pact _cons	.3684035	.0317363	-11.59 -37.14	0.000	.3111692	.4361651

logistic cvd pact if sex==1

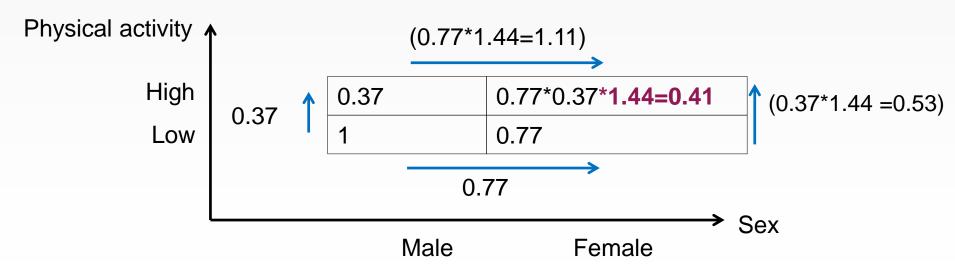
cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
pact _cons	.5318518 .1811128	.0462782			.4484611	.630749



Logistic regression with interaction

STATA COMMAND: xi:logistic cvd i.sex*i.pact

cvddef1	Odds Ratio	Std. Err.	z	P> z	[95% Conf.	Interval]
_Isex_1	.7683977	.0402843	-5.03	0.000	.693363	.8515525
_Ipact_1	.3684035	.0317363	-11.59	0.000	.3111692	.4361651
_IsexXpac_1_1	1.443666	.1767673	3.00	0.003	1.135646	1.835231
_cons	.2357019	.0091722	-37.14	0.000	.2183931	.2543825



Interpretation

- The interaction term between sex and pact has odds ratio 1.44
 - The odds ratio for physical activity is different between men and women
 - The odds ratio fir sex is different between active and non-active
- Among those less active (the baseline of pact) the odds ratio for women vs men is 0.77
- Among those active (not at the baseline) the odds ratio for women vs men is
 0.77 multiplied by the interaction parameter 1.44 = 1.11
- Among men (the baseline of sex), the odds ratio for the effect of pact (active vs less active) is 0.37
- Among women, the odds ratio for the effect of pact (active vs less active) is
 0.37 multiplied by 1.44 = 0.53

Again, this can be confirmed by stratified analyses



Note!

The odds ratio for sex diverges according to the different levels of physical activity

- •0.77 (< 1) in less active
- •1.1 (> 1) in highly active

but for both genders, the modifiable risk factor of high (vs low) activity is beneficial



Important

- In the first example of interaction between diabetes and age, the baseline ORs are greater than 1 and the interaction is negative (OR < 1)
 - this implies that the effect of diabetes tends to decrease with age (3.1 and 2.5)
- In the second example of interaction between sex and physical activity, the baseline ORs are less than 1 and the interaction is positive (OR > 1)
 - this implies that the effect of sex is diverging according to different levels of physical activity (0.77 and 1.1)



Interaction with a continuous variable

diabetes 6.08410154 2.60797383 13.64613360

diabetes:age 0.98530604 0.97323994 0.99800089

1.04801623 1.04498230 1.05109221

age



Interpretation

- Diabetes = 6.08 is the odds ratio for CVD in those with diabetes vs no-diabetes, holding age constant
- Age = 1.04 is the increase in the odds of CVD per each year increase in age, amongst non-diabetics
- diabetes:age = 0.98 is the interaction term between diabetes and age (one year increase)
- Note for STATA users: using i.diabetes*age tells STATA
 we want interaction between diabetes and age (where age
 is continuous)
 - Beware: STATA doesn't understand age*i.diabetes, only i.diabetes*age



LIKELIHOOD RATIO TEST FOR INTERACTIONS



Likelihood ratio test

- We can perform the LR test for the null hypothesis that there is no interaction
- We do this by comparing the log likelihoods of the model with the interaction term and the model without
 - LRT = 2 ($L_1 L_0$)
 - L₁ is the log likelihood of model with the variable that you want to test
 - L₀ is the log likelihood of the model without that variable



Interaction term involving a variable with more than 2 categories

cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]
 _Isex_1 Ismoking 2	1.092743 2.346264	.0797532	1.22	0.224	.9470947	1.260789
 Ismoking3	.8582719	.08505	-1.54	0.123	.7067658	1.042256
_IsexXsmo_1_2	.7069234	.0766261	-3.20	0.001	.5716199	.8742534
_IsexXsmo_1_3	.9895677	.1287282	-0.08	0.936	.7668611	1.276951
_cons	.1342282	.0077527	-34.77	0.000	.1198616	.1503167



LRT test

Null hypothesis: There is no interaction between sex and smoking status

We test it with LRT, if p < 0.05 we reject the null hypothesis



cvddef1	Odds Ratio	Std. Err.	z	P> z	[95% Conf.	Interval]
_Isex_1	.9616179	.0459716	-0.82	0.413	.8756077	1.056077
_Ismoking_2	1.970778	.105413	12.68	0.000	1.774633	2.188602
_Ismoking_3	.8460627	.0542723	-2.61	0.009	.7461061	.9594106
_cons	.1452046	.0066206	-42.32	0.000	.1327913	.1587782

. est store b

. lrtest a b

Likelihood-ratio test LR chi2(2) = 11.80 (Assumption: b nested in a) Prob > chi2 = 0.0027



cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]	. xi:logistic cvd i.smoking if sex==0
Ismoking 2	2.346265	.182454	10.97	0.000	2.014581	2.732559	
Ismoking 3	.8582718	.08505	-1.54	0.123	.7067658	1.042256	
cons	.1342282	.0077527	-34.77	0.000	.1198616	.1503167	
cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]	. xi:logistic cvd i.smoking if sex==1
_Ismoking_2	1.65863	.1252463	6.70	0.000	1.430453	1.923204	
_Ismoking_3	.8493182	.0715772	-1.94	0.053	.7200032	1.001858	
_cons	.1466769	.0065444	-43.02	0.000	.1343949	.1600812	
<u> </u>							
cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]	. xi:logistic cvd sex if smoking==0
sex	1.092742	.0797531	1.22	0.224	.9470943	1.260788	. Alliogistic eva Sex II Smoking0
_cons	.1342283	.0077527	-34.77	0.000	.1198617	.1503168	
cvddef1	Odds Ratio	Std. Err.	Z	P> z	[95% Conf.	Interval]	. xi:logistic cvd sex if smoking==1
sex	.7724846	.0619073	-3.22	0.001	.6601979	.9038691	
_cons	.3149351	.0163984	-22.19	0.000	.2843804	.3487727	
cvddef1	l Odds Ratio	Std. Err.	Z	P> z	[95% Conf	. Interval]	
sex	1.081343	.1164413	0.73	0.468	.8755966	1.335434	. xi:logistic cvd sex if smoking==2
_cons	.1152043	.0092764	-26.84	0.000	.0983849	.1348991	
							•



Interpretation

- _Isex_1: the odds of having CVD is 1.09 times higher in women compared to men in the non-smokers category
- _Ismoking_2: the odds of having CVD is 2.34 times higher among men who are ex-smokers compared to men who are non-smokers. For women, this is 2.34 * 0.71 = 1.65
- _Ismoking_3: the odds of having CVD is 0.85 times lower among men who are current smokers compared to men who are non-smokers For women, this is 0.86 * 0.99 = 0.85
- _IsexXsmo_1_2 and _IsexXsmo_1_3 are interaction terms
- OR comparing women to men among ex-smokers 1.09*0.71 = 0.77.
 For current smokers, this is 1.09*0.99 = 1.08



Suggested readings

- Tabachnick B, Fidell L. Using Multivariate Statistics. 4th Edition. London, Allyn & Bacon, 2001
- Clayton D, Hills M. Statistical Methods in Epidemiology. Oxford University Press 1993
- Hosmer D W, Lemeshow S. Applied logistic regression. 2nd Edition. New York, Chichester Wiley, 2000
- Long JS, Freese J Regression Models for Categorical Dependent Variables Using Stata, 2nd edition, Stata Press, 2006

47