Categorical clinical outcomes Classical approaches vs Binary Logistic Regression

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Preamble

- Today we will focus on studies that consider categorical outcome variables
- In particular I will focus on **Binary outcomes** (*aka* dichotomous outcomes)
  - EG: Yes/No; Live/Deal; cured/not cured; etc etc
- However I will also comment briefly on other types of categorical outcomes:
  1. **Nominal (Non-ordered) outcomes** such as Cancer type: Lung cancer, Colon cancer, Breast cancer; and
  2. **Ordinal (ordered) outcomes** such as remission status: Full remission, partial remission, no remission

Preamble

I will focus on three main aspects:

1. Naive approaches: Classical (but non-informative) statistical tests (i.e. χ^2 test of independence)
2. Describing categorical data (gauging effect size)
3. Model-based approaches (i.e. Logistic regression)

Today, I will use a case study approach demonstrate the relative strengths and weaknesses of these different approaches.

What we will cover....

1. Thinking about categorical data
2. Eyeballs
3. Statistical inference for categorical data
4. Binary Logistic regression
   - A better look at the odds ratio
   - Example of Logistic regression analysis

Case study: Blood sugar control in Type 2 diabetese patients

Today we will focus on comparing the relative success in achieving blood sugar control ($HbA1c < 7\%$) in patients attending two hospitals. So,

- **Outcome** HbA1c control
  - HbA1c $> 7\% \Rightarrow$ NO;
  - HbA1c $\leq 7\% \Rightarrow$ YES
- **Study effect** Hospital
  - A large BKK tertiary care hospital; vs
  - A small Khon Kaen community hospital
- **Other covariates** mainly measured at the patient level

The first thing we should note is that this is an **observational study**.

Using our eyes

- The first thing we will do (and the first thing we should always do) is to use our eyes
- By this, I mean simple graphs and tables of summary statistics
- This way we can gauge if there is a **real** (i.e. clinically important) difference in blood sugar control in patients attending the two hospitals
- I will focus on three statistics:
  1. Difference in proportions (*aka* Risk difference, prevalence difference, excess or attributable risk)
  2. Relative risk (*aka* risk ratio)
  3. Odds ratio
- All three of these values represent a **measure of association** and give us an idea of the **Effect size**

Measures of association for Binary outcomes

Now if we cross-tabulate our data into the form:

	Outcome			
Exposed	yes	no	Total	Risk of outcome
yes	a	b	a + b	a/(a + b)
no	c	d	c + d	c/(c + d)
Total	a +c	b + d	a + b + c + d	

Difference in proportions (prevalence): $p_1 - p_2 = \frac{a}{a+b} - \frac{c}{c+d}$

Relative risk: $RR = \frac{(\frac{a}{a+b})}{(\frac{c}{c+d})}$

Odds Ratio: $OR = \frac{(\frac{a}{b})}{(\frac{c}{d})}$

Looks complicated but really very simple

A first look at our data

Now let's look at a simple cross-tabulation of our data:

	$>7\%$	$\leq 7\%$
BKK.big	144	178
KK.small	42	18

Not very informative (a lot more patients at the big hospital). Let's consider the proportions ('risk' of blood sugar control)

	$>7\%$	$\leq 7\%$
BKK.big	0.45	0.55
KK.small	0.70	0.30

We can see that at our large Bangkok hospital, 55% of patients managed to control their blood sugar, whereas in the small Khon kaen hospital only 30% had $HbA1c \leq 7$

Measure 1: Difference in proportions (Risk difference)

$$p_1 - p_2 = \frac{178}{144+178} - \frac{18}{42+18} = \frac{178}{322} - \frac{18}{60}$$

$$= 0.55 - 0.30 = 0.15$$

The 'prevalence' of blood sugar control was 15% higher in the large BKK hospital (55% achievement) than in the small KK hospital (30% achievement)

Does this seem substantial to you???

Difference in proportions

Advantages and disadvantages

Difference in proportions is a nice measure of association as it:

- is readily interpretable
- gives us an idea of effect size

However, also has a **major disadvantage**:

- As an ABSOLUTE measure, the magnitude of the effect depends on the (baseline) prevalence.

Consider the following situations...

Difference between two proportions

For example, consider two different randomized controlled trials of a new therapy. In both cases, the prevalence is reduced by 5%

1. In the first case prevalence in control is 6 % and in treatment group is 1 %
2. In the second case prevalence in control is 56 % and in treatment group is 51 %

Do you think this is the same effect size??????

If not, which effect is more profound?

The 'relative' measures of effect size

Risk ratios and Odds ratios

Recall the other two measures of association I mentioned:

Risk Ratio:

$$RR = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)}$$

Odds Ratio:

$$OR = \frac{\left(\frac{a}{b}\right)}{\left(\frac{c}{d}\right)}$$

Measures of association
Risk ratios and Odds ratios

- Advantage of the RR and OR (over difference in proprotions) is they are relative
- i.e. they account for the baseline prevalence:
  For example,
  - RR and OR would show a lower association where 5% prevalence difference between control = 56% and treatment = 51%
  - RR and OR would show a higher association where 5% prevalence difference where control = 6% and treatment = 1%

In this respect, RR and OR (unlike difference in proportions) account for the level of baseline prevalence.

Measure 2: Risk ratios = Relative risk

Now lets consider the risk (of HbA1c target achievement) in the our large hospital **relative** to the small hospital:

$$RR = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)} = \frac{\frac{178}{322}}{\frac{18}{60}} = \frac{0.55}{0.30} = 1.8333$$

This means, (in our sample) the 'risk' of achievement in our BKK hospital patients is 1.8333 time higher than in the KK hospital patients (The BKK patients almost have twice the chance of achieving the HbA1c target, relative to the KK patients).

Again: Does this seem like a substantial effect??

Measures of association

Risk ratios

The relative risk has some advantages:

- it is a relative measure
- it is intuitive

Unfortunately it has some mathematical properties that make it difficult to model, especially when we want to account for more than one risk factor (i.e. multivariable modeling)

Measures of association

Odds ratios

Finally we come to the odds ratio (OR).

- not as intuitive as the RR and risk difference
- but has desirable mathematical properties
- In fact, **ORs are the measure of association underpinning Logistic regression models**. For this reason, they are very important to understand.

Now for our HbA1c target data:

$$OR = \frac{\left(\frac{a}{b}\right)}{\left(\frac{c}{d}\right)} = \frac{\frac{178}{144}}{\frac{18}{42}} = \frac{1.254}{0.429} = 2.925$$

Measures of association

Interpretation: Odds ratios

How do we interpret $OR = 2.925$

- The **ODDS** of blood sugar control in the BKK patients is 2.925 times the odds of control in the KK patients
- Note: That an OR is always more extreme than RR (except when prevalence in both groups is low)

Pitfall:

Be careful with words like chance, likelihood, probability and risk when discussing odds ratios. Note that the odds of an event is different from the probability(risk) of an event.
Hint: OR and RR move in the same direction, but not at the same rate.

Where to from here

- Our summary statistics (Risk difference, Relative Risk and Odds ratio) all **suggest** substantially better control in our BKK patients than in the KK patients.
- So are my results **definitive**?
- Can I conclude that is a 'real' effect?
- If I repeated study, will I see the same effect?

Although we have a shown a 'clinically' important difference in our SAMPLE, we can't really conclude that the populations are different. For that we need a hypothesis testing approach (statistical inference).

Clinical vs Statistical significance

Clinical significance vs statistical significance

Clinical significance is about the magnitude of the effect size and its clinical importance. **Statistical significance**, however, is about ruling out a chance difference (due to our sampling) so we can make an inference about populations (a 'replicable' result)

So in our example:

- 15% higher achievement in the BKK patients seems like a scientifically important difference⇒**Clinically significant**
- **BUT** are we confident that the (population of)patients that attend the BKK hospital have a better chance of controlling their blood sugar NOT JUST THE ONES IN OUR SAMPLE⇒ **Statistical significance**

Statistical imference for categoical data

We will consider two approaches for the inferential analysis of categorical data:

1. χ^2 **test of independence:** A very widely used, but rather naive and uninformative way test test for associations
2. **Logistic regression:** A model based approach which is much more flexible, useful and informative BUT a little bit trickier to understand (at least at first)

Take home message

A very important point I want you to take home today is that the χ^2 **test of independence and other classical bivariate methods are almost useless in observational studies**. These studies require much more then such a simplistic bivariate approach.

χ^2 test of independence

A test statistic (for any method) is a statistic (measure calculated from the sample) that gives us an idea whether we should (or should not) reject the null hypothesis (H_0).
For the χ^2 test of independence.....

$$\chi^{2*} = \sum_{i=1} \frac{(O_i - E_i)^2}{E_i}$$

where O = observed and E = expected frequencies (if H_0 true)
Typically, large test statistics suggest that we have strong evidence to reject the null hypothesis.

Test statistic for the χ^2 test of independence

χ^{2*} above tells us how much our data (reality) differs from expectation (a 'reality' of independence)

χ^2 test: Blood sugar control vs hospital

Recall our observed frequencies:

	>7%	<=7%
BKK.big	144	178
KK.small	42	18

Now if there TRULY wasn't a relationship (null hypothesis true), we would expect the frequencies to be:

	>7%	<=7%
KK.small	29.21	30.79
BKK.big	156.79	165.21

Now we conduct of χ^2 test of independence (software) and get: $\chi^2 = 11.945$, $df = 1$, $p < 0.001$

χ^2 test: Blood sugar control vs hospital

We should note:

H_0 : Blood sugar control and hospital type are independent

H_A : Blood sugar control is associated with hospital type

Now what do our results tell us?

From $\chi^2 = 11.945$, $df = 1$, $p < 0.001$ we can reject ($p < 0.05$) the null hypothesis (H_0) and conclude that **there is indeed a relationship between blood sugar control in patients and the hospital they attend.**

ANY PROBLEMS???

χ^2 test: Two main problems

1. **Clinical importance:** We have a **statistically significant** association, but is it clinically important.
2. **Crude associations and confounding:**Even more importantly, from our results we might (mistakenly) assume that it is differences in the quality of care between the two hospitals. **Are there major differences in the patients attending the two hospitals**.

Statistical significance, Magnitude and nature of effect

1. It is very important to remember that (unless N exactly right) Statistical significance $\not\Rightarrow$ Clinical significance
2. With the exception of well designed experimental studies (such as RCTs), a bivariate association is not sufficient to describe a relationship (and can even be misleading).

Solving the limitations of χ^2 test

- We could (unsatisfactorily) solve the first problem by also providing the risk difference or relative risk:
  ...We demonstrated that there was a significant association between hopsital and blood sugar control in the patients ($\chi^2 = 11.945$, $df = 1$, $p < 0.001$) with patients at the Khon Kaen community hospital exhibiting a 15% lower chance of achieving the HbA1c clinical target compared to patients at Bangkok tertiary care facility
- However, there is no way (using the χ^2 test) that we can control for confounders (i.e. The other explanations for the differences)

We need a better approach!!!!

Binary logistic regression

So finally we come to the statistical method that can save the day (and the main reason for this lecture): **Binary logistic regression**, as an analytical approach, has a number of distinct advantages:

1. It provides measures of effect size: Odds ratios (ORs)
2. We can run multivariable models, allowing us to consider:
   - Other risk factors
   - Confounders
   - Effect modifiers
3. Also (unlike the χ^2 test) we can consider continuous (not just categorical) predictors

Binary logistic regression

- Binary logistic regression is VERY widely used model and is a child of a family of methods called **Generalized Linear Models**
- Binary logistic regression is used when our outcome is binary (e.g. HbA1c target: $> 7\%$, $\leq 7\%$)
- There are other types of logistic regression models too:
  - **Nominal (Multinomial) logistic regression** which is for nominal variables (e.g. Type of cancer: Lung, Breast, Colon); and
  - **Ordinal Logistic regression** which is used when we have an ordinal outcome (e.g. Level of remission: Full, Partial, None)
- Unfortunately, these other types of logistic regressions are not within the scope of today's lecture (not enough time)

Logistic regression in a GLM framework

- Classical model was developed for a binary outcome
- Involves modelling the Odds ($\text{Odds} = \frac{\text{Those who do}}{\text{Those who don't}}$)
- Uses the **logit** link, which is simply the **log of the odds**. That is:

$$\ln(Odds) = \mathbf{X}\beta + \epsilon$$

Or,

$$\ln\left(\frac{N_+}{N_-}\right) = \mathbf{X}\beta + \epsilon$$

Use of Binary Logistic Regression in clinical studies

Binary logistic regression is a VERY commonly used method in clinical studies. It has two main uses:

1. **Association studies**: Is an Exposure/Treatment **associated** with (**cross-sectional studies**) or a **risk factor** for (**Cohort sudies**) a particular disease outcome?
2. **Predictive studies**: Can we **PREDICT** disease (+/-) based on patient characteristics (**eg diagnostic studies**)?

- In the first case we are working at the population level.
  - For an exploratory study: What ARE the factors associated with the outcome; or
  - For a hypothesis testing study, is our **Study effect 'A'** associated with our **Disease outcome 'B'**
- This type of study uses Logistic regression in the form presented on the previous slide

Predictive studies

Alternatively, when predicting whether a patient is diseased (diagnosis), the model changes (with a little algebra) to:

$$Prob(Diseased) = \frac{e^{(\beta_0+\beta_1 X_{i,1}+\beta_2 X_{i,2}+...+\beta_{k-1} X_{i,k-1}+\epsilon_i)}}{1+e^{(\beta_0+\beta_1 X_{i,1}+\beta_2 X_{i,2}+...+\beta_{k-1} X_{i,k-1}+\epsilon_i)}}$$

and

$$Prob(Non-diseased) = \frac{1}{1+e^{(\beta_0+\beta_1 X_{i,1}+\beta_2 X_{i,2}+...+\beta_{k-1} X_{i,k-1}+\epsilon_i)}}$$

Purpose of logistic regression:

The above representation not that helpful for standard logistic regression analysis (hypothesis testing about associations), but is for **risk scoring** such as in diagnostic studies

Old concepts and new approaches

Now in terms of interpreting ORs (especially in observational studies) let's dig a little deeper

- Odds ratios: What's an OR, and how do we interpret it?
- Confounding: To adjust or to not adjust (that is the question)
- Effect modification: Is our OR (of interest) constant across subgroups?

The Odds Ratio

If we represent the association of our binary outcome (disease: +/-) with a 2-level risk factor (e.g. Exposed / non-exposed)

	Disease	
Exposure	+	-
+	a	b
-	c	d

EVERY epidemiology text book written will provide you this table.

Odds Ratio:Prevalence studies

Then we can calculate the odds ratio

- Odds of outcome(exposed): $\frac{a}{b}$
- Odds of outcome(unexposed): $\frac{c}{d}$
- Odds ratio: $\frac{(\frac{a}{b})}{(\frac{c}{d})} = \frac{ad}{bc}$

Confounding: Are there alternative explanations

Are the crude and adjusted ORs similar??

- Old methods: Crude OR vs Mantel-Haenzel adjusted OR
- New Logistic Regression approach:
  - Is the OR from a Bivariate (Simple) Logistic Regression (i.e. crude OR) the same as the adjusted OR we get from a 'Multi-variable' Logistic regression
  - We can adjust for multiple potential confounders
  - Confounders can be continuous and/or categorical
  - We can test the significance (and report ORs) of the confounders as potential (independent) risk factors in their own right

Confounding: Example

Study to explore whether high cholesterol (+/-) represents a risk factor for CHD(+/-):

- **Crude OR**: We find that the OR = 5.9
  - Individuals with high cholesterol have 5.9 time the odds of CHD (relative to those without high cholesterol)

When we adjust for demographics(Sex, Age, SES):

- **Adjusted OR**: OR = 2
  - After adjusting for demographics, individuals with high cholesterol have 2 time the odds of CHD (relative to those without high cholesterol)

We find that demographics has substantial confounding effect(e.g.$\triangle$OR $\gg$ 10%). **Which estimate is appropriate?**

In terms of Logistic regression models

"Simple" (Bivariate) Logistic Regression model

$$\ln(Odds) = \beta_0 + \beta_{Chol} Chol_i$$

gives crude $OR = e^{\beta_{Chol}} = 5.9$

Multi-variable Logistic Regression model....

$$\ln(Odds) = \beta_0 + \beta_{Chol} Chol_i + \beta_{Fem} Fem_i + \beta_{Age} Age_i + \beta_{Mid} Mid_i + \beta_{Up} Up_i \quad (1)$$

gives $e^{\beta_{chol}} = 2.0$

Note:

Chol, *Fem*, *Mid* and *Up* are dummy variables (0/1) indicating class membership: As in GENERAL linear model lecture

Effect modification

Effect modification is where the effect of a risk factor varies with the **level** of another predictor. That is, if we ran a model with interaction term(s) (to determine whether effect modification was occurring) and observed a significant interaction(s). For example:

$$\ln(Odds) = \beta_0 + \beta_{Chol} Chol_i + \beta_{Fem} Fem_i + \beta_{Chol \times Fem}(Chol \times Fem)$$

and we found we reject H_0: $\beta_{Chol \times Fem} = 0$ then we would conclude that Sex modifies the effect of high cholesterol on the Odds (and risk) of CHD.

Effect modification

After identifying effect modification (A significant interaction), the simplest way of gauging the modification effect of Sex on the risk factor (cholesterol) is to run an individual Logistic Regression for each gender. That is,
For males (only), run:

$$\ln(Odds) = \beta_0 + \beta_{Chol} Chol_i$$

and for females (only), run:

$$\ln(Odds) = \beta_0 + \beta_{Chol} Chol_i$$

We might find that for males: $OR_{Chol} = 10$ ($p < 0.05$), and for females $OR_{Chol} = 1.2$ ($p \not< 0.05 \Rightarrow$ns) suggesting that cholesterol only represents a significant risk factor (for CHD) for males (i.e males with high cholesterol have 10 times the odds of CHD, relative to males without high cholesterol).

Effect modification vs. confounding

Many people get confused about the difference between **Confounding** and **Effect modification**.

Take home message: Confounding vs. effect modification

Confounding is where the effect of a risk factor (or treatment) changes with the **PRESENCE** of another (confounding) risk factor in the model. **We need to adjust**. **Effect modification** is where the effect of a risk factor (or treatment) changes with the **LEVEL** of another risk factor in the model

- We should also note that effect modification 'trumps' confounding. Since interpretation of the main effects is inappropriate when there is effect modification, the notion of confounding is no longer relevant.

Effect modification vs. confounding

For example:

- If GENDER confounds with our treatment effect we need to include it in our model (i.e. adjust for it)
- If GENDER is an effect modifier (of our treatment), then the efficacy our treatment is different for men (e.g. more effective) than women (e.g. less effective). We may need a logistic regression model for each gender.

Back to our diabetes patients

- As with all our previous analysis today, our objective is to compare blood sugar control among patients attending two different types of hopsitals
- HOWEVER, we have admitted that there are likely to be some fundamental differences between the patients (i.e. ABOVE the health care setting). We believe, we will probably need to adjust for several confounders.
- Regardless of whether confounding is present (or not), we are also interested in the effects of other factors that might be associated with bloodsugar control.

In such an observational study I would NEVER use a χ^2 test of independence for my front line analysis.

Bivariate analysis: 'Simple' Logistic Regression

Now fitting the model:

$$\ln(Odds) = \beta_0 + \beta_{BKK} BKK_i + \epsilon_i$$

where $BKK_i = 1$ where the patient attends the Bangkok hospital, and 0 otherwise

Which group is the referent?

Bivariate analysis: 'Simple' Logistic Regression

When we run our model we find:

Those attending the BKK hospital have 2.88 times the odds of acheiving their HbA1c target relative to the KK patients ($OR = 2.884$, $95\% CI : 1.589, 5.235$, $p < 0.001$)

However, this is a **crude** effect (unadjusted). This assumes that the patients are pretty much the same in BKK and KK, and differ only in the health care setting (something unlikely to be true).

Let's dig a little deeper. Let's start by runing bivariate models for all other patient characteristics too.

Bivariate models: Part 1

Effect				
	OR	L95	U95	p.val
BKK.big	2.88	1.59	5.24	0.00
Age (10 years)	1.58	1.29	1.93	0.00
Duration (5 years)	1.01	0.90	1.12	0.92
Female	0.99	0.65	1.51	0.95
Marital Status	$\chi^2_{LRT} = 10.223$	$df = 2$	$p = 0.006$	
Mar: Married	0.43	0.21	0.86	0.02
Mar: Wid, Sep, Div	0.78	0.37	1.68	0.53
Education	$\chi^2_{LRT} = 8.745$	$df = 3$	$p = 0.033$	
Edu: Primary	0.34	0.15	0.75	0.01
Edu: Secondary	0.47	0.20	1.10	0.08
Edu: Bach+	0.50	0.21	1.17	0.11

Bivariate models: Part 2

Effect		OR	L95	U95	p.val
Income grp	$\chi^2_{LRT} = 7.847$	$df = 4$	$p = 0.097$		
Inc: 5-9.99K		0.59	0.30	1.18	0.13
Inc: 10-14.99K		0.41	0.20	0.83	0.01
Inc: 15-24.99K		0.89	0.47	1.67	0.71
Inc: 25+K		0.72	0.41	1.25	0.24
BMI class	$\chi^2_{LRT} = 1.759$	$df = 3$	$p = 0.624$		
BMI: <18.5		2.14	0.53	8.56	0.28
BMI: 25-29.9		0.90	0.57	1.42	0.65
BMI: 30+		0.89	0.50	1.57	0.68
Familiy hist DM		1.02	0.68	1.53	0.91

Bivariate models: Part 3

Effect		OR	L95	U95	p.val
Diabetes treatment	$\chi^2_{LRT} = 68.71$	$df = 3$	$p < 0.001$		
Treat: OHA		0.21	0.03	1.73	0.15
Treat: Ins		0.06	0.01	0.53	0.01
Treat: OHA+Ins		0.03	0.00	0.23	0.00
Smoking status	$\chi^2_{LRT} = 0.335$	$df = 2$	$p = 0.846$		
Smo: Previous		1.17	0.66	2.08	0.59
Smo: Current		1.17	0.35	3.93	0.80
Alcohol status	$\chi^2_{LRT} = 0.392$	$df = 2$	$p = 0.822$		
Alc: Prev		1.09	0.62	1.94	0.76
Alc: Current		0.81	0.36	1.82	0.61
Cormorbidity		1.26	0.55	2.90	0.58

χ^2_{LRT}: **Likelihood ratio test**. Global test for multiclass predictors

Building the multivariable model

Without going into too much detail about the research problem. First we note that there are **many other covariates significantly associated with HbA1c control** including: **Age**, **Marital status**, **Education**, **Current diabetes treatment**. What should go into my full multivariable model:

- **The study effect**: As my research question resolves around 'health care setting', I will FORCE the variable, **Hospital** into my model
- **Empirical considerations**: Several variables associated ($p < 0.05$) with HbA1c control. BUT THIS IS PROBABLY NOT ENOUGH. Instead I will use $p < 0.25$ to decide what goes in the final model (Think of $p < 0.25$ as indicating potentially important covariate)

Building the MV model: Thinking about the research problem

Another thing is **Contextual considerations** (we shouldn't be driven purely by p-values). Probably the trickiest variable there is **Current DM treatment**.

Remembering that comparing the hospitals (not the patients) is the main research objective, we could argue...

- The propensity and approach of doctors to treat patients is (partially) driven by the health care setting.
- However, probably much more importantly, a doctor is likely to be predominantly driven by the health care needs of the patients. A clinic that tends to see (on average) sicker patients is likely to be one for which treatment approach is (on average) more profound.

The multivariable model

So in my final model I will include the study effect, **Hospital** and all the variables whose $p < 0.25$ in the bivariate analysis: **Age**, **Marital status**, **Education**, **Current diabetes treatment**, and **Income group**.

The art and science of model building

The practice of model building is a quite subtle and detailed topic. How we build a model should depend on Research objective, empirical considerations, a strong understanding of both the clinical context and the research design. **This will be the topic of my lecture next month**

Multivariable model: Part 1

Effect		OR	L95	U95	p.val
BKK.big		1.977	0.893	4.376	0.092
Age (10 years)		1.360	1.046	1.767	0.021
Marital status	$\chi^2_{LRT} = 6.082$		$df = 3$	$p = 0.048$	
mart: Married		0.393	0.168	0.919	0.031
mart:Wid, Div, Sep		0.594	0.224	1.577	0.294
Education	$\chi^2_{LRT} = 4.717$		$df = 3$	$p = 0.194$	
edu: Primary		0.441	0.170	1.144	0.091
edu: Secondary		0.723	0.250	2.089	0.547
edu: Bach+		0.778	0.245	2.472	0.670

Multivariable model: part 2

		OR	L95	U95	p.v
Income	$\chi^2_{LRT} = 3.838$		$df = 3$	$p = 0.4284$	
inc: 5-9.99K		1.247	0.525	2.959	0.61
inc: 10-14.99K		0.632	0.261	1.535	0.31
inc: 15-24.99K		0.587	0.259	1.327	0.19
inc: 25+K		0.572	0.255	1.282	0.17
Diabetes treatment	$\chi^2_{LRT} = 67.46$		$df = 3$	$p < 0.001$	
Treat; OHA		0.206	0.024	1.786	0.15
Treat: Ins		0.055	0.006	0.498	0.01
Treat: OHA+Ins		0.023	0.003	0.211	0.00

Interpreting the results

- **When we adjust for patient characteristics and treatment between the hospitals**, we can no longer say that blood sugar control IS significantly better at the large hospital, relative to the smaller hospital (An inference: A statement about the population).
- However, in the patients we collected (our sample) we did see about twice the odds of achieving blood sugar control in the big hospital patients, relative to the small hospital ($OR_{adjusted} = 1.977$)
- In the end we could **demonstrate Age**, **Marital status** and **DM treatment** were associated with achieving the HbA1c in this population

Interpreting the results...and to be fair

- For the most part, the study design has major limitations in terms of it's ability to answer our research question. It provides limited (and even questionable) evidence about whether larger hospitals have better clinical target outcomes
- This data was derived from a real study in which I am involved, but **to be fair**, I deliberately selected only two hospitals that differed in many ways (i.e. lots of confounding effects).
  - For example, it is well established that T2DM is considerably more prevalent in the northeast (relative to the rest of Thailand)
- In the full study we took much more care to select different sized hospitals from all the provinces included in the study

Things to ask yourself

- **Why did I deliberately choose this biased subset of data?**
- What would my conclusions have been had I have just used the χ^2 test of independnce
- Which approach (that I used) was:
  1. More informative,
  2. Painted a more realistic picture
  3. Identified 'interpretations' to treat with care

Concluding remarks

- Binary Logistic regression represent a very versatile, and perhaps one of the most useful models in biostatistics
- It has major advantages over methods like the χ^2 test of independence because:
  - It provides a measure of effect size
  - It can be multivariable so provides adjusted estimates
  - It also allows us to include other predictors (categorical and continuous)
  - We can also examine more complex interplays between variables (confounding and effect modification)

What I didn't cover

- One argument for the χ^2 test of independence (over binary logistic regression) is that the χ^2 test allows the analysis of other types of categorical outcomes (i.e. Nominal and Ordinal)
- However, Binary Logistic regression can be extended to deal with this situation too. Specifically:
  - Nominal Logistic regression (for nominal outcomes)
  - Ordinal Logistic regression (for ordinal outcomes)
- All of these models (again) can be further extended for more complex study designs, such as longitudinal data

To be continued....

MODEL BUILDING

Watch this space!!!!