Applied Epidemiology I: Tables and interpreting results

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Acknowledgements

This course material is based on my learning from Anastasia Lam's teachings in last year's Applied Epidemiology I lab sessions, and readings from *Epidemiology* by Gordis [1], *A First Course in Probability and Statistics* by Goldsman and Goldsman [2], *Principles of Biostatistics* by Pagano and Gauvreau [3], and *Biostatistics I* by Gabriel and Frumento [4]. I especially want to thank Marlene Stratmann for reviewing the slides and Prof. Paul Dickman for providing me with suggestions to improving the teaching.

Outline

How to deal with missing values?

- Types of missing data [5]
  - Missing completely at random
  - Missing not at random

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  - Missing not at random
- I don't know.

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  - Sensitivity analysis. [5]
  - Be aware of what you are doing !
  - Whatever you do is merely assumption to your data.
  - You have to
    1. **illustrate your assumption** in the methods part
    2. **explain the influence of the assumption** in the discussion part
    3. make a flow chart to say what you kicked out (recommended).

Good epidemiologists

Migeal A Hernán [a], "Epidemiologists are trained to generate, integrate, analyse, interpret data."

"And description is the foundation."

[a] Professor at Harvard University T.H. Chan Public Health School

Tables: Bad example

What is the problem here?

Table 5

Simulation results for using full data, CRs only, and proposed method under four missing mechanisms

	Bias[a]		Variance[b]		95% CI[c]	
Method	$(\hat{\beta}_W)$	$(\hat{\beta}_X)$	$(\hat{\beta}_W)$	$(\hat{\beta}_X)$	$(\hat{\beta}_W)$	$(\hat{\beta}_X)$
(M.1) $P(R=1)=0.66$						
Full	0.01346	0.02229	0.04008	0.03685	0.955	0.950
Comp	0.03062	−0.003561	0.1149	0.06732	0.960	0.955
Impu	0.01431	0.021	0.04088	0.05169	0.980	0.975
(M.2) logit $P(R=1)=2Y$						
Full	0.007908	−0.02116	0.03838	0.03624	0.975	0.925
Comp	0.01945	0.07096	0.107	0.06581	0.960	0.950
Impu	0.006966	0.01597	0.04227	0.05226	0.975	0.985
(M.3) logit $P(R=1)=2X$						
Full	0.007908	−0.02116	0.03838	0.03624	0.975	0.925
Comp	0.01225	0.0589	0.08856	0.06818	0.980	0.975
Impu	0.009563	−0.04699	0.03865	0.04923	0.985	0.970
(M.4) logit $P(R=1)=X+Y$						
Full	0.01346	0.02229	0.04008	0.03685	0.955	0.950
Comp	0.02404	1.613	0.1102	0.08202	0.955	0.580
Impu	0.01814	0.08289	0.0578	0.06075	0.955	0.970

[a]Bias $= (\hat{\beta}-\beta_0)/\beta_0$.

[b]Simulation variance.

[c]Confidence interval using jackknife standard error.

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  - self-explanatory and informative
  - placed above the tables.
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Table 1: Baseline characteristics of colon cancer patients diagnosed during 1981-1990, Sweden.

		<50	50-59	60-69	70-79	≥80	All
Colon cancer							
1981-1990	Patient size (n)	1 148	2 485	6 227	9 381	5 442	24 683
	Female (%)	51.74	52.43	50.09	51.61	59.28	53.01
	Proportion of censoring[1] (%)	34.41	15.69	3.12	0.22	0.09	4.07

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- We use cancer data still.

```
sysuse cancer, clear
keep if drug ==1 | drug == 2
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- One-way table of frequencies with mean and sd of age

```
. table died, contents(freq mean age sd age)
```

```
-----------------------------------------------
1 if       |
patient    |
died       |      Freq.   mean(age)     sd(age)
-----------+-----------------------------------
         0 |           9     55.1111    5.487359
         1 |          25       56.88    6.227091
-----------------------------------------------
```

Tables: One-way tables

- One-way table of frequencies

```
. tabulate died
```

1 if patient died	Freq.	Percent	Cum.
0	9	26.47	26.47
1	25	73.53	100.00
Total	34	100.00	

Tables: One-way tables

- Create table I of baseline characteristics using `table1_mc`
- This command is useful. Play it on your own!
- See `help table1_mc`

```
. ssc install table1_mc, replace
. table1_mc, vars(age conts)
  +-----------------------------------------+
  |                                  Total  |
  |-----------------------------------------|
  |                                  N=34   |
  |-----------------------------------------|
  | Patient's age at start of exp.   56 (51-61) |
  +-----------------------------------------+
Data are presented as median (IQR).
```

Tables: Two by two tables

- 2 by 2 table for drug and died with relative frequency by column or row

```
. tabulate died drug, col row

      1 if |
   patient | Drug type (1=placebo)
      died |         0          1 |     Total
-----------+----------------------+----------
         0 |         8          1 |         9
           |     88.89      11.11 |    100.00
           |     57.14       5.00 |     26.47
-----------+----------------------+----------
         1 |         6         19 |        25
           |     24.00      76.00 |    100.00
           |     42.86      95.00 |     73.53
-----------+----------------------+----------
     Total |        14         20 |        34
           |     41.18      58.82 |    100.00
           |    100.00     100.00 |    100.00
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Tables: Two by two tables

- 2 by 2 table with chi-square test and fisher's exact test

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. tabulate died drug, col row chi2 exact
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- How to interpret the results?
- Chi-square test: testing the association between two binary variables.
- Using placebo has association with that the patients died or not.

Tables: Two by two tables

- 2 by 2 tables straitified by sex

```
. bysort sex: tab died drug, col row chi2

-> sex = 0

      1 if |
   patient | Drug type (1=placebo)
      died |         0          1 |     Total
-----------+----------------------+----------
         0 |         6          1 |         7
           |     85.71      14.29 |    100.00
           |     75.00       9.09 |     36.84
-----------+----------------------+----------
         1 |         2         10 |        12
           |     16.67      83.33 |    100.00
           |     25.00      90.91 |     63.16
-----------+----------------------+----------
     Total |         8         11 |        19
           |     42.11      57.89 |    100.00
           |    100.00     100.00 |    100.00

          Pearson chi2(1) =   8.6466   Pr = 0.003

-> sex = 1
      1 if |
   patient | Drug type (1=placebo)
      died |         0          1 |     Total
-----------+----------------------+----------
         0 |         2          0 |         2
           |    100.00       0.00 |    100.00
           |     33.33       0.00 |     13.33
-----------+----------------------+----------
         1 |         4          9 |        13
           |     30.77      69.23 |    100.00
           |     66.67     100.00 |     86.67
-----------+----------------------+----------
     Total |         6          9 |        15
           |     40.00      60.00 |    100.00
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          Pearson chi2(1) =   3.4615   Pr = 0.063
```

Tables: Stata tool for Epidemiology

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- But before demonstrating how this works, a recapture on basic epi terms!

Basic Epidemiology terms: Rate vs. proportion

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- Survival (proportion/probability) ~~rate~~:

$$\frac{\text{no. of alive persons (since diagnosis)}}{\text{no. of initially disease-free persons (since diagnosis)}}$$

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3. Is risk a rate or a proportion?

Basic Epidemiology terms: Risk, risk difference, risk ratio

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Cumulative hazard $= 1-$Survival proportion $=$ Cumulative probability of death

$$F(t) = 1 - S(t) = P(T \leq t)$$

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- Risk ratio: the ratio of the probabilities of an event between the exposed group and non-exposed group
- **Caution!** Relative risk could be either risk ratio or rate ratio!

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	Female (Exposed)	Male (Unexposed)	Total
shiba (Case)	2	2	4
guinea pig (Noncase)	2	1	3
Total	4	3	7

Epidemiologists love two by two tables!

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- Interpretation: Females have ~~16.67 % lower risk of having shiba~~ 16.67 less per 100 subjects of having shiba than males.

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- Risk ratio between females having shiba and males having shiba $= \widehat{p_F} \div \widehat{p_M} = 2/4 \div 2/3 = 0.75.$
- Interpretation: The risk of females having shiba is 0.75

Basic Epidemiology terms: Odds, odds ratio

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$$Odds = \frac{p}{1-p}$$

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- Why is there no odds difference?

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- The odds of having shiba among females is

$$\widehat{odds}_F = \frac{p(\text{having shiba}|\text{female})}{p(\text{having guinea pig}|\text{female})} = \frac{(2/4)}{(2/4)} = 1$$

- The odds of having shiba among males is 2 (calculation ignored).

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- OR of having shiba (females to males)
- $\text{OR} = \frac{Odds_f}{Odds_m} = \frac{1}{2}$
- Interpretation: there is a 50% decrease in the odds of having shiba among females compared to males. Higher odds of shiba ownership among males than females!
- It seems that females instead love guinea pigs more.

Interpreting results: Principles

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- Example:
  1. Females have a risk ratio of 0.75 having shiba compared to males.

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- When describing a ratio, it can ideally be illustrated by
  1. Exposed group
  2. Ratio (exact value, higher or lower percentage)
  3. Outcome
  4. Unexposed
- Example:
  1. Females have a risk ratio of 0.75 having shiba compared to males.
  2. Females have a 50% decrease in the odds of having shiba compared to males.

Interpreting results: Ratio $>$ or $<$ 1

Ratio

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Ratio

- As ratio < 1,
  - $(1 - \text{RR/OR}) \times 100\%$
  - E.g., RR $= 0.75$, $(1 - 0.75) \times 100\% = 25\%$
  - 25% lower risk

Interpreting results: Ratio $>$ or $<$ 1

Ratio

- As ratio < 1,
  - $(1 - \text{RR/OR}) \times 100\%$
  - E.g., RR $= 0.75$, $(1 - 0.75) \times 100\% = 25\%$
  - 25% lower risk
- As ratio > 1,
  - $(\text{RR/OR} - 1) \times 100\%$
  - E.g., OR $= 2.05$, $(2.05 - 1) \times 100\% = 105\%$
  - 105% higher odds
  - The odds is 2 times higher.
  - Twice the odds

Interpreting results: More examples

Diabetes Is a Risk Factor for Pulmonary Tuberculosis: A Case-Control Study from Mwanza, Tanzania (Faurholt-Jepsen, 2011)

	OR (95% C.I.)	OR (95% C.I.)	OR (95% C.I.)
		Model 1	Model 2
	Unadjusted	Adjusted for age, sex, socio-demography [2]	Model 1 + AGP [3]
HIV negative (n = 770)			
Glucose intolerance status [1]			
normal glucose tolerance	ref.	ref.	ref.
IFG/IGT	2.26 (1.50;3.41)	2.34 (1.52;3.61)	2.65 (1.00;7.06)
diabetes	2.15 (1.35;3.42)	2.14 (1.32;3.46)	4.23 (1.54;11.57)

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1. People with diabetes had a higher odds of TB (OR 2.15, 95% CI: 1.35-3.42) relative to people without diabetes.

Interpreting results: More examples

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1. People with diabetes had a higher odds of TB (OR 2.15, 95% CI: 1.35-3.42) relative to people without diabetes.
2. Having diabetes was associated with more than a 2-fold increase (OR: 2.15, 95% CI: 1.35; 3.42) in the odds of TB compared to not having diabetes.

Interpreting results: More examples

Bidirectional association between physical activity and symptoms of anxiety and depression: the Whitehall II study (Azevedo Da Silva, 2012)

Table 3 Cross-sectional associations between physical activity at recommended levels and anxiety and/or depression symptoms at phase 1 (1985–1988) (N = 9,309)

	OR (CI 95 %)	*P* value
Anxiety symptoms		
Model 1		
Physical activity		
Yes	0.71 (0.54, 0.91)	0.01
No	1 (reference)	
Model 2		
Physical activity		
Yes	0.71 (0.55, 0.93)	0.01
No	1 (reference)	
Depression symptoms		
Model 1		
Physical activity		
Yes	0.63 (0.48, 0.81)	<0.001
No	1 (reference)	
Model 2		
Physical activity		
Yes	0.63 (0.49, 0.82)	0.001
No	1 (reference)	

Interpreting results: More examples

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1. Patients who conducted recommended levels of physical activity had a 29% lower odds of anxiety (OR: 0.71, 95% CI: 0.54-0.91) and a 37% lower odds of depression (OR: 0.63, 95% CI: 0.48-0.81) relative to those who did not.

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1. Patients who conducted recommended levels of physical activity had a 29% lower odds of anxiety (OR: 0.71, 95% CI: 0.54-0.91) and a 37% lower odds of depression (OR: 0.63, 95% CI: 0.48-0.81) relative to those who did not.
2. Our results showed that individuals who practiced recommended levels of physical activity were less likely to have anxiety (OR: 0.71, 95% CI: 0.54-0.91) and depression (OR: 0.63, 95% CI: 0.48-0.81) in comparison with those who did not.

Interpreting results: Avoid dehumanising language use

What is the problem of the following sentences?

1. Patients that have diabetes have a higher risk of developing cardiovascular disease.

Interpreting results: Avoid dehumanising language use

What is the problem of the following sentences?

1. Patients that have diabetes have a higher risk of developing cardiovascular disease.
2. Our study suggests diabetic patients control their blood sugar level.

Interpreting results: Avoid dehumanising language use

What is the problem of the following sentences?

1. Patients that have diabetes have a higher risk of developing cardiovascular disease.
2. Our study suggests diabetic patients control their blood sugar level.
3. Each observation in this Stockholm Public Health cohort was recruited through cross-sectional surveys done in 2002, 2006, and 2010.

Interpreting results: Avoid dehumanising language use

What is the problem of the following sentences?

1. Patients that have diabetes have a higher risk of developing cardiovascular disease.
2. Our study suggests diabetic patients control their blood sugar level.
3. Each observation in this Stockholm Public Health cohort was recruited through cross-sectional surveys done in 2002, 2006, and 2010.
4. The normal individuals (the control group) showed a lower risk of developing lung cancer.

Interpreting results: Avoid dehumanising language use

What is the problem of the following sentences?

1. Patients ~~that~~ **who** have diabetes have a higher risk of developing cardiovascular disease.

Suggested reading: Leopold s et al, Editorial: Words Hurt – Avoiding Dehumanizing Language in Orthopaedic Research and Practice. Clin Orthop Relat Res. 2014 Sep; 472(9). [6]

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1. Patients ~~that~~ **who** have diabetes have a higher risk of developing cardiovascular disease.
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3. Each ~~observation~~ **individual** in this Stockholm Public Health cohort was recruited through cross-sectional surveys done in 2002, 2006, and 2010.
4. The ~~normal~~ **individuals of the control group** showed a lower risk of developing lung cancer.

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Calculate ratios using Stata: Risk ratio

- Finally we come back to Stata again!

Calculate ratios using Stata: Risk ratio

- Finally we come back to Stata again!
- cs case exposed

```
. cs died drug
```

```
                | Drug type [1=placebo]   |
                |   Exposed   Unexposed   |      Total
----------------+-------------------------+-----------
          Cases |        19           6   |         25
       Noncases |         1           8   |          9
----------------+-------------------------+-----------
          Total |        20          14   |         34
                |                         |
           Risk |       .95    .4285714   |   .7352941
                |                         |
                |      Point estimate     |    [95% Conf. Interval]
                |-------------------------+------------------------
 Risk difference |         .5214286       |     .245166    .7976911
      Risk ratio |         2.216667       |    1.200631    4.092525
 Attr. frac. ex. |         .5488722       |    .1671043    .7556521
 Attr. frac. pop |         .4171429       |
                +-------------------------------------------------
                           chi2(1) =    11.50  Pr>chi2 = 0.0007
```

Calculate ratios using Stata: Odds ratio

- cs case exposed, or

```
. cs died drug, or
```

```
                | Drug type [1=placebo]   |
                |   Exposed   Unexposed   |      Total
----------------+-------------------------+-----------
          Cases |        19           6   |         25
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      Risk ratio |         2.216667       |    1.200631    4.092525
 Attr. frac. ex. |         .5488722       |    .1671043    .7556521
 Attr. frac. pop |         .4171429       |
      Odds ratio |         25.33333       |    3.189793           . (Cornfield
                +-----------------------------------------------------
                                  chi2(1) =    11.50  Pr>chi2 = 0.0007
```

Calculate ratios using Stata: Incidence rate ratio

- ir case exposed studytime

```
. ir died drug studytime
Incidence-rate comparison
                 | Drug type [1=placebo]  |
                 |   Exposed   Unexposed  |      Total
-----------------+------------------------+-----------
1 if patient die |        19            6 |         25
Months to death  |       180          209 |        389
-----------------+------------------------+-----------
                 |                        |
  Incidence rate |   .1055556    .0287081 |   .0642674
                 |                        |
                 |      Point estimate    |    [95% Conf. Interval]
                 |------------------------+------------------------
 Inc. rate diff. |         .0768474       |    .0241182    .1295766
 Inc. rate ratio |         3.676852       |    1.411772    11.24864 (exact)
 Attr. frac. ex. |         .7280282       |    .2916701    .9111003 (exact)
 Attr. frac. pop |         .5533014       |
                 +-----------------------------------------------------
Mid p-values for tests of incidence-rate difference:
  Adj Pr(Exposed 1 if patient die <= 19) = 0.9985 (lower one-sided)
  Adj Pr(Exposed 1 if patient die >= 19) = 0.0015 (upper one-sided)
                       Two-sided p-value = 0.0031
```

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