

Biost 517
Applied Biostatistics I

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Second Quiz and Discussion

November 14, 2011

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Question 1

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- In considering the correlation between DSST and Age in two different studies:
 - Study 1: Least squares slope is -2
 - Study 2: Least squares slope is -1
- If all other aspects stay constant, which of the following statements is most likely to be true.
 - A. Study 1 has a higher sample correlation.
 - B. Study 2 has a higher sample correlation.
 - C. The sample correlations will tend to be equal.

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Question 2

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- In considering the correlation between DSST and Age in two different studies:
 - Study 1: Age is sampled over the range of 70 to 80
 - Study 2: Age is sampled over the range of 60 to 90
- If all other aspects stay constant, which of the following statements is most likely to be true.
 - A. Study 1 has a more extreme sample correlation.
 - B. Study 2 has a more extreme sample correlation.
 - C. The sample correlations will tend to be equal.

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Question 3

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- In considering the correlation between DSST and Age in two different studies:
 - Study 1: The study is restricted to college graduates
 - Study 2: The study takes all education levels
- If all other aspects stay constant, which of the following statements is most likely to be true.
 - A. Study 1 has a more extreme sample correlation.
 - B. Study 2 has a more extreme sample correlation.
 - C. The sample correlations will tend to be equal.

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Question 4

- In considering correlation between DSST and Age in two different studies:
 - Study 1: The study sample size is 1,000
 - Study 2: The study sample size is 5,000
- If all other aspects stay constant, which of the following statements is most likely to be true.
 - A. Study 1 has a higher sample correlation.
 - B. Study 2 has a higher sample correlation.
 - C. The sample correlations will tend to be equal.

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Question 5

- When presenting a single number to describe any association between DSST and Age, the most useful descriptive statistic to present is
 - A. Mean
 - B. Median
 - C. Geometric mean
 - D. Standard deviation
 - E. Minimum, maximum
 - F. None of the above

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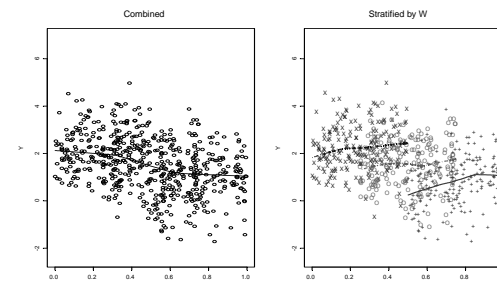
Question 6

- In considering associations between DSST and Age, we are interested in whether education level modifies any such association:
 - College graduates: Sample correlation is -0.3
 - Non-college graduate: Sample correlation is -0.8
- Which of the following statements best describes your conclusion about the possibility of effect modification.
 - A. Education modifies DSST-Age association.
 - B. Education does not modify DSST-Age association.
 - C. There is insufficient information to assess this.

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Question 7

- Plot of Y vs X: **Stratification variable W appears to be**
 - A. An effect modifier
 - B. A confounder
 - C. A precision variable

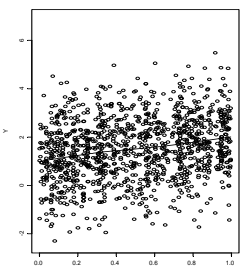
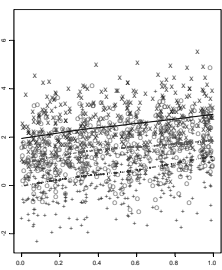


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Question 8

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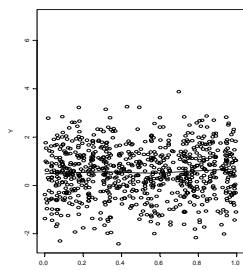
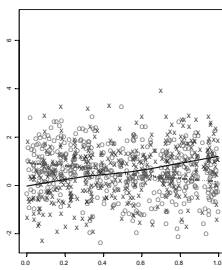



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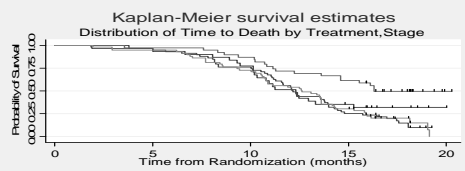



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Question 10

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- Plot of KM curves: Relative to treatment effect, **stage of disease appears to be**
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Kaplan-Meier survival estimates
Distribution of Time to Death by Treatment, Stage

Number at risk		5	10	15	20
tx = 0/advdis = 0	31	30	24	10	1
tx = 0/advdis = 1	59	57	45	15	0
tx = 1/advdis = 0	39	38	34	24	1
tx = 1/advdis = 1	59	56	43	18	0

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Question 11

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- Summary statistics for selected laboratory variables

	N	Mean	SD	Min	Mdn	Max
cholest	50000	301	40.1	128	311	474
albumin	40	3.99	0.48	2.86	4.08	4.97
AST	400	30.4	8.96	6.44	30.7	58.7
- Which variables might have **substantial outliers**?
 - Cholesterol
 - Albumin
 - AST
 - None of the above
 - Cannot tell

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Answers and Discussion

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Inference for Means

- Most common parameter used as a basis for statistical inference is the mean
 - Proportions = mean of binary variable
 - log Geometric mean = mean of log transformed data
- Tends to reflect a wide variety of differences between distributions
 - E.g., extremely sensitive to changes in the tail of distributions
- Statistical theory allow us to know the sampling distribution, and thus allows us to do inference

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Measures of Association

- Most commonly we contrast summary measures across groups
 - Difference (ratio) of means
 - Difference (ratio) of medians
 - Ratio of geometric means
 - Difference (ratio) of proportions
 - Odds ratio
 - Difference (ratio) of rates
 - Hazard ratio

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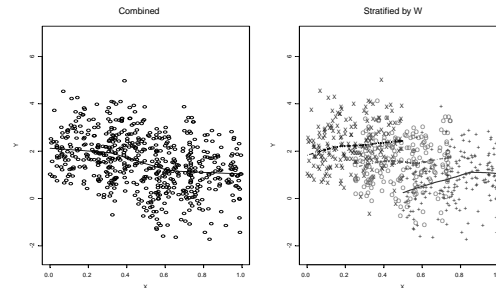
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Question 7

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(Pure) Confounders

- Estimates of treatment effect the same across strata, AND
 - Confounder is causally associated with Response, AND
 - Confounder associated with POI in the sample
- When analyzing difference of means of continuous data
 - Stratified smooth curves of data are parallel
 - Distribution of POI differs across strata
 - Unadjusted, adjusted analyses give different estimates

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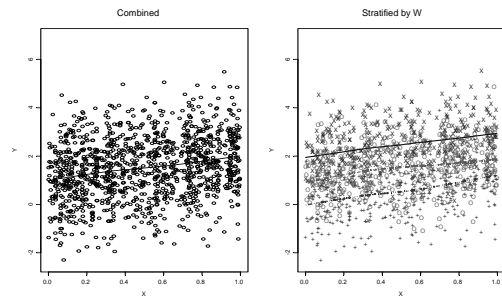
Interpreting Scatterplots

- W associated with Y independent of association between Y and X?
 - Vertical separation between lowest curves for strata
 - Causally?
 - Cannot get this from the data, much less the scatterplot
- W associated with X
 - Preponderance of X values different for the strata

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Question 8

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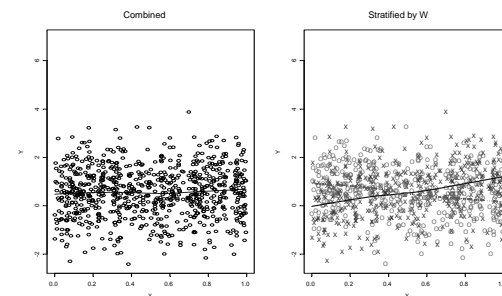
(Pure) Precision Variables

- Estimates of treatment effect the same across strata, AND
 - Variable is causally associated with Response, AND
 - Variable not associated with POI in the sample
- When analyzing difference of means of continuous data
 - Stratified smooth curves of data are parallel
 - Distribution of POI same across strata
 - Unadjusted, adjusted analyses give similar estimates

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Question 9

- Plot of Y vs X: **Stratification variable W appears to be**
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 - B. A confounder
 - C. A precision variable



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Effect modifiers

- Estimates of treatment effect differ among the strata
 - When analyzing difference of means of continuous data
 - Stratified smooth curves of data are nonparallel
 - (Graphical techniques difficult in other settings)
- We do not always care about effect modifiers
 - Sometimes we just average across it
 - In those cases, we may care about confounding effects

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Example

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- A hypothetical agricultural experiment is conducted to assess the effect of fertilizer on the size of fruit produced
- Plants are randomly assigned to receive either fertilizer or a sham treatment
 - Randomization in some sense precludes the possibility of confounding
- Response variable
 - At the end of the study, the diameter of the fruit produced by the plants is measured.

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Example: Predictor of Interest

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- The scientific question translates into a statistical question comparing the distribution of fruit sizes across groups defined by fertilizer treatment
- Predictor of interest:
 - A binary variable indicating whether the corresponding fruit was obtained from a plant receiving fertilizer (1) or a sham treatment (0)

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Example: Hypothetical Data (Case 1)

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Fruit sizes by treatment group

	Fert	Sham	Diff
	3.7, 12.5,	41.6, 10.3,	
	13.7, 44.2,	0.9, 40.5,	
	43.8, 43.5,	9.8, 10.2,	
	4.3, 14.0,	11.1, 1.1,	
	4.6, 43.9,	39.9, 1.3,	
	13.8, 4.2	40.7, 1.4	
Mean	20.5	17.4	3.1
SD	17.7	17.6	

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Example: Conclusions (Case 1)

.....

- No conclusive evidence that fertilizer improves size
 - The difference in the average size of fruit (mean difference 3.1) was not very large compared to the variability in the size of the fruit within groups
 - $\text{Var}(\text{Size} | \text{Trt}) = 311.5$ (SD = 17.65)
 - (P value = 0.67)
 - Thus with these small sample sizes, we cannot rule out that the difference in means was not just a chance observation when no real effect exists
 - (A larger sample size might make such an observed difference conclusive)

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Example: Adjusted Analysis (Case 1)

.....
Fruit sizes by treatment group and type of fruit

	Fert	Sham	Diff
Berry	3.7, 4.3, 4.6, 4.2	0.9, 1.1, 1.3, 1.4	
Mean(SD)	4.2 (0.37)	1.2 (0.22)	3.0
Apple	13.8, 12.5, 13.7, 14.0,	9.8, 10.2, 11.1, 10.3,	
Mean(SD)	13.5 (0.68)	10.4 (0.54)	3.1
Melon	44.2, 43.8, 43.5, 43.9	41.6, 40.5, 39.9, 40.7	
Mean(SD)	43.8 (0.29)	40.7 (0.70)	3.1

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Example: Adjusted Conclusions (Case 1)

-
- This second analysis suggests very conclusive evidence that fertilizer improves size of fruit
 - More precision was gained by comparing similar types of fruits ("Apples with apples")
 - Var (Size | Trt, Fruit) = 0.25 (SD = 0.50)
 - The average difference of 3.1 across types of fruit is large compared to the within group standard deviation of 0.50
 - (P value < .0001)
 - (Randomization did protect us from confounding: Each treatment group had four plants of each kind)

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Example: Case 2 - Confounding

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- We can use this example to illustrate how confounding would appear different
 - In Case 1, we imagined that randomization worked perfectly (perhaps we stratified on type of plant)
 - If we used complete randomization, we might have been unlucky and ended up with imbalance between treatment groups with respect to type of plant

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Example: Hypothetical Data (Case 2)

.....
Fruit sizes by treatment group

	Fert	Sham	Diff
	3.7, 12.5,	41.6, 10.3,	
	13.7, 44.2,	0.9, 40.5,	
	3.8, 43.5,	9.8, 10.2,	
	4.3, 14.0,	11.1, 1.1,	
	4.6, 43.9,	39.9, 41.3,	
	13.8, 4.2	40.7, 1.4	
Mean	17.2	20.7	-3.5
SD	16.6	18.1	

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Example: Conclusions (Case 2)

- No conclusive evidence that fertilizer improves size of fruit
- The difference in the average size of fruit (mean difference -3.1) was not very large compared to the variability in the size of the fruit (standard deviation 16.6 and 18.1 in the two groups)
 - (P value = 0.62)
- In fact, the point estimate of treatment effect actually suggests that the fertilizer treatment makes things worse

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Example: Adjusted Analysis (Case 2)

Fruit sizes by treatment group and type of fruit

	Fert	Sham	Diff
Berry	3.7, 4.3, 3.8, 4.6, 4.2	0.9, 1.1, 1.4	
Mean(SD)	4.1 (0.37)	1.1 (0.25)	3.0
Apple	13.8, 12.5, 13.7, 14.0,	9.8, 10.2, 11.1, 10.3,	
Mean(SD)	13.5 (0.68)	10.4 (0.54)	3.1
Melon	44.2, 43.5, 43.9	41.6, 40.5, 41.3, 39.9, 40.7	
Mean(SD)	43.9 (0.35)	40.8 (0.67)	3.1

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Example: Adjusted Conclusions (Case 2)

- This second analysis suggests very conclusive evidence that fertilizer improves size of fruit
- More accuracy was gained by comparing similar types of fruits (“Apples with apples”)
 - In this case, also gained precision, though not as much as when fruit type was balanced
- The average difference of 3.1 across types of fruit is large compared to the standard deviations with groups defined by type of fruit and treatment
 - (P < .0001)

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Example: Case 3 – Effect Modification

- We can also use this example to illustrate how effect modification would appear different
- In Cases 1 and 2, we imagined that the treatment worked equally well for all types of fruit
- We can now examine what would happen if that were not the case

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Example: Hypothetical Data (Case 3)

Fruit sizes by treatment group

	Fert	Sham	Diff
	3.7, 12.5,	45.6, 10.3,	
	13.7, 44.2,	0.9, 44.5,	
	43.8, 43.5,	9.8, 10.2,	
	4.3, 14.0,	11.1, 1.1,	
	4.6, 43.9,	43.9, 1.3,	
	13.8, 4.2	44.7, 1.4	
Mean	20.5	18.7	1.8
SD	17.7	19.6	

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Example: Conclusions (Case 3)

- No conclusive evidence fertilizer improves size of fruit
- The difference in the average size of fruit (mean difference 1.8) was not very large compared to the variability in the size of the fruit (standard deviation 17.6 and 19.6 in the two groups)
 - (P value = 0.82)
- Thus with these small sample sizes, we cannot rule out that the difference in means was not just a chance observation when no real effect exists
 - (A larger sample size might make such an observed difference conclusive)

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Example: Adjusted Analysis (Case 3)

Fruit sizes by treatment group and type of fruit

	Fert	Sham	Diff
Berry	3.7, 4.3,	0.9, 1.1,	
	4.6, 4.2	1.3, 1.4	
Mean(SD)	4.2 (0.37)	1.2 (0.22)	3.0
Apple	13.8, 12.5,	9.8, 10.2,	
	13.7, 14.0,	11.1, 10.3,	
Mean(SD)	13.5 (0.68)	10.4 (0.54)	3.1
Melon	44.2, 43.8,	45.6, 44.5,	
	43.5, 43.9	43.9, 44.7	
Mean(SD)	43.8 (0.29)	44.7 (0.70)	-0.8

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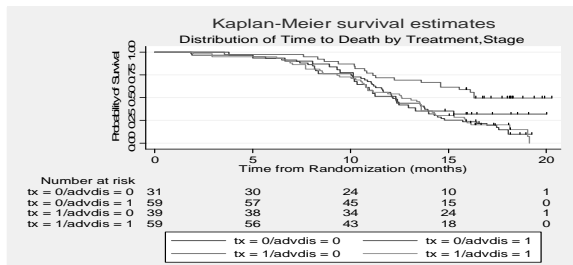
Example: Adjusted Conclusions (Case 3)

- A stratified analysis suggests the question about fertilizer effect should be answered by stratum
- Two basic approaches to analysis are possible
 - Average the stratum specific effect of fertilizer across strata
 - Treatment effect of 1.8 is large compared to within group variation (P=.0009)
 - Analyze each stratum separately
 - Improvement of 3.1 for berries, apples is large compared to within group variation (P <.0001, P<.0001)
 - Decrease of 0.8 for melons is marginal (P=0.032 without adjustment for multiple comparisons)

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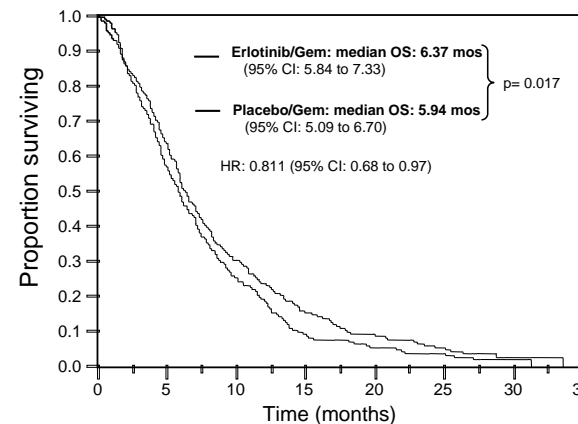
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- Plot of KM curves: Relative to treatment effect, **stage of disease appears to be**
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 - A precision variable



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Kaplan Meier Survival Curve Erlotinib/Gem vs Placebo/Gem (504 deaths)



* Stratified log-rank test

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Comparing Survival Curves

- In the presence of **censored observations**, it is never **possible to compare population**
 - Median (horizontal difference)
 - Mean (area under curve)
 - Geometric mean (area: log x- axis)
 - Standard deviation (complicated)
 - 25th and 75th Percentiles (horizontal difference)
 - Prob of exceeding thresholds (vertical difference)
 - Hazard ratio (related to slopes)

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Question 11

- Summary statistics for selected laboratory variables

	N	Mean	SD	Min	Mdn	Max
cholest	50000	301	40.1	128	311	474
albumin	40	3.99	0.48	2.86	4.08	4.97
AST	400	30.4	8.96	6.44	30.7	58.7

- Which variables might have **substantial outliers**?
 - Cholesterol
 - Albumin
 - AST
 - None of the above**
 - Cannot tell

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