Section B

Confounding, More Examples

Example 1: Arm Circumference and Height

- An observational study to estimate association between arm circumference and height in Nepali children
  - 94 randomly selected subjects (ages 3 months—6.5 years) had arm circumference, weight, and height measured
  - This study is observational—it is not possible to randomize subjects to height groups!

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Example: Arm Circumference and Height

- The data
  - Arm circumference range: 11.6–16.5 cm
  - Height range: 57–109 cm
  - Weight range: 5–18 kg
- To perform analysis
  - Dichotomize height at median (i.e., subjects will be classified as "less than" or "greater than or equal to" median height of 87 cm)
  - Dichotomize weight at median (i.e., subjects will be classified as "less than" or "greater than or equal to" median weight of 11.4 kg)

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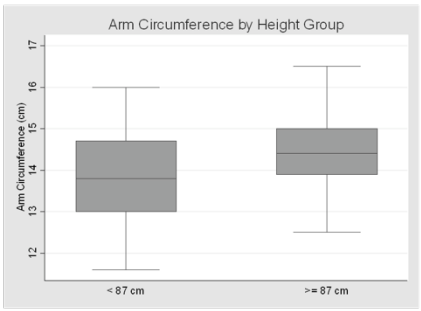
Example: Arm Circumference and Height

- Boxplot arm circumference by height group



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Example: Arm Circumference and Height

- Mean arm circumference (AC) by height group

Height group	n	Mean AC	SD
< 87 cm	47	13.8	1.1
≥ 87 cm	47	14.5	0.9
Difference	-0.7 cm		

  - Shorter subjects have arm circumferences on average .7 cm lower than taller subjects (mean difference = -0.7 with 95% CI -1.1 cm to -0.3 cm)

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Example: Arm Circumference and Height

- However, it is very likely that arm circumference and height are both related to a child's weight
- Some of the relationships between arm circumference and height could be because of, or masked by, these "behind the scenes" relationships to weight

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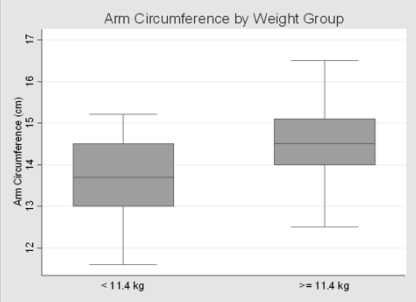
Example: Arm Circumference and Height

- What about weight?
  - Boxplot: arm circumference by weight group



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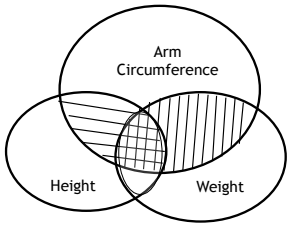
Example: Arm Circumference and Height

- Possible diagram of this scenario



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Example: Arm Circumference and Height

- Recall the original finding—children below the median height had arm circumferences of .7 cm lower on average than children (equal to or) above the median height
- To investigate whether this estimate is being fueled (or lessened) in part by weight differences in the height groups, and the arm circumference/weight relationship, let's stratify by weight group, and estimate the arm circumference/height association in each weight group

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Example: Arm Circumference and Height

- Mean arm circumference (AC) by height group
  - Children below median weight

	Lower weight group		
Height group	n	Mean AC	SD
< 87 cm	41	13.65	1.1
≥ 87 cm	6	13.63	0.6

  - Shorter subjects below the median weight have average arm circumferences on average .02 cm larger than taller subjects below the median weight (95% CI: -.64 cm (lower) to .68 cm [higher])

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Example: Arm Circumference and Height

- Mean arm circumference (AC) by height group
  - Children above median weight

	Higher weight group		
Height group	n	Mean AC	SD
< 87 cm	6	14.65	0.92
≥ 87 cm	41	14.59	0.87

  - Shorter subjects at or above the median weight have average arm circumferences (on average) .06 cm larger than taller subjects at or above the median weight (95% CI: -.90 cm [lower] to 1.0 cm [higher])

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Example: Arm Circumference and Height

- A recap
  - Ignoring weight, children below the median height had arm circumferences of .69 less (on average) than children at or above the median height and this difference was statistically significant
  - When stratified by weight children below the median height had arm circumferences marginally larger (on average) than children with or above the median height in both weight groups, but these estimates were very close to 0 and not statistically significant

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Example: Arm Circumference and Height

- So, it appears as though the association between arm circumference and height "disappears" or at least gets much smaller after accounting for weight
- Associations: (mean difference in arm circumference, shorter subjects compared to taller)
  - Crude/unadjusted -0.7 cm (95% CI -1.1 to -0.3)
  - Adjusted?
  - One possibility: taking weighted average of weight specific AC /height associations, weighted by inverse of SE's of weight specific associations

$$\frac{\frac{1}{\widehat{SE}(\bar{x}_{short\ low\ weight} - \bar{x}_{tall\ low\ weight})} \times (\bar{x}_{short\ low\ weight} - \bar{x}_{tall\ low\ weight}) + \frac{1}{\widehat{SE}(\bar{x}_{short\ high\ weight} - \bar{x}_{tall\ high\ weight})} \times (\bar{x}_{short\ high\ weight} - \bar{x}_{tall\ high\ weight})}{\frac{1}{\widehat{SE}(\bar{x}_{short\ low\ weight} - \bar{x}_{tall\ low\ weight})} + \frac{1}{\widehat{SE}(\bar{x}_{short\ high\ weight} - \bar{x}_{tall\ high\ weight})}}$$

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Example: Arm Circumference and Height

- Associations: (mean difference in arm circumference, shorter subjects compared to taller)
  - Crude/unadjusted -0.7 cm (95% CI -1.1 to -0.3)
  - Adjusted?
  - One possibility: taking weighted average of weight specific associations, weighted by SEs of weight specific associations

$$\frac{\frac{1}{0.46} \times .02 + \frac{1}{0.40} \times .06}{\frac{1}{0.46} + \frac{1}{0.40}} \approx 0.04$$

  - Can get 95% CI for this adjusted estimate: -0.30 cm to 0.38 cm

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Example: Arm Circumference and Height

- One approach—take a weighted average of the average arm circumference differences between subjects below and above the median weight within weight groups (weighted by size of each group)
- However, this is a pain, and if there are more potential confounders we could spend our life stratifying and computing such estimates
- Better approach—multiple regression methods (forthcoming!)

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Example: Arm Circumference and Height

- Just FYI:
  - A weighted overall average height adjusted difference in arm circumference between the two weight groups is .98 cm (children below median weight have smaller arm circumference on average) with 95% CI .40 cm to 1.55 cm
- Interesting:
  - When adjusted for weight, the arm circumference/height association disappears
  - When adjusted for height, the arm circumference/weight association is almost the same as the unadjusted arm circumference/weight association

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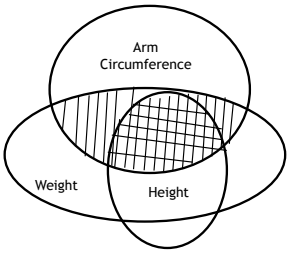
Example: Arm Circumference and Height

- This is an interesting case, perhaps better illustrated by this picture:



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Example: Arm Circumference and Height

- This is not always the case—many times when there is confounding between an outcome and two (or more) grouping variables, all of the adjusted outcome/group relationships will differ from the unadjusted associations

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Example 2: South African Study

- A longitudinal study from South Africa: birth cohort, followed up five years after birth
- Participation by medical aid status at birth, all baseline participants

	All subjects		
	Medical aid	**No medical aid**	**Total**
Follow-up participation	46	370	416
No follow-up participation	195	979	1,164
Total	241	1,349	1,590

$$\hat{RR}_{f\ ollowup} = \frac{\hat{p}_{medical\ aid}}{\hat{p}_{no\ medical\ aid}} = \frac{46/241}{370/1,349} = \frac{0.19}{.27} \approx 0.70$$

- 95% CI: 0.53 to 0.92

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Example 2: South African Study

- A longitudinal study from South Africa: birth cohort, followed up five years after birth
- Participation by medical aid status at birth, black participants

	Black subjects		
	Medical aid	**No medical aid**	**Total**
Follow-up participation	36	368	404
No follow-up participation	91	957	1,048
Total	127	1,325	1,452

$$\hat{RR}_{f\ ollowup\ Blcak} = \frac{\hat{p}_{medical\ aid\ Black}}{\hat{p}_{no\ medical\ aid\ Black}} = \frac{36/127}{368/1,325} = \frac{0.28}{.28} \approx 1.0$$

- 95% CI: 0.76 to 1.36

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Example 2: South African Study

- A longitudinal study from South Africa: birth cohort, followed up five years after birth
- Participation by medical aid status at birth, white participants

	White subjects		
	Medical aid	**No medical aid**	**Total**
Follow-up participation	10	2	12
No follow-up participation	104	22	126
Total	114	24	138

$$\hat{RR}_{f\ ollowup\ White} = \frac{\hat{p}_{medical\ aid\ White}}{\hat{p}_{no\ medical\ aid\ White}} = \frac{10/114}{2/24} = \frac{0.088}{.083} \approx 1.05$$

- 95% CI: 0.25 to 4.5

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Example 2: South African Study

- Recap

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Example 2: South African Study

- What's going on?
- Race
  - Majority of sample black subjects (91%)
- Race and follow-up participation
  - 26% of black subjects completed follow-up as compared to 9% of white subjects
- Race and medical aid
  - 9% of black subjects had medical aid compared to 83% of white subjects

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