Confounding

2004 Epidemiology, Biostatistics and Clinical Research Methods Summer Session

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Part 12

Adjustment of Rates

- Assume that mortality rates have been obtained for a one-year period for two communities: Community A, located in the developed world, and Community B, located in the developing world.

Adjustment of Rates

	Community A			Community B		
Age	# of deaths	Pop.	Annual rate per 10,000	# of deaths	Pop.	Annual rate per 10,000
Young	1	1,000	10	20	10,000	20
Middle	25	5,000	50	50	5,000	100
Old	100	10,000	100	20	1,000	200
Total (crude)	126	16,000	78.8	90	16,000	56.3

Calculating Age-adjusted (Standardized) Rates

1. Pick a reference population distribution. One (of many) ways to do this is to combine the two populations:

Young	=	1,000	+	10,000	=	11,000
Middle	=	5,000	+	5,000	=	10,000
Old	=	10,000	+	1,000	=	11,000

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Calculating Age-adjusted (Standardized) Rates

2. Apply age-specific rates for each population under study to the reference population, and add up the expected deaths (This is the number that would be expected if the community's age-specific rates had operated on the reference population's size and age distribution).

Community A					Community B				
Rate per 10,000		Reference population		Expected deaths	Rate per 10,000		Reference population		Expected deaths
10	x	11,000	=	11	20	x	11,000	=	22
50	x	10,000	=	50	100	x	10,000	=	100
100	x	11,000	=	110	200	x	11,000	=	220
				171					342

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Calculating Age-adjusted (Standardized) Rates

3. Divide the number of expected deaths in each group by the reference population:
   - Community A: 171/32,000 = 53.4 per 10,000
   - Community B: 342/32,000 = 106.9 per 10,000

   - The rates calculated are adjusted for age and allow an evaluation of the contribution of "community" to mortality independent of the age distributions of the communities being studied.

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Confounding vs. Effect Modification

- For ease of communication, comparisons of rates between “exposed” and “non-exposed” groups should, whenever possible, be aggregated across subgroups
- For example, it’s a lot easier to say, just once, that the rate of a disease in country A is half that in country B than to say the same thing for each age subgroup separately

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Confounding vs. Effect Modification

- However, while this type of rate summarization permits information to be conveyed more easily, it is probably a poor idea if important information is lost in the summarization process
- Furthermore, even after deciding to summarize, there are situations in which rate adjustment offers no particular benefit over presenting crude rates

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Confounding vs. Effect Modification

- You wish to portray the difference between the rates in Towns X and Y concisely and accurately. For each of the following figures, indicate whether:
  1. The age-adjusted rate is more appropriate than the crude rate;
  2. The crude and age-adjusted rates are equally appropriate; or
  3. Neither the crude nor age-adjusted rates are appropriate

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Population Distributions

Age	Town X	Town Y
≤ 20	48%	36%
21-64	40%	33%
65+	12%	31%

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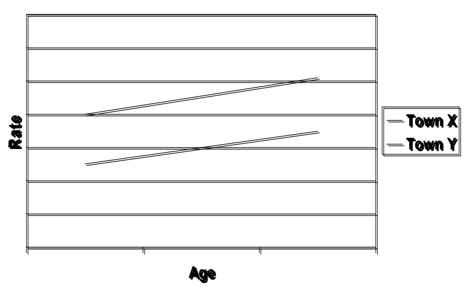

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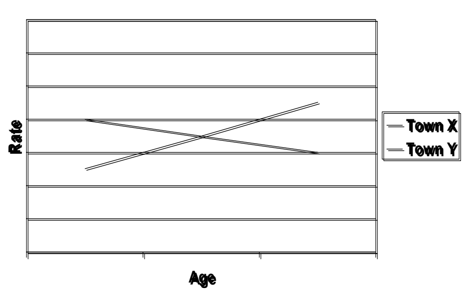

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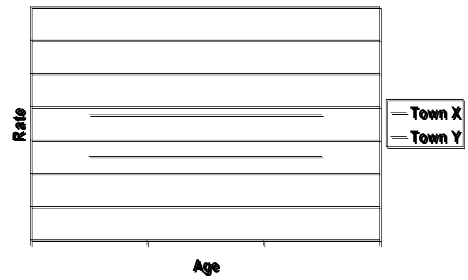


Effect-modification and Confounding

- Effect-modification (interaction) exists when the magnitude of the association between an exposure (or characteristic) and disease (or other outcome) is influenced by one of more other factors. For example:

		CD mortality per 100,000 woman years
Smoker	OC user	51.90
	OC nonuser	11.76
	Rate difference	40.14
Nonsmoker	OC user	15.12
	OC nonuser	5.19
	Rate difference	9.93

Effect-modification and Confounding

- In the presence of “important” effect-modification, such as in the above example (in which 40.14 and 9.93 are different to an “important” degree), summarization of the data into a single table is inappropriate
- In this instance the effect of smoking on the OC-circulatory-death association would be missed

Effect-modification and Confounding

- Once effect-modification has been sought and found to be absent or small in magnitude, it is reasonable and convenient to summarize
- Summarization can be done either by pooling data from the component tables into just one, or by standardizing in some way
- Pooling is appropriate only if the factor that is being ignored (summed over) is non-confounding

		CD deaths	Woman-years (x 100K)	CD rate	Rate difference	Rate ratio
Low parity	OC user	6	.40	15.0 0	9.44	2.70
	OC nonuser	1	.18	5.56		
High parity	OC user	7	.46	15.2 2	10.14	3.00
	OC nonuser	3	.59	5.08		
All women	OC user	13	.86	15.1 2	9.93	2.91
	OC nonuser	4	.77	5.19		

Effect-modification and Confounding

- The small amount of effect-modification is not likely to be important (rate difference of 9.44 versus 10.14), so the presentation of stratum-specific information is unnecessary
- In order to determine whether OC use is associated with altered CD mortality, it’s necessary to calculate the RR, and the pooled data give an RR respectably intermediate to the component RRs
- Thus, no important degree of confounding is present

Effect-modification and Confounding

- Another way of inferring the relative absence of confounding is to see if "parity" meets the minimal criteria for confounding, i.e., relationship both to OC use and CD:

	Woman-years (x 100,000) among OC users	Woman-years (x 100,000) among OC non-users
High parity	.46	.59
All women	.86	.77
% high parity	53% (=.46/.86)	77%

		CD rate	RR
OC users	High parity	15.22	1.01
	Low parity	15.00	
OC nonusers	High parity	5.08	0.91
	Low parity	5.56	

Effect-modification and Confounding

- Though parity and OC use are associated, there is no relation between parity and CD, and so we would not expect parity to be a confounding variable

		CD deaths	Woman-years (x 100K)	CD rate	Rate difference	Rate ratio
Inactive	OC user	6	.29	20.69	13.87	3.03
	OC nonuser	3	.44	6.82		
Active	OC user	7	.57	12.28	9.25	4.05
	OC nonuser	1	.33	3.03		
All women	OC user	13	.86	15.12	9.93	2.91
	OC nonuser	4	.77	5.19		

Effect-modification and Confounding

- No reasonable method of averaging the two rate ratios, 3.03 and 4.05, gives 2.91, so confounding must be present
- Standardization must be employed when summarizing these tables

Effect-modification and Confounding

- To satisfy ourselves that "physical activity" indeed met our minimal criteria for confounding, we might examine the following tables:

	Woman-years (x 100,000) among OC users	Woman-years (x 100,000) among OC non-users
Inactive	.29	.44
All women	.86	.77
% inactive	31%	57%

		CD rate	RR
OC users	Inactive	20.69	1.68
	Active	12.28	
OC nonusers	Inactive	6.82	2.25
	Active	3.03	

Effect-modification and Confounding

- A higher percentage of OC users than nonusers are active,a relationship that makes the elevated CD rate in users smaller than it "ought" to be if they had the same level of activity as nonusers
- Thus, the OC-CD association is (to some extent) confounded by the influence of physical activity

Calculation of Adjusted Rate Ratio in Cohort Studies

	OC+	OC-	Total
Inactive			
CD deaths	**6**	**3**	**--**
Woman-years ($x10^5$)	**.29**	**.44**	**.73**

	OC+	OC-	Total
Active			
CD deaths	**7**	**1**	**--**
Woman-years ($x10^5$)	**.57**	**.33**	**.90**

Calculation of Adjusted Rate Ratio in Cohort Studies

Adjusted rate ratio $= \frac{\sum a_i \; N_{0i} \div T_i}{\sum b_i \; N_{1i} \div T_i}$

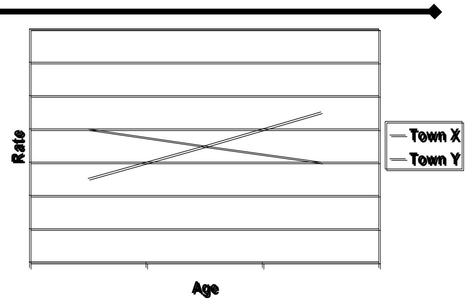
$= \frac{(6(.44) \div .73) + (7(.33) \div .90)}{(3(.29) \div .73) + (1(.57) \div .90)}$

$= 3.39$

	CD deaths	Woman-years (x 100,000)	CD rate	Rate difference	Rate ratio
Inactive					
OC user	6	.29	20.69	13.87	3.03
OC nonuser	3	.44	6.82		
Active					
OC user	7	.57	12.28	9.25	4.05
OC nonuser	1	.33	3.03		
All Women					
OC user	13	.86	15.12	9.93	2.91
OC nonuser	4	.77	5.19		

Exercises - Confounding

A. In order to assess the efficacy of faceguards in preventing the occurrence of facial injury in Little League Baseball in the U.S., the rate of these injuries (for which insurance compensation claims were paid) was compared between leagues that did and did not use faceguards. The results of this research, stratified by Division of play (each Division represents a separate age group) are as follows:



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Exercises - Confounding

	Faceguard used		No faceguard used	
Division	# of injuries	Player-seasons	# of injuries	Player-seasons
T-ball	0	328,245	1	1,035,105
Minor	9	484,830	33	1,442,340
Regular	14	278,685	84	891,270
Upper	5	66,705	37	444,060

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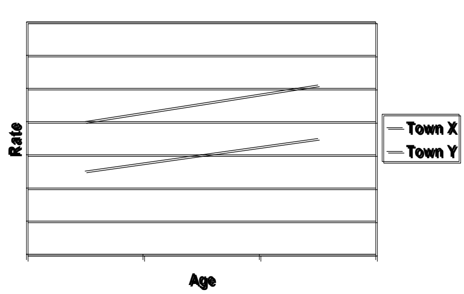

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Exercises - Confounding

1. What was the crude incidence of facial injury among players in leagues that used faceguards? In those that did not? What was the rate difference?

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Exercises - Confounding

2. What is the corresponding rate difference that is adjusted for Division? (Use the Division distribution of faceguard users as the standard population.)

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Exercises - Confounding

3. Why is the difference between the adjusted rates smaller than the difference between the crude rates?

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Adjusted rate of facial injuries among participants in Little League Baseball who did not use faceguards

Division	Rate	Standard Population	*wt*	# of injuries expected in standard population
T-ball	1 / 1,035,105	328,245	*.283*	.317
Minor	33 / 1,442,340	484,830	*.419*	11.093
Regular	84 / 891,270	278,685	*.241*	26.265
Upper	37 / 44,060	66,705	*.058*	5.558
		1,158,465	*1.001*	43.233

Adjusted rate = 43.233 / 1,158,465

= 37.319 per million player-seasons

Exercises - Confounding

B. Among the employees who have worked in a certain industry, some have been exposed to a substance, S, that you suspect to be a cause of bladder cancer. You conduct a cohort study in which the mortality from bladder cancer in exposed and nonexposed persons is compared. The results are as follows:

Exercises - Confounding

Sex	Exposure status	Deaths	Person-years
Male	S+	36	31,819
	S-	45	79,631
Female	S+	2	4,634
	S-	8	41,187

Exercises - Confounding

1. What is the rate ratio associated with exposure to S in males? In females? In both sexes combined? What is the rate ratio adjusted for sex? Why does it differ from the crude rate ratio?

Epidemiologic Perspectives

- Ed Boyko, MD, MPH, Seattle ERIC Director, interviews Polly Newcomb, PhD, Member and Program Head, Cancer Prevention Program, Fred Hutchinson Cancer Research Center, about her study on Pregnancy Termination in Relation to Risk of Breast Cancer.