Lab: Cohort Study Design

Angry Temperament and Coronary Heart Disease Risk

Instructions

1. Read pages 191 – 208 in Chapter 11 on cross-sectional and cohort designs. In addition, read or re-read pages 125 – 131 on incidence proportion (cumulative incidence) and incidence rate (incidence density).
2. Carefully review slides 1 – 21 in the Chapter 11 .PPT file.
3. Complete a "self-test" of the material with the Chapter 11 Review Questions for §11.1 – §11.4.
4. Look over the lab questions.
5. Download this article: Janice E. Williams, F. Javier Nieto, Catherine P. Stanford and Herman A. Tyroler. Effects of an angry temperament on coronary heart disease risk: The Atherosclerosis Risk in Communities Study. *American Journal of Epidemiology* 2001; 154(3):230-235. [Link to full text] Read the abstract and scan or read the rest of the article. I do not expect you to understand every element of this study.
6. Discuss lab questions online.
7. Submit your answers to the question using the assignment tool.

Background: The Atherosclerosis Risk in Communities Study (ARIC) is a multi-site epidemiologic project funded by the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) to study cardiovascular disease in the U.S. population. The study enrolled people in four communities, each studied by a different team of investigators, who worked under the direction of a steering committee for the study. People who enrolled in the study had thorough medical examinations and completed extensive questionnaires. Participants were re-examined after several years and again several years later. One of the examinations that participants underwent was measurement of the thickness of the walls of their carotid arteries, with B-mode ultrasound, a technique that was fairly new when ARIC began. Atherosclerosis in the carotid arteries serves as an indicator of atherosclerosis elsewhere in the arterial bed, so this measurement provided a non-invasive measure of subclinical (prior to symptoms) atherosclerosis that could lead to coronary events and strokes. The studies by Williams and coworkers (2001) were carried out using data from the ARIC study. This particular study looked at angry temperament in relation to coronary heart disease risk.

Questions

(NOTE: For some of these questions there may not be one "right answer".)

1. [Thought question; not graded.] What are advantages and disadvantages of conducting a study of angry temperament and anger reaction as part of a large, multi-center investigation designed for multiple purposes?

2. [Thought question; not graded.] A total of 14,348 persons were examined at the second clinic visit. A previous article by Williams and coworkers explains that these participants represented about 93% of those examined at baseline. Williams et al. apparently excluded 1,140 participants with a history of myocardial infarction (MI), coronary bypass surgery, or electrocardiographic

evidence of MI, as well as an additional 222 participants most of whom were missing data on hypertension or the anger scale, leaving 12,990 participants for analysis (the arithmetic does not quite work out, so perhaps several people listed as excluded in the earlier article, which says 12,896, were retained after all).

(a) What is the reason for excluding the 1,140 participants with evidence of clinical coronary heart disease?

(b) How might losing 7% of the original cohort by the second visit affect the study results?

3. Table 1 (p. 231) presents selected characteristics of study subjects for each category of hypertension and anger.

(a) Are there marked differences between those with low and high anger trait? What are the implications of these differences?

(b) Use data in Table 1 to determine the number of normotensive males with low anger-temperament.

(c) Use data in the table to determine the percentage of hypertensives that are female.

4. Participants were followed from the date of their second clinic examination visit through December 31, 1995. How many person-months are contributed to follow-up by each of three different study participants whose second clinic exam visit took place on December 31, 1990, June 30, 1991, and January 31, 1992, respectively? None of these three participants experienced a CHD event.

5. Table 3 (p. 232) shows the total number of participants in each category of hypertension and Spielberger trait anger-temperament score range at the time of the second examination visit and the number in each category experiencing an incident event. What was the cumulative incidence (incidence proportion) for the four subgroups: (a) normotensive, low trait anger, (b) normotensive, high trait anger (c) hypertensive, low trait anger (d) hypertensive, high trait anger.

State the meaning of these incidences.

Cumulative incidence of CHD events by anger-temperament and hypertension

	Spielberger trait anger-temperament scores			
	Normotensive		Hypertensive	
	Low (≤8)	High (>8)	Low (≤8)	High (>8)
Population	8,021	456	4,231	282
No. with events	167	23	213	13
Incidence proportions	(a)	(b)	(c)	(d)

6. If participants who did not have a CHD event were followed for an average of 54 months and those who did have an event contributed an average of 27 months before the event, what would the total number of person-years have been for participants in each of the four groups identified in the previous problem? What was the incidence rate (a.k.a. [also known as], incidence density) in each of the four groups?

Hint: Here is how to calculate the person-years in the low anger, normotensive group:
Person-years = [(27 months)(167) + (54 months)(8,021−167)] /12 months per year = 428,625/12 = 35,719 person-years Now complete this process for the other three groups and calculate the rates for all four groups using this information.

Incidence density of CHD events by anger-temperament and hypertension

	Spielberger trait anger-temperament scores			
	Normotensive		Hypertensive	
	Low (≤8)	High (>8)	Low (≤8)	High (>8)
Population	8,021	456	4,231	282
No. with events	167	23	213	13
Person-years	(a)	(b)	(c)	(d)
Incidence density	(e)	(f)	(g)	(h)

Because the disease is rare (risk less than 5%), the approximate relationships between the incidence proportions reported in the first table and the incidence rates in the second table is described by this formula:

$$\text{incidence proportion} = \text{incidence rate} \times \text{time of follow-up}$$

The justification for this relationship is described in Formula (6.7) on p. 133 in the text.

7. What are the incidence rate ratios (RR) for high trait anger in (a) normotensive persons and (b) hypertensive persons? Recall that the rate ratio is the ratio of the rate in the "exposed" to the rate in the "unexposed". Write down the formula and the calculation as well as the result. Then translate the result into terms a layman would understand. What do these ratios show?

8. Compare the crude rate ratios that you just calculated to the rate ratios (referred to in the paper as "hazard ratios") for CHD events combined, age-adjusted as reported in Table 3 (p. 232) of the article. Are the crude and adjusted rate ratios similar?

9. In the article, under Results (page 232, col 1), Williams et al. write: "There was a monotonic increase in CHD risk as a result of trait anger-temperament in the multivariate-adjusted models. Normotensive persons experienced a 68 percent greater risk of CHD (age-adjusted, hard events)

for each four-unit increase in trait anger-temperament (95 percent confidence interval: 1.53, 1.84). "

Since the authors used Cox proportional hazards regression, which estimates rate ratios, by "68 percent greater risk" they are referring to a 68 percent greater incidence rate of CHD. To what incidence rate ratio (or "hazard ratio") does a 68 percent increase correspond?

Hint: See the text, p. 157, paragraph 2 that starts "*Relative* comparisons can be expressed in various equivalent ways." Especially note point 3 in this paragraph. Then refer to p. 160 starting in paragraph 6 that begins "Relative Rate Difference." Notice, for instance, that a relative risk of 1.5 represents a 50% increase in risk (in relative terms). This because the baseline RR is 1.0, not 0. Discuss this point among yourselves, if necessary, as this method of discussing risk is extremely different in the lay and professional press.

11. Examine Figures 1 through 3 in the article. Besides providing an easy way to see the difference in CHD incidence in the groups being compared, what additional information do the figures provide that is not available from the tables?

12. Cohort studies are considered observational studies, whereas clinical trials are considered experimental. Could a randomized intervention trial be conducted to test the hypothesis that anger-temperament increases CHD risk? Would it provide stronger evidence for a causal relation?