EPID600 (Spring 2007) module on Cohort Studies

Objectives:

- List the characteristics of cohort studies.
- Identify the advantages and disadvantages of cohort studies.
- Define the terms risk ratio, rate ratio, attributable risk (exposed population), attributable risk (total population), attributable risk percent (exposed population), and attributable risk percent (total population).
- Calculate risk ratio, rate ratio, attributable risk (exposed population), attributable risk (total population), attributable risk percent (exposed population), and attributable risk percent (total population).
- Interpret 95% confidence intervals.
- Interpret risk ratio, rate ratio, attributable risk (exposed population), attributable risk (total population), attributable risk percent (exposed population), and attributable risk percent (total population) calculations.
- Identify a statistically significant RR.
- Interpret the meaning of a statistically significant RR.
- Differentiate cohort studies from clinical trials.
- Distinguish between crude and adjusted RRs.

Instructions:

1. **Read**: Aschengrau and Seage, ch. 8 - Cohort Studies . Answer the practice questions at the end of the chapter or at http://publichealth.jbpub.com/aschengrau/student_resources.cfm and check your answers (recommended, but optional) (animated flashcards, weblinks, and Powerpoint slides from the authors] can also be found at that URL)

2. Look over the case study questions and then read the case study reading: 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, *Am J Epidemiol* 2001; 154(3):230-235. (abstract, full text)

3. (Optional, but earns credit) Before lab, submit the answers to the starred case study questions (numbers 3, 10, 11, 12, and 13).

4. Read the lecture slides and attend the lecture (or read the speaker notes).

5. Work on the rest of the case study questions in **lab** and afterwards.

6. Agree on the answers, so the facilitator can submit the group's consensus answers by the following Sunday evening (EST).

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

1. The Atherosclerosis Risk in Communities Study (ARIC) is a major, multi-site project funded by the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) to study cardiovascular disease in the general 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 overall 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 *et al.* were carried out using data from the ARIC study. What are advantages and disadvantages of conducting a study of anger temperament and anger reaction as part of a large, multi-center investigation designed for multiple purposes?

2. 14,348 persons were examined at the second clinic visit. A previous article by Williams *et al.* 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 presents various participant characteristics 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 the table to derive the number of normotensive males with low anger-temperament.

c. Use data in the table to derive the percentage of hypertensives who are female.

4. Participants were followed up from the date of their second clinic examination visit through December 31, 1995. How many person-months would be contributed to the follow-up by each of 3 participants whose second clinic exam visit took place on December 31, 1990, June 30, 1991, and January 31, 1992, assuming that none of them experienced a CHD event?

5. Table 3 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: normotensive, low trait anger ("CInL" in the table); normotensive, high trait anger (CInH); hypertensive, low trait anger (CIhL); hypertensive, high trait anger (CIhH)? State the meaning of these incidences. Do these incidences require units? Why not?

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
Cumulative incidence	CInL	CInH	CIhL	CIhH

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 (labelled nL, nH, hL, and hH in the table below)? What was the incidence rate (a.k.a. [also known as], incidence density) in each of the four groups? (See table below.)

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	PYnL	PYnH	PYhL	PYhH
Incidence density	IDnL	IDnH	IDhL	IDhH

7. What is the approximate relationship between the incidence proportions in the first table and the incidence rates in the second table? (You can find an interactive example of the relation between incidence rates and incidence proportions at www.epidemiolog.net/studymat/).

8. What are the incidence density ratios (IDR, a.k.a. incidence rate ratios) for high trait anger in (a) normotensive persons and (b) hypertensive persons? (A rate ratio is usually 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 English or a language of your choice. What do these ratios appear to show?

9. Compare the incidence rate ratios that you computed for the preceding question to the incidence rate ratios (referred to in the paper as "hazard ratios") for CHD events combined, Age-adjusted in Table 3. What does their similarity imply in regard to the age distributions of participants with low and high trait anger? Explain.

**10. In the text, 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)."

a. 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? In other words, what is the rate ratio for a 4-point increase in trait anger-temperament in these data?
b. Based on this statement, what was the estimated rate ratio for an **8-point** increase in trait anger-temperament?

**11. What are appropriate interpretations of the 95% confidence interval referred to in the preceding question and of "statistically significant" in the authors' following sentence ("In contrast, the association between trait anger-temperament and CHD risk among hypertensives was not statistically signficant.")?

**12. Examine Figures 1-3. 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?

**13. The appendix to this paper contains the Spielberger subscales used as the exposure measures for this article. How would you establish the reliability and validity of a scale?

14. 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?

12/9,11/2003vs, 2/18/2004vs, 5/28/2004vs

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Effects of an Angry Temperament on Coronary Heart Disease Risk

The Atherosclerosis Risk in Communities Study

Janice E. Williams,[1] F. Javier Nieto,[2] Catherine P. Sanford,[3] and Herman A. Tyroler[4]

The objective of the study was to determine which component of an anger-prone personality more strongly predicts coronary heart disease (CHD) risk. Proneness to anger, as assessed by the Spielberger Trait Anger Scale, is composed of two distinct subcomponents—anger-temperament and anger-reaction. Participants were 12,990 middle-aged Black men and women and White men and women from the Atherosclerosis Risk in Communities Study who were followed for the occurrence of acute myocardial infarction (MI)/fatal CHD, silent MI, or cardiac revascularization procedures (average = 53 months; maximum = 72 months) through December 31, 1995. Among normotensive persons, a strong, angry temperament (tendency toward quick, minimally provoked, or unprovoked anger) was associated with combined CHD (acute MI/fatal CHD, silent MI, or cardiac revascularization procedures) (multivariate-adjusted hazard ratio = 2.10, 95% confidence interval: 1.34, 3.29) and with "hard" events (acute MI/fatal CHD) (multivariate adjusted hazard ratio = 2.28, 95% confidence interval: 1.29, 4.02). CHD event-free survival among normotensives who had a strong, angry temperament was not significantly different from that of hypertensives at either level of anger. These data suggest that a strong, angry temperament rather than anger in reaction to criticism, frustration, or unfair treatment places normotensive, middle-aged persons at increased risk for cardiac events and may confer a CHD risk similar to that of hypertension. *Am J Epidemiol* 2001;154:230–5.

coronary disease; prospective studies; stress; survival analysis

A recent analysis of the Atherosclerosis Risk in Communities Study (ARIC) cohort reported that normotensive persons who were highly predisposed to anger and free of coronary heart disease (CHD) at baseline were slightly greater than two times more likely to experience a CHD event than were their less-anger-prone counterparts (1). Proneness to anger was assessed by the Spielberger Trait Anger Scale, which is composed of two distinct subscales: anger-temperament and anger-reaction (2). Compared with persons who are prone to angry reactions, those who have a strong, angry temperament experience anger longer, more frequently, more intensely, and in a broader range of situations and express it more quickly, needing little or no provocation. Persons prone to angry reactions, on the other hand, typically experience anger when frustrated, mistreated, or negatively evaluated by others. This study assessed the association between each trait anger component and CHD risk among persons enrolled in the ARIC cohort (3).

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Abbreviations: ARIC, Atherosclerosis Risk in Communities; CHD, coronary heart disease; MI, myocardial infarction.

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Reprint requests to Dr. Janice E. Williams, Cardiovascular Health Branch, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Highway NE, Mailstop K-47, Atlanta, GA 30341–3717 (e-mail: jwill22@bellsouth.net).

MATERIALS AND METHODS

ARIC is a large, population-based, prospective study of cardiovascular disease and its risk factors among residents aged 45–64 years in the US communities of Washington County, Maryland; suburban Minneapolis, Minnesota; Forsyth County, North Carolina; and Jackson, Mississippi. Baseline clinical examinations were conducted from 1987 to 1989 (visit 1), and follow-up examinations were given every 3 years thereafter (visits 2–4) (3). The population for this study was selected from the ARIC cohort who returned to visit 2 between 1990 and 1992 (n = 14,348). After exclusions, 12,990 persons remained for these analyses.

Using Spielberger's trait anger-temperament and trait anger-reaction subscales (see Appendix), respondents rated the frequency of their experience with anger on a Likert-type scale as: almost never = 1, sometimes = 2, often = 3, and almost always = 4. Responses to the four items in each subscale were summed to yield a score.

Covariates analyzed were age, race/ethnicity, gender, waist-to-hip ratio, plasma low density lipoprotein and high

Principles of Epidemiology for Public Health (EPID600)

Study designs: Cohort studies

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Cohort studies

Intuitive approach to studying disease incidence and risk factors:

1. Start with a population at risk
2. Measure characteristics at baseline
3. Follow-up the population over time with a) surveillance or b) re-examination
4. Compare event rates in people with and without characteristics of interest

Cohort studies

Can be large or small

Can be long or short

Can be simple or elaborate

For rare outcomes need many people and/or lengthy follow-up

May have to decide what characteristics to measure long in advance

Case example – Atherosclerosis Risk in Communities (ARIC) Study

Prospective study in four U.S. communities to investigate:

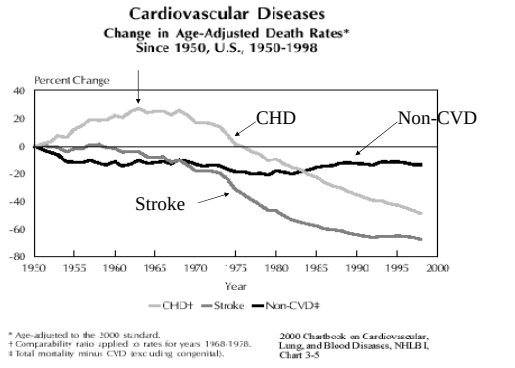
1. etiology and natural history of atherosclerosis
2. etiology of clinical atherosclerotic diseases
3. variation in CVD risk factors, medical care and disease by race, sex, place, and time.

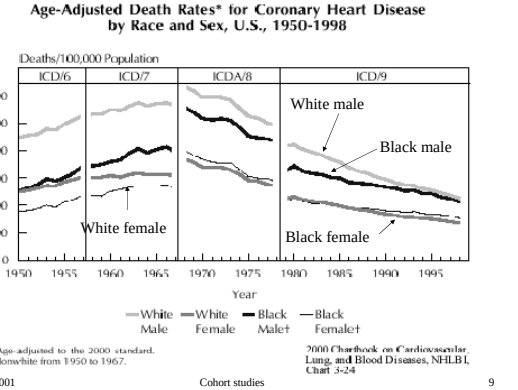
Background to ARIC Study – the CVD epidemic of the 20th century

- Heart disease became the leading cause of death in men and women
- Major CVD cohort studies, e.g.:
  - Framingham, MA
  - Tecumseh, MI
  - Evans County, GA
  - Honolulu, HI
  - British Civil Servants
  - Paris
  - …

Background to ARIC Study – the CVD epidemic of the 20th century

- CVD death rate peaked in 1963, then fell by over one-half (56%)
- Death rates from coronary heart disease (CHD) and stroke fell most





1978 National Heart, Lung and Blood Institute (NHLBI) Workshop on the Decline in Coronary Heart Disease Mortality

1. Is the decline in CVD mortality real?
2. How much of the decline reflects lower <u>incidence</u> (blood pressure control, smoking cessation, dietary change)?
3. How much reflects lower <u>case fatality</u> rate (better survival due to emergency medical services and coronary care units)?

Conclusion: The decline is real

Recommendations:

- Need data on incidence and risk factor change in order to determine causes
- NHLBI Community Cardiovascular Surveillance Program (1980-1984) developed and pilot-tested protocol for community surveillance

Atherosclerosis Risk in Communities Study (ARIC)

"the Framingham of the 1990's"

Two components:

1. Community surveillance – estimate CVD incidence
2. Cohort – validate and facilitate interpretation of surveillance data

(See http://www.cscc.unc.edu/aric/)

Communities in ARIC Study

- Forsyth County, North Carolina (biracial)
- Jackson, Mississippi (blacks)
- Suburban Minneapolis, Minnesota
- Washington County, Maryland

Defined geographical entities, well-delineated medical care referral patterns, black and white, urban and rural

Demographics of ARIC study communities, 1980

Study community	Pop. age 35-74	Total pop.	% Black	% Urban	% educ 12+ yrs	Median income
Forsyth Cnty NC	95,863	243,683	24	75	63	$16,600
Jackson MI	68,303	202,895	48	100	71	$14,800
Minn. subrbs MN	69,338	192,004	1	100	85	$24,165
Wash. Cnty MD	45,539	113,068	4	57	60	$16,863
Total	279,043	751,668				

Age-adjusted mortality rates in ARIC study communities, 1980

ARIC Study	All-cause		Heart disease	
communities	Men	Women	Men	Women
Forsyth Cnty NC	16.3	8.7	6.7	2.7
Jackson MI (Black)	20.8	10.0	6.6	2.9
Minn. subrbs MN	9.4	6.3	4.2	1.3
Wash. Cnty MD	16.1	8.2	7.8	2.8
Total	14.4	8.0	5.7	2.6

Cohort study added to enhance ARIC community surveillance

Cohort study – more and better data:

1. More data: provides information on risk factors and out-of-hospital medical care
2. Better data: uses standard methods for ascertaining events (surveillance relies on health care system)

Measure preclinical CVD (atherosclerosis) and CVD precursors

1. assess association of risk factors with both underlying and clinical diseases
2. assess value of ultrasound diagnosis in predicting clinical diseases
3. store blood in hope of discovering unsuspected precursors of CVD

Community surveillance enhances generalizability of cohort findings

1. Cohort → Community: compare incidence rates and characteristics of events in residents who do and who do not participate in cohort
2. Communities → Cohort: compare the study community CHD experience with areas in the U.S.

ARIC community surveillance for hospitalized MI and CHD death in age 35-74

- Hospital records with discharge diagnosis of MI or related “screening” diagnoses
- Death certificates with various CHD manifestations coded as the cause of death
- Interviews with physician and next-of-kin for deaths outside the hospital

ARIC cohort study – 1

- Different sampling scheme in each community
- Map & enumerate households
- Interview all eligible persons in household
- Recruit 16,000 age 45-64, clinic examination (1986-1989)

ARIC cohort study – 2

- Review medical records
- Interview participants annually
- Contact health care providers, family members
- Re-examine every 3 years after first exam (1990-92, 1993-95)

ARIC cohort study – home interview

- Health status, CVD risk factors
- Family health status, past history of CVD, cancer or diabetes
- Smoking status and amount
- Current employment status
- Level of education
- Participant's cooperation, literacy/comprehension, interview quality

ARIC cohort study – clinic examination

- 3 l/2 hours, 2 or 3 simultaneous exams
- Fasting and 12-hour abstinence (tobacco, alcohol) required prior to blood pressure and venipuncture
- Sitting blood pressure must be measured before venipuncture
- Interview and exam must precede the Medical Review

ARIC cohort study clinic exam – 1

- Greet participant; determine fasting status; collect medications
- Obtain informed consent
- Measure sitting blood pressure
- Measure weight, height, skinfolds, girths, and wrist breadth
- Blood samples for lipid, hemostasis, hematology, and chemistries

ARIC cohort study clinic exam – 2

- Snack (no caffeine or stimulants)
- Obtain a digitized 12-lead ECG and 2-minute rhythm strip
- Collect medical history (incl. Rose Quest.; stroke, TIA, respiratory symptoms, reproductive history) and food frequency
- Brief systems review incl. neck, neurological, chest and lungs, breast (optional), heart, extremities.

ARIC cohort study clinic exam – 3

- Digitized spirometric measurements of timed pulmonary function (FVC, FEV1).
- B-mode ultrasound scans for wall measurements in carotids and a popliteal artery
- Supine brachial and ankle blood pressure; heart rate and blood pressure changes as participant arises

(www.cscc.unc.edu/aric/visit/General_Description_and_Study_Management.1_1.pdf)

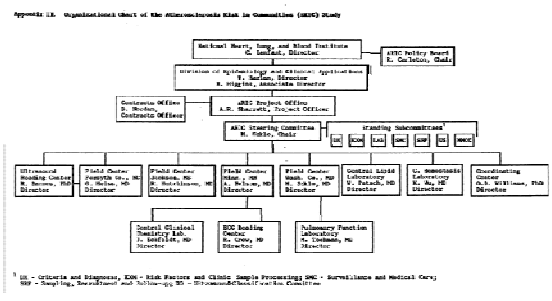
Central laboratories & Coordinating Center

- Central lipid laboratory
- 2 ECG reading cntrs (Dalhousie, U of Minn)
- Pulmonary function center
- Ultrasound reading center
- Study coordinating center (data monitoring, data mgmt, quality control, data analysis)

ARIC committees and subcommittees

- Steering Committee
- Laboratory and Sample Processing
- Ultrasound Subcommittee
- Risk Factors and Clinic Operations
- Sampling, Recruitment, and Follow-Up
- Criteria and Diagnoses
- Morbidity and Mortality Classification

ARIC committees and subcommittees



Anger proneness predicts coronary heart disease risk

Prospective analysis from the Atherosclerosis Risk in Communities (ARIC) Study

Janice E. Williams, Catherine C. Paton, Ilene C. Siegler, Marsha L. Eigenbrodt, F. Javier Nieto, and Herman A. Tyroler

Circulation 2000;101:2034

Background

- Persons "with trait anger have rage and fury more often, more intensely, and with longer-lasting episodes."
- Studies have linked trait anger with CHD risk factors.
- Studies have found associations between CHD and suppressed anger and difficulties with controlling anger.

Study population

- 14,348 participants (92.9% of baseline) returned to the ARIC visit 2 (1990-92) exam
- Exclusions for this study:
  1,140 with clinically manifest CHD (incl ECG)
  38 with ethnicity other than black or white
  40 with missing data on hypertension
  144 with incomplete anger questionnaire
- 12,986 participants available for this analysis

Spielberger's 10-item trait anger scale

(1=never, 2=sometimes, 3=often, 4=almost always)

1. I am quick tempered.
2. I have a fiery temper.
3. I am a hotheaded person.
4. I get angry when I am slowed down by others' mistakes.
5. I feel annoyed when I am not given recognition for doing good work.

Spielberger's 10-item trait anger scale

6. I fly off the handle.
7. When I get angry, I say nasty things.
8. It makes me furious when I am criticized in front of others.
9. When I get frustrated, I feel like hitting someone.
10. I feel infuriated when I do a good job and get a poor evaluation.

Measures

- Age, Gender, Race/ethnicity, Education
- Alcohol, Cigarette smoking
- Waist-to-hip ratio
- Diabetes (fasting serum glucose >= 140 mg/dL or history of diabetes, insulin, or diabetes medication)
- Plasma LDL & HDL cholesterol

Hypertension

- Blood pressure measured as average of 3 sitting measurements with a random-zero sphygmomanometer, after 5 min. rest period
- Hypertension if any of the following
  - Diastolic pressure >= 90 mm Hg
  - Systolic >= 140 mm Hg
  - Use within past 2 weeks of hypotensive medication

Follow-up for events

- Participants were followed from date of their first clinic reexamination in ARIC (1990-92) through December 31, 1995
- Median 53 months, maximum 72 months
- Abstraction of death certificates and hospital discharge records

"Incident CHD event"

1. acute myocardial infarction (MI) or fatal CHD ("hard" events)
2. cardiac revascularization procedure (percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery)
3. silent MI

Table 1. Distribution of Population Characteristics by Level of Trait Anger: ARIC Study, 1990 to 1992

	Spielberger Trait Anger Scores			
	Low: 10–14	**Mod: 15–21**	**High: 22–40**	**p[1]**
Participants, n (%)	**4,821 (37)**	**7,165 (55)**	**1,000 (7.7)**	
Age, yrs, mean	**57.3**	**56.6**	**56.3**	**<0.001**
Male, n (%)	**41.9**	**43.0**	**46.4**	**0.03**
% < high school educ.	**22.0**	**19.0**	**29.2**	**<0.01**
White, n (%)	**72.2**	**77.4**	**73.1**	**<0.01**
Current smokers, n (%)	**18.0**	**23.8**	**31.1**	**<0.01**
Current drinkers, n (%)	**51.9**	**59.9**	**61.2**	**<0.01**

Table 1. Distribution of Population Characteristics by Level of Trait Anger: ARIC Study, 1990 to 1992

	Spielberger Trait Anger Scores			
	Low: 10–14	Mod: 15–21	High: 22–40	p[1]
Participants, n (%)	4,821 (37.1)	7,165 (55.2)	1,000 (7.7)	
Hypertensive, n (%)	35.5	34.0	36.7	0.09
Diabetic, n (%)	11.4	10.2	13.6	<0.01
LDL chol., mg/dL, mean	133.1	133.2	132.1	0.66
HDL chol., mg/dL, mean	50.4	50.0	49.0	0.05
Waist-to-hip ratio, mean	0.918	0.925	0.939	<0.001

From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores			
	Low: 10–14	Mod: 15–21	High: 22–40	p[1]
Participants, n (%)	3,110	4,731	633	
Individuals with event	53	110	27	
Hazard ratio age-adjust	1.0	1.40	2.61	<0.001
Hazard ratio multivar.	1.0	1.32	2.20	0.02

From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores		
	Low: 10–14	Mod: 15–21	High: 22–40
Participants, n (%)	3,110	4,731	633
Individuals with event	53	110	27
CI (crude)	____	____	____
Hazard ratio age-adjust	1.0	1.40	2.61

From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores		
	Low: 10–14	Mod: 15–21	High: 22–40
Participants, n (%)	3,110	4,731	633
Individuals with event	53	110	27
CI (crude)	0.017	0.023	0.043
Hazard ratio age-adjust	1.0	1.40	2.61

From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores			
	Low: 10–14	Mod: 15–21	High: 22–40	
Number of persons	3,110	4,731	633	(x 4.4)
Individuals with event	53	110	27	
CI (crude)	0.017	0.023	0.043	
Person-years (hypothet)	13,736	20,895	2,796	
ID / 1,000py (crude)	____	____	____	
Hazard ratio age-adjust	1.0	1.40	2.61	

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Individuals with event	53	110	27
CI (crude)	0.017	0.023	0.043
ID / 1,000py (crude)	3.9	5.3	9.7
IDR (hazard ratio)	____	____	____
Hazard ratio age-adjust	1.0	1.40	2.61

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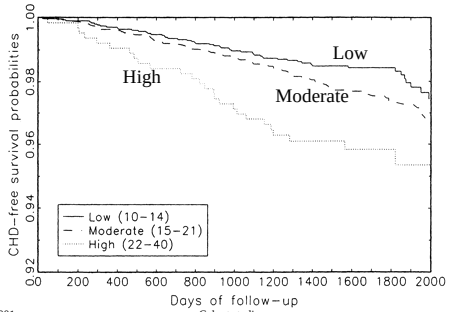
Person-years (hypothet.)	13,736	20,895	2,796
Individuals with event	53	110	27
ID / 1,000py (crude)	3.9	5.3	9.7
IDR (hazard ratio)	1.0	**1.4**	**2.5**
Hazard ratio age-adjust	1.0	1.40	2.61

From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores		
	Low: 10–14	Mod: 15–21	High: 22–40
Person-years (hypothet.)	13,736	20,895	2,796
Individuals with event	53	110	27
ID / 1,000py (crude)	3.9	5.3	9.7
IDR	1.0	1.4	2.5
IDD per 1,000 py	**0**	**1.4**	**5.8**

Figure 1. CHD event-free survival probabilities among normotensive individuals by trait anger scores



From table 2. Hazard Ratios (95% CI) for association between trait anger and all CHD – Normotensives

	Spielberger Trait Anger Scores			
	Low: 10–14	Mod: 15–21	High: 22–40	p[1]
Participants, n (%)	3,110	4,731	633	
Individuals with event	53	110	27	
CI (crude)	0.017	0.023	0.043	
Hazard ratio age-adjust	1.0	1.40	2.61	<0.001
Hazard ratio multivar.	1.0	1.32	2.20	0.02

From table 2. Hazard Ratios (95% CI) for association between trait anger and "hard" CHD – Normotensives

	Spielberger Trait Anger Scores			
	Low: 10–14	Mod: 15–21	High: 22–40	p[1]
Participants, n (%)	3,110	4,731	633	
Individuals with event	31	63	18	
CI (crude)	0.010	0.013	0.028	
Hazard ratio age-adjust	1.0	1.36	2.97	0.005
Hazard ratio multivar.	1.0	1.35	2.69	0.02

Relating risk factors to health outcomes – questions

- Is this health condition associated with this exposure?
  - Association not = causation but may reflect it
- How strongly are these two factors related?
  - Strong association more likely causal
- How much of a disease can be attributed to a causative factor?

What is an association?

Factors are associated if:

- the distribution of one factor is different for different values of another.
- knowing the value of one factor gives information about the distribution of the other.

Example – oral contraceptives and CHD

	OC	No OC	Total
CHD	30	20	50
No CHD	30	70	100
Total	60	90	150

Example – oral contraceptives and CHD

(positive association)

60% (30/50) of CHD cases used OC

	OC	No OC	Total
CHD	(30)	20	50
No CHD	(30)	70	100
Total	60	90	150

30% (30/100) of controls OC, overall

Example – oral contraceptives and breast cancer

	OC	No OC	Total
Cancer	15	35	50
No cancer	30	70	100
Total	45	105	150

Example – oral contraceptives and breast cancer (no association)

30% (15/50) of cases used OC

	OC	No OC	Total
Cancer	15	35	50
No cancer	30	70	100
Total	45	105	150

30% (30/100) of noncases used OC

Measures of association

- Can compare incidences (rate or proportion), prevalences
- Look at differences (e.g., "incidence difference") (retains units)
- Look at ratios (e.g., "incidence ratio") (no units)

Translating measures of association

If incidence ratio for runners / non-runners = 3.0:

- "Incidence in runners was 3 times that in non-runners."
- "Incidence in runners was 3 times as great as in non-runners."
- "Incidence in runners was 200% greater than incidence in non-runners." [(3.0 – 1.0) / 1.0 = 200%]

Translating measures of association

"Incidence in runners was 3 times greater than incidence in non-runners" is ambiguous

- Does it mean incidence ratio = 3.0 ?
- Does it mean incidence ratio = 4.0 ?

Translating measures of association

If incidence for runners / non-runners = 0.30:

- "Incidence in runners was 0.30 times that in non-runners."
- "Incidence in runners was 30% of that in non-runners."
- "Incidence in runners was 70% lower [or "less"] than incidence in non-runners." [(1.0 – 0.30) / 1.0 = 0.70 = 70%]

Translating measures of association

Or, can say "Incidence in *non-runners* was 3.3 times as great as incidence in *runners*".

Measures of impact

Concept of attributable risk

- How much of a disease can be attributed to a causative factor?
- What is the potential benefit from intervening to modify the factor?

Important for

- Public health policy
- Legal liability
- Clinical/individual decisions

Example questions

- Now that I am 35 years old, my CHD risk from taking oral contraceptives is twice as great as when I was 25. But how much more risk do I have due to taking the pill?
- How much of the risk of heterosexual transmission of HIV might be eliminated through eliminating bacterial sexually transmitted diseases?

Example questions

- How many cases of asthma are due to ambient sulfur dioxide?
- What proportion of motor vehicular deaths can be prevented by mandatory seat belt use.
- What proportion of perinatal HIV transmission has been prevented through the use of prenatal, intrapartum, and neonatal zidovudine (AZT)?

Simplifying assumptions

1. "Exposure" either causes or prevents the outcome, but not both (no two-edged swords)
2. "Exposed" and "unexposed" groups are alike in all other respects (no *confounding*)
3. No other causes "compete" with the exposure

Several concepts

Concepts

- "Absolute" versus "relative"
- Exposed versus total population
- Disease caused, disease prevented

Many terms, many meanings

E.g., "attributable risk" can mean:

- Risk difference
- Population attributable risk percent
- Concept of assessing impact

"Absolute" perspective

How much risk?

- In exposed persons:
  risk difference ($I_1 - I_0$)
- In the total population:
  ($I_1 - I_0$) x exposure prevalence (P_1)

How many cases?

($I_1 - I_0$) x # of exposed persons (n_1)

Relative perspective

What proportion of the risk is attributable? (What proportion of cases could be eliminated?)

In exposed persons: $(I_1 - I_0) / I_1 = (IR - 1) / IR$

(Relative strength of association)

In the population: $(I - I_0) / I$

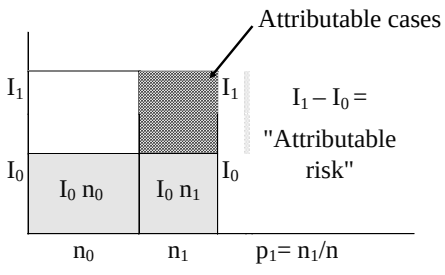
(Strength of association and prevalence)

How much risk? What %? How many cases? What %?

	E	$\overline{E}$	Total
D	40	20	60
$\overline{D}$	960	1,980	2,940
Total	1,000	2,000	3,000

$I_1 =$___ $I_0 =$___ $I =$___

Attributable risk diagram



Prevented fraction diagram