First Year Medical Exams
Second Semester

Epidemiology

BI 372

Final: 2002, 2000
1. Which of the following is an advantage of a case control study?

- Bias in the assessment of exposure to the factor of interest is minimized.
- Multiple disease outcomes following a selected exposure can be readily studied.
- Dependence on recall by subjects in the study is minimized.
- It is possible to determine the true incidence of the disease.
- It may be used to study etiology of a rare disease.

2. A study was published in the late 1990s indicating a possible increase in endophthalmitis related to glaucoma filtering surgery. In this surgery a filtering bleb is surgically created to allow drainage from the eye. The suspected cause of infection in this study was mitomycin C, an antifibrosis agent that prevents wound healing. Prevention of wound healing helps maintain drainage but also leads to a compromise of the barriers normally in place to prevent bacteria from entering the eye. A recent study was conducted to assess a new drug that prevents wound healing but which is also designed to reduce the incidence of postoperative endophthalmitis. The incidence of endophthalmitis in this study was found to be 12% in 25 patients given the new drug and 20% for 20 patients given the mitomycin C. The difference in efficacy between the two drugs was not statistically significant. Thus, it may be concluded that

- The new procedure is effective in reducing postoperative endophthalmitis.
- The new procedure is ineffective in reducing postoperative endophthalmitis.
- The results are probably affected by information bias and cannot be considered reliable.
- The results are clinically significant.
- The evidence is insufficient to demonstrate that the new drug is effective in reducing endophthalmitis.
3. A report of a clinical trial comparing a new drug versus placebo noted that the new drug gave a higher proportion of success than did the placebo. The report ended with the statement $\chi^2 = 4.72$, $P < 0.05$. In light of this information, we may conclude:

a. Fewer than 1 in 20 will fail to benefit from the drug.

b. The chance that an individual patient will fail to benefit is less than 0.05.

c. If the drug were effective, the probability of the reported finding is less than 1 in 20.

d. If the drug were ineffective, the probability of the reported finding is less than 0.05.

4. Since 1948, the Framingham Study has followed 2,336 males and 2,873 females in order to investigate the relationship between risk factors and the development of cardiovascular disease. Data from the Framingham Study on serum cholesterol levels and coronary heart disease (CHD) in men and women are shown in Table 1. Calculate the values for boxes labeled A through N in this table. Use the lowest level of serum cholesterol as the reference category for calculation of relative risks and risk differences.

**Table 1. Incidence of Coronary Heart Disease (CHD) by serum cholesterol at baseline, Ages 40-59, Framingham Study**

<table>
<thead>
<tr>
<th>Serum Cholesterol (mg/100 mL)</th>
<th>New CHD Cases</th>
<th>Population at Risk</th>
<th>Incidence (per 1000)</th>
<th>Relative risk</th>
<th>Risk difference (per 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 210</td>
<td>16</td>
<td>454</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>210 - 244</td>
<td>29</td>
<td>455</td>
<td>A 35 (Reference)</td>
<td>1 (Reference)</td>
<td>F 28</td>
</tr>
<tr>
<td>245 or more</td>
<td>51</td>
<td>424</td>
<td>B 64</td>
<td>D 1.8</td>
<td>G 85</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 210</td>
<td>8</td>
<td>445</td>
<td>H 18 (Reference)</td>
<td>1 (Reference)</td>
<td></td>
</tr>
<tr>
<td>210 - 244</td>
<td>16</td>
<td>527</td>
<td>I 30</td>
<td>K 1.68</td>
<td></td>
</tr>
<tr>
<td>245 or more</td>
<td>30</td>
<td>689</td>
<td>J 43</td>
<td>L 2.42</td>
<td></td>
</tr>
</tbody>
</table>

$$RR = \frac{\text{Incidence in exposed}}{\text{Incidence in unexposed}}$$

$$\text{Risk Diff} = \frac{\text{Incidence in exposed} - \text{Incidence in unexposed}}{\text{Exp}}$$
For each of the brief study descriptions in questions 5-7 presented below, identify whether the study is experimental or observational and, if observational, its design.

5. Some studies have identified a behavior pattern called Type A (characterized by a hard-driving time urgency) which they have associated with myocardial infarction (MI). Type A behavior was assessed for a group of men in a post-MI rehabilitation program. All men not falling into the Type A group were classified as Type B. Type A and Type B men were followed for 5 years to assess MI recurrence rates.

   a. (  ) Experimental
      (✓) Observational

   b. If observational, is the design:
      (  ) Cross sectional
      (x) Case control
      (  ) Retrospective cohort
      (✓) Prospective cohort

6. Investigators are studying employees at a bus company to test their hypothesis that occupational stress causes high blood pressure. Two major groups of employees are of interest: bus drivers and office workers in the same salary range. The investigators measure the blood pressure of all bus drivers and of a group of office workers matched to the bus drivers on age, sex, ethnicity, and length of employment. The mean blood pressure of the drivers is higher than that of the office workers and the investigators conclude that stress causes high blood pressure.

   a. (  ) Experimental
      (✓) Observational

   b. If observational, is the design:
      (✓) Cross sectional
      (  ) Case control
      (  ) Retrospective cohort
      (  ) Prospective cohort
7. One hundred persons with hepatitis A and 100 healthy neighbors were questioned regarding their history of eating raw clams or oysters in the preceding 3 months.

a. (    ) Experimental
       (    ) Observational

b. If observational, is the design:
   (    ) Cross sectional
   (    ) Case control
   (    ) Retrospective cohort
   (    ) Prospective cohort

8. Figure A shows 95% confidence intervals from 10 cohort studies on total fat intake and the relative risk of breast cancer. For most studies, the relative risk of high versus low quartiles of fat intake are shown. In some, quartiles or tertiles are used.

Figure A. Estimated relative risks of breast cancer associated with high total fat intake, 10 separate cohort studies. (Data source: Hunter & Willett, 1993, Table 1 p. 113.)
a. Which of these studies provides the most precise estimate of the size of the association? 
   1.7
b. Which of these studies provides the least precise estimate of the size of the association? 
   

  
   c. Which studies are statistically significant at p<.05? 
   None - all cross 1

  
   d. When the data from these studies are taken as a whole, do you think these studies support 
   or refute the proposed association between dietary fat and breast cancer? 
   Refute

  
   9. A screening test for diabetes, where a blood glucose of ≥180 mg/dl is considered positive, 
   has a known sensitivity of 22.5% and a known specificity of 99.7%. The prevalence of 
   diabetes in Town X is 2.2% and in Town Y is 1.5%.
   
   The proportion of all positive test results which are false positives is (circle one):

   a. Higher in Town X than in Town Y
   b. Lower in Town X than in Town Y
   c. The same in Town X as in Town Y
   d. Equal to the sensitivity of the test
   e. Equal to the specificity of the test

  
   10. Assuming there are 10,000 people living in Town Y, how many people will test positive and 
   be referred for additional testing (circle one)?

   a. 34
   b. 64
   c. 74
   d. 150
   e. 200
   f. 9936
   g. None of the above
For the following questions (11-15) please circle all that apply

11. You have a family practice in Groton Connecticut with a large proportion of your patients who are retired shipyard workers. You have read that people working with asbestos (as shipyard workers did), may be at increased risk of several cancers, including lung cancer. You go to MEDLINE and search for the best study that provides data on the topic. One of the studies you identify is a case-control study investigated asbestos exposure (E), lung cancer deaths (D), and cigarette smoking (F) in men living in a community with an asbestos plant. Data appear in Table 2.

a. Calculate the overall odds ratio for the study.
   \[ \frac{21}{3} \]

b. Calculate the odds ratio for smokers.
   \[ \frac{60}{4} \]

c. Calculate the odds ratio for nonsmokers.
   \[ \frac{2}{1} \]

d. Based on these data, which of the following is true of the men studied?

1. Asbestos workers who never smoked are at greater risk of dying from lung cancer than nonworkers who smoked \[ \frac{5/85}{5/23} \]
2. Asbestos workers who never smoked are at lower risk of dying from lung cancer than nonworkers who smoked
3. The odds of dying from lung cancer is increased by asbestos exposure to a greater extent in smokers than in nonsmokers \[ \frac{75/80}{5/15} \]
4. Smoking contributes independently of asbestos to the risk of dying from lung cancer.
   The increased odds of dying from lung cancer in asbestos workers as compared to nonworkers is accounted for by smoking \[ \frac{5/80}{5/15} \]

Table 2. Case-Control Study of Lung Cancer and Asbestos, Stratified by Smoking Status

<table>
<thead>
<tr>
<th></th>
<th>Stratum 1 (Smokers)</th>
<th>Stratum 2 (Nonsmokers)</th>
<th>All men in study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer +</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbestos +</td>
<td>75</td>
<td>5</td>
<td>80</td>
</tr>
<tr>
<td>Asbestos -</td>
<td>a</td>
<td>b</td>
<td>15</td>
</tr>
<tr>
<td>Lung Cancer -</td>
<td>20</td>
<td>80</td>
<td>152</td>
</tr>
</tbody>
</table>

\[ \chi^2 = \frac{ad}{bc} \]

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12. "Matching" is undertaken in a case-control study so that

1. Variables already known to influence the distribution of the disease under study are controlled for in both case and comparison groups.
2. The influence of the variables matched for may be studied.
3. The result may not be attributed to the influence of the matched variables.
4. The study results may include inferences about the influence of preselected matching variables.

13. You are interpreting the results of a randomized clinical trial testing the effectiveness of prostate specific antigen (PSA) screening for reducing mortality due to prostate cancer. Which of the following are appropriate conditions for exclusion of patients from study analyses?

1. Men who fail to comply with a pre-randomization (before random allocation) rectal exam.
2. Men who fail to comply with the PSA intervention after having been randomly allocated to study groups.
3. Men who had already had an earlier PSA test through their regular doctor before being randomly allocated to groups.
4. Men allocated to the regular care group who subsequently received PSA testing via their regular doctor.

14. Data from the Deaconess Hospital and Harvard Medical School in Boston show that since the widespread introduction of screening mammography in the mid 1970's, the mean diameter of breast tumors at the time of diagnosis has decreased markedly from approximately 3 cm to less than 2 cm. From many other studies, we know that smaller tumor size is significantly associated with improved survival. These data provide:

1. Reliable evidence of the effectiveness of screening mammography
2. Evidence of the effectiveness of screening mammography that is at a higher "level" than data from randomized trials where women may have not complied with their treatment as assigned
3. Unreliable evidence of the effectiveness of mammography because we have no data on mortality for individual patients
4. Unreliable evidence of the effectiveness of mammography because patients with smaller tumors may be different from patients with larger tumors in other ways that might affect their mortality
5. Unreliable evidence of the effectiveness of mammography because we cannot rule out a type I error.
15. In May 2001, *Cancer*, the peer-reviewed journal published by the American Cancer Society, published an article comparing breast cancer mortality in two counties in Sweden, for women 20 to 69 across three time periods: 1968 to 1977, when no screening was taking place because mammography had not been introduced; 1978 to 1987, when the two-county randomized trial of women 40-74 was taking place in the two counties; and 1988 to 1996, when all women 40-69 in the two counties were invited to screening. Breast cancer mortality in the two counties studied (total = 1863 over all years) was significantly reduced for patients actually screened between 1988 and 1996 compared to mortality in the time when no screening was available (1968 to 1977) (RR=0.37; 95% CI=0.30 to 0.46). Based on these results, we:

1. Cannot be confident that mammography screening is superior to no screening for preventing breast cancer death because the power of the study is not great enough to rule out a beta (Type II) error

2. Cannot be confident that mammography screening is superior to no screening for preventing breast cancer death because the reduction in breast cancer mortality observed in the later time period might have been lower for reasons other than mammography.

3. Can be confident that screening mammography is effective in preventing breast cancer mortality

4. Can be confident that screening mammography is not effective in preventing breast cancer mortality because p>.05.
Title: Acupuncture for the Treatment of Cocaine Addiction

Authors: Arthur Margolin, Herbert Kleber, S. Kelly Avants, Janet Konefal, Frank Gawin, Elena Stark, James Sorensen, Eleanor Midkiff, Elizabeth Wells, T. Ron Jackson, Milton Bullock, Patricia Culliton, Sharon Boles, Roger Vaughn


Cocaine addiction is a large problem in the United States. There is a lack of pharmacological agents to use for treatment, and psychological and behavioral approaches have not been entirely explored. Auricular acupuncture is one of the most widely used treatments for cocaine addiction. Previously conducted research has not lead to conclusive evidence as to whether or not this form of treatment is effective. This randomized control trial conducted over the span of three years in several cities across the United States attempts to evaluate the effectiveness of this auricular acupuncture therapy as a treatment for cocaine addiction. Knowing the answer to this questions will contribute greatly to the future direction of cocaine addiction treatment.

The primary hypothesis of the study was clearly stated and read as follows: "Compared with those in two control conditions, patients, assigned to the NADA (National Acupuncture Detoxification Association) treatment conditions would be more likely to provide negative urine screens throughout the course of the study and at follow-up and more likely to complete treatment and be retained in treatment longer."

The article addresses the following clinically relevant question: Is auricular acupuncture as prescribe by NADA more effective in treating cocaine addiction other forms of treatment among adult cocaine users in urban centers? The answer to this question would help a healthcare professional determine the best treatment option for her or his patient. The study population included males and females, and members of different races from all over the United States. It also included those with co-addictions with opiates and nicotine. The study is relevant to a large percentage of the population suffering with cocaine addiction because of the range of participants.

The study was approved by institutional review boards of all the study sites, and obtained written informed consents from all participants.

An a priori sample size was calculated at 620 participants to be randomized. This number provided the needed statistical power of >.80; alpha of .05. This sample size allowed the researchers to detect small differences (as small as .20) in treatment effect. Participants were recruited to the RCT at community-based clinics, hospital affiliated clinics, and methadone maintenance programs. In order to be eligible for the study, participants had to be 18 or older, and be diagnosed as cocaine dependent according to the SCID criteria, and must have used cocaine within the two weeks prior to recruitment. Exclusion criteria included those who were dependent on substances other than opiates and nicotine, currently receiving treatment for cocaine dependence, currently taking
benzodiazapine, other psychotropic drugs started in the last 90 days, or those currently receiving acupuncture therapy.

Participants were randomized using a computer model to three forms of treatment—auricular acupuncture (NADA approved), non-NADA sites needle insertion, and relaxation technique. This was a single-blinded study in that those assessing the results—urine sample analysts did not know which category the participant was randomized to. Because of the impossibility of the task due to difference in procedures, patients and those giving them the treatment could not be blinded. Patients in the the treatment and comparison group had similar known prognostic factors like length, amount, and frequency of cocaine use. The paper does not indicate how many people were approached and what the precise recruitment procedures were. This is a weakness in the article, and could conceal selection bias.

The experimental and control groups retained similar prognosis after the study started. There was no significant difference in the completion rate of treatment, or the length of time the participants were retained. Though there were no differences between treatment groups, there was a significant difference between completers and non-completers. It does not seem likely that information bias was introduced. Patients in the methadone maintenance program received more drug counseling as part of their methadone treatment, outside the study, than did primary cocaine users.

Outcomes to be measured were clearly defined by the study and they were cocaine use during treatment and at 3- and 6- month post-randomization follow-up based on urine toxicology screening, and retention in treatment. Cocaine was assessed by urine screening for the presence of cocaine metabolites. Cocaine use and severity of craving was also assessed by self-reporting. Retention in treatment was documented by attendance and scheduled treatment sessions and weekly administration of treatment services review (TSR), which collected self-reported information regarding attendance at treatments sessions, on site drug counseling sessions, and off-site meetings.

Statistical analysis used included the Kaplan-Meier method and log rank test, Chi squared analysis and many other analytical methods. While there was an overall modest decrease in cocaine use after treatment, there was no treatment effect, meaning the acupuncture method was not more or less effective than the other two methods. Among all three treatment arms, the number of cocaine positive urine screens declines moderately over time. (z=3.0; P=.002) and the overall OR for a negative screen was 1.40 (95%; Confidence Interval: 1.11-1.74).

The article concludes that NADA approved acupuncture treatment for cocaine addiction was not more effective than needle-insertion or relaxation control in reducing cocaine use. This study does not support the use of acupuncture as a stand-alone treatment for cocaine addiction, or in contexts where patients receive minimal concurrent psychological treatment. This answers the initial question posed by the hypothesis. These conclusions are justified given the results presented. If they had found a treatment effect, it would have been questionable given the high attrition rates. Urine samples were taken from fewer than 1/3 of those who did not complete the study, and so the small decrease in cocaine positive urine test maybe due to artifact.

The study addresses most, if not all, the clinically relevant outcomes. There does not seem to be much potential harm to this treatment method, but there seems to be a very high economic cost to these programs, that may not have any benefit at all. As a doctor, I
would not recommend NADA prescribed auricular acupuncture to my patients as treatment for cocaine. However, this study is a valuable with rigorous analysis and contributes to the literature.

This well-designed, comprehensive study is a significant contribution to the literature because it answers an important question regarding cocaine addiction. The study suggests that more research can be done regarding the contribution of acupuncture to addiction treatment when provided in an ancillary role, along with counseling and other interventions.
Epidemiology for the Practice of Medicine
BC 372
Final Quiz March 13, 2000

1. Match the situation description with the study design. Place appropriate design code in parenthesis next to situation description. Questions refer to timeline below, such that time A precedes time B which precedes time C.

**Design** | **Situation description**
---|---
1. | Investigator at time C selects study group with exposure at time A.
2. | Investigator selects study groups at time B according to disease status and asks participants about exposure at time A
3. | Investigator at time A selects study groups according to exposure status and follows them to time C
4. | Investigator assigns exposure at time A and follows participants to time C
5. | Investigator measures exposure and disease simultaneously at time C

**Design codes**
1. Prospective cohort
2. Clinical trial
3. Case-control
4. Cross-sectional
5. Retrospective cohort

![Timeline]

A  B  C

⇒ Time

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Epidemiology for the Practice of Medicine - BC 372
Final Quiz March 13, 2000 (cont’d)

2. In a clinical trial, 9 of 50 patients (18%) taking penicillin three times per day for streptococcal pharyngitis had bacteriologic treatment failures. In the group taking penicillin two times per day, 14 of 49 (28.5%) had treatment failures. A two sided t-test comparing the two groups’ treatment failures had a p-value of 0.21. What is the best conclusion (check one)?

( ) a. Twice a day therapy is better than three times a day since they are equally efficacious and twice a day therapy is cheaper and has better compliance.

( ) b. Three times a day therapy is better than twice a day but the power of the study was too small to demonstrate this result conclusively. No stat sig result. Can’t make this statement until we actually test with a large group.

( ) c. Since the p value was greater than .05, the null hypothesis of no difference between treatments cannot be rejected. It should be investigated as to whether these findings are the result of a type II error and insufficient power to detect a true difference.

( ) d. Since the p value of the study was greater than .05, the evidence indicates that doctors should be advising patients to take penicillin three times a day.

( ) e. Both b and d.

3. In a prospective cohort study of coffee and coronary heart disease (CHD), 5 cups of coffee or greater was associated with RR=1.5 (95% CI = 1.2 to 1.8). When the data were stratified by smoking status the following results were obtained:

Smokers: Non-smokers:
RR=1.1 (95% CI = 0.8 to 1.6) RR=0.8 (95% CI = 0.6 to 1.2)

These findings most likely represent an example of (check one):

( ) Confounding of smoking on the coffee to CHD relationship
( ) Random error
( ) Recall bias where smokers differentially recall coffee drinking
( ) Non-differential misclassification bias of CHD
( ) Selection bias with regard to coffee drinkers

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03/12/00
2 of 6
4. When a new treatment is developed that prevents death from an otherwise highly fatal disease, but does not produce cure from the disease, which of the following will occur (check one)?

- Prevalence of the disease will decrease
- Incidence of the disease will increase
- Prevalence of the disease will increase
- Incidence of the disease will decrease
- Incidence and prevalence of the disease will decrease

A study reported on 37 patients admitted for thyroid cancer ("cases") and 50 "controls" admitted during the same time period for treatment of pneumonia. Only the cases were interviewed, and 16 of the cases were found to have been exposed to x-ray therapy in the past, based on the interviews and medical records. The "controls" were not interviewed, but a review of medical records of their admission(s) for pneumonia revealed that only 1 "control" and been exposed to x-ray therapy in the past.

What is the odds ratio for the association between thyroid cancer and x-ray therapy (check one)?

- 71.1
- 43.3
- 37.3
- 7.1
- 5.1

Questions 6 and 7 are based on the information given below:

A school nurse routinely tests all new children ages 6-14 for strabismus (having crossed-eyes). The prevalence of this condition at this age group is approximately 5%. The nurse’s examination has a sensitivity and a specificity of 90%. She refers those who test positive to the ophthalmologist, whose examination also has a sensitivity and specificity of 90%.
Epidemiology for the Practice of Medicine - BC 372
Final Quiz March 13, 2000 (cont’d)

6. If this nurse examines 2000 children, she is going to refer to the ophthalmologist:

(   ) 100 children
(   ) 200 children
(  ) 270 children
(   ) 1720 children
(   ) None of the above

7. The predictive value of a positive test by the nurse is:

(   ) 0.6%
(   ) 10%
(   ) 32%
(   ) 90%
(   ) None of the above

---

K-Type questions

Key

\( a \quad b \quad c \quad d \quad e \)

\[ 1, 2, 3 \quad 1 \text{ and } 3 \quad 2 \text{ and } 4 \quad \text{only } 4 \quad \text{all } 4 \]
are correct \quad are correct \quad are correct \quad is correct \quad are correct

---

Question 8 is based on the information given below.

Comparison of mortality rates due to cancer of the uterus in users and non-users of supplemental estrogen revealed:

Mortality rates (per 100,000)

<table>
<thead>
<tr>
<th></th>
<th>Aged 40-54</th>
<th>Aged 55-70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Users of estrogen</td>
<td>3.0</td>
<td>17.0</td>
</tr>
<tr>
<td>Non-users</td>
<td>1.0</td>
<td>6.0</td>
</tr>
</tbody>
</table>
8. Valid conclusions derived from the above data concerning mortality among estrogen users include (write your response, which should be a letter from the K-type questions key above, in the space provided):  

1. The mortality rates for cancer of the uterus are higher in estrogen users than in non-users in both age groups studied

2. A causal relationship is demonstrated between the use of estrogen and incidence of uterine cancer

3. Mortality from cancer of the uterus rises with age regardless of whether or not estrogen is used

4. The mortality rate is lower in non-users than users because the symptoms of uterine cancer are detected earlier in the former group of women

**Question 9 is based on the information given below.**

The following table shows the relationship between initial serum cholesterol levels and risk of coronary artery disease by age and sex in the Framingham study (first 12 years):

<table>
<thead>
<tr>
<th>Cholesterol (mg%)</th>
<th>Incidence rates for coronary artery disease per 1,000 persons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men 30-49</td>
</tr>
<tr>
<td>&lt;190</td>
<td>38</td>
</tr>
<tr>
<td>190-219</td>
<td>44</td>
</tr>
<tr>
<td>220-249</td>
<td>95</td>
</tr>
<tr>
<td>&gt;250</td>
<td>157</td>
</tr>
</tbody>
</table>
9. Which of the following statement(s) is/are correct (write in your response, which should be a letter from the K-type questions key above, in the space provided)?

1. The risk of coronary artery disease is associated with increasing cholesterol levels in men and women, ages 30-49.

2. The risk of coronary artery disease is associated with increasing age at all cholesterol levels in men.

3. Within a given age group men have a higher risk of coronary artery disease than women at each cholesterol level.

4. At a cholesterol level of 220-249 mg%, the relative risk of coronary artery disease for older women compared to younger women is less than the relative risk for older men compared to younger men.

\[ \text{older women have a higher relative risk} \]