

Figure 9.19. EXPERIMENTAL PLANS: An Example from Breast Cancer Research

EM8701: Kitchener-Waterloo Record, January 10, 1987, page C4

Link between high-fat diet, breast cancer sought

TORONTO (CP) – At least two Canadian cancer research centres are considering taking part in an expensive and ambitious study to determine whether a high-fat diet increases the incidence of breast cancer.

British Columbia's Cancer Control Agency will apply to enroll about 2,000 women in the study by U.S. researchers, and Toronto's Princess Margaret Hospital is in the process of deciding whether to take part.

Dr. Ross Prentice, associate director of the Fred Hutchinson Cancer Research Center in Seattle and the study's principal investigator, was in Ottawa Thursday to talk to federal Health and Welfare officials about the project.

The 30,000 women who will participate will be followed for between seven and 10 years to see whether cutting down on fats reduces the incidence of breast cancer.

It is estimated that one in 14 North American women will contract breast cancer and evidence suggests that diet plays a role in promoting the disease.

Prentice is recruiting women between 45 and 69 – when breast cancer most commonly strikes – who are at increased risk because of family history, who gave birth for the first time after 30, or who have had two or more benign breast tumours.

To enter the study, women must show a diet high in fats. About 40 per cent of their food intake must be fats from sources including red meat, dairy products and desserts.

The women will be divided into two groups: 60 per cent of them will maintain their normal fat consumption and the rest will be required to reduce their fat intake by half. A particular target will be

saturated fats such as butter and some margarines.

The two groups will receive nutrition counselling and regular mammograms during the course of the study.

"The average North American diet is 40 per cent fat and international studies suggest that if that amount can be reduced to 20 per cent, we may be able to cut the incidence of breast cancer by half," Prentice said.

Studies of Polish and Japanese women, who have low rates of breast cancer in their native countries, show that when they immigrate to North America and adapt to its high-fat diet, their incidence of breast cancer increases quickly.

"Diet seems like a logical place to look," Prentice said.

He said the goal of the study "is not to reduce calories. It won't be necessary to go around hungry all day or prepare meals differently for the rest of a family."

So far, clinics in Seattle, Houston and Cincinnati have agreed to take part in the \$100-million study, which is sponsored by the National Cancer Institute.

There have been several U.S. breast-cancer studies in which the diets of women were monitored but not changed and these have yielded mixed results.

The most recent study, done by researchers at Harvard University and described this month in *The New England Journal of Medicine*, found no link between dietary fat and incidence of the disease.

Dr. Kenneth Carroll, professor of biochemistry at the University of Western Ontario in London, has been studying diet and breast cancer in rats since the late 1960s.

REFERENCE: Willett, W.C., Stampfer, M.J., Colditz, G.A., Rosner, B.A., Hennekens, C.H. and F.E. Speizer: Dietary Fat and the Risk of Breast Cancer. *New Engl. J. Med.* **316**(#1): 22-28 (1987). [DC Library call number: PER R11.B7]

- 1 Identify the matter(s) mentioned in the article which are components of an adequate Plan for such an investigation.
- 2 Identify matter(s) *not* explicitly mentioned in the article which are components of an adequate Plan for such an investigation.
 - For each missing component you identify, indicate whether it would be practicable to incorporate it into this investigation; give reason(s) in each case.
- 3 Explain why it was necessary to carry out this investigation using an *experimental* Plan rather than an *observational* Plan.
 - Would there be any *advantages* of an observational Plan in this context? Explain briefly.
- 4 Do you know, or can you suggest, the type(s) of evidence that has led to the hypothesis of a link between level of dietary fat and the incidence of breast cancer?
 - What is the weakness(es) of the existing evidence for such a link?
 - Why is breast cancer a matter of appreciable concern to medical research?
- 5 Some time after this article appeared, the U.S. National Cancer Institute decided *not* to go ahead with this investigation; suggest possible reasons for this decision.
- 6 The last paragraph of the article mentions the use of laboratory rats to investigate diet and breast cancer. For investigating diseases like human cancers:
 - what are the *advantage(s)* of using laboratory rats or other animals?
 - what are the *disadvantage(s)* of using laboratory rats or other animals?

The article reprinted below contains information relevant to the articles reprinted in Figures 9.18 and 9.16.

EM9035: The Globe and Mail, November 10, 1990, page D4

Spine-chilling to look at: another stat

IT is too late this year, but when Halloween rolls around again, I recommend that kids think about dressing up as something that really frightens adults: Statistics. Whooo – BELL CURVES. Whooo – DELTA FUNCTION.

The fact is that the misunderstanding of statistics continually guts grownups. We get led around by the nose and don't sense the "yeah, but what about these things" questions.

In this column, I am going to lead you through a couple of examples of statistical hamstringing and then pose a modest solution. Last week, speakers at a conference on gender bias in science attacked a 1988 study in the United States in which 20,000 men were tested to try to determine the effect that a small daily dosage of the active component in aspirin had on heart attacks.

The background document described it as a perfect example of how women are mindlessly excluded from biological testing – a situation that created the anomaly that "doctors could recommend the treatment for men and not for women." Not exactly right.

The first thing to understand was the sample. The "men" involved were in fact U.S. doctors. They were considered to be particularly good candidates because they were likely to take their daily medication and because they paid attention to their health. In 1983, when the mailings went out, there were approximately 450,000 registered male doctors to sample.

Because the incidence of heart disease rises with age, only the 261,248 men between 40 and 84 were contacted. Of those, 59,280 said they would participate. Adverse medical problems and a lack of real commitment reduced this to 22,071 men.

They were divided into two groups, one taking the aspirin and the other a placebo. At the end of a year, of all the non-fatal heart attacks that occurred in the two groups during that time, a third of those were suffered by

SCIENCE

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aspirin-takers. Moreover, there were five heart attack deaths in that group compared with 18 in the control (placebo) group. It was, as they say, statistically significant.

However, if one were to get about the same answer in women, a sampling problem arose. Not only do women have half as many heart attacks percentage-wise and have them later than men but there were only roughly 70,000 women doctors in the United States.

No more than 28,000 of them met the age requirements. Assuming the same kind of patterns of response and health discrimination, more or less, 2,400 women doctors would have qualified. In a given year, on average, only two or three of them might have died from heart attacks. Obviously, this is too few for statistical significance.

Well, you say, maybe a different and larger group of women could have been sampled. That makes sense until one looks at the outcome of the supposedly sexist study. Yes, indeed aspirin did seem to reduce the number of heart attacks, but when the total number of deaths from cardiovascular disease was looked at – oh, statistical horror of horrors – the control group and the aspirin group both produced EXACTLY THE SAME number – 44.

The sadder-but-wiser statisticians concluded that even 22,000 male doctors weren't going to be a large enough group to prove conclusively that aspirin reduced heart attacks, at least when death was the criterion.

The second statistical boomerang involves the risk of AIDS to women. On October 19, a Toronto AIDS conference was told that women were "the fastest growing AIDS risk group" and women were the "last to accept

they are at risk."

Evidence was presented suggesting 50 per cent of the women who are infected with AIDS through heterosexual intercourse. A breakout of AIDS among heterosexual women is something I have been closely looking for but just couldn't remember seeing. Therefore, I went to my collection of statistics produced by the Federal Centre for AIDS, and teased out the root of the misinformation. It was true that on Oct. 1, 1990, 127 out of 227 women with AIDS in Canada had gotten the disease heterosexually. However, nearly two-thirds (83) of these women were in a special risk sub-group. They were either Haitians or the wives and girl friends of Haitian men.

They were special, because, for some reason, AIDS is easily passed back and forth between men and women in Africa and the Caribbean but not in temperate climates. The best guess is that other untreated venereal diseases, different sex practices, fewer circumcisions and more penile and vaginal sores vastly increase the AIDS risks from heterosexual sex in the tropics.

What this all means is that in Canada since 1981 when the first cases of sexually transmitted AIDS were reported in women, only 44 non-Haitian-linked cases have appeared. Is even that rate increasing? Let the figures speak. In 1987, 25 women – Haitian connection and all – contracted AIDS through heterosexual intercourse. There were 28 in 1988 and 23 in 1989, although final numbers are not in.

Finally, though it will undoubtedly turn out to be a statistical fluke, of the 254 gender-classified cases of AIDS reported in 1990 so far, none, let me repeat, NONE of them has been in women through heterosexual intercourse. The moral of all this is: before giving algebra, geometry, calculus and trigonometry, Canadian schools should teach their students how to navigate the shoal-filled mathematics of everyday life.

As Ian Fleming might have put it: Statistics is forever.

- 1 What sample selecting method was used to obtain the 22,000 male U.S. doctors? Identify explicitly the place(s) in the article from which you take your information.
 - Outline how this selecting method affects the *precision* of the Answers(s) from the investigation.
- 2 Explain, in non-technical language, the meaning of the last statement in the third paragraph of the second column: *this is too few for statistical significance*.