



Case Control Study

Step 1: Learning Objectives

- A. Apply the principles of case-control studies:
 - 1. Formulate research hypotheses
 - 2. Define population at risk for disease
 - 3. Define eligibility criteria for cases and controls
 - 4. Describe methods of accrual of cases and controls
 - 5. Define exposure
 - A. Timing and measurement
 - 6. Define outcome
 - A. Ascertainment of outcome
- B. Employ steps in data analysis of case-control studies to analyze the data:
 - 1. Administrative procedures before start of the study
 - 2. Calculate disease odds ratio
 - A. Interpret your estimate
 - 3. Calculate exposure odds ratio
 - A. Interpret your estimate
- C. Explain your findings and discuss problems in data analysis:
 - 1. Explain how the size of the odds ratio influences your conclusions about the association between exposure and outcome
 - 2. Give your suggestions for carrying out this case-control study
 - 3. Discuss the importance of defining the underlying population for selection of cases and controls
 - 4. Discuss the importance of exchangeability of cases and controls
 - 5. Explain why exposure odds ratio is identical to the disease odds ratio
 - 6. Discuss the relationship between odds ratio and relative risk
 - 7. Discuss the value of statistical data analysis in reaching conclusions about causality of the exposure-outcome relationship

Step 2: Introduction to the Study

Susser Syndrome, a rare and debilitating neurological disease, is striking the People of Epiville!

You have just begun your internship at the Epiville Department of Health and your supervisor has been called in to investigate the possible causes of the sudden increase in Susser Syndrome cases. After careful thought, she wants you to lead the investigation and report to her continuously. Armed with your trusty Gordis textbook and your love of epidemiology, you decide upon a plan of action.

Step 3: Student Role - Your Plan of Action

You need to gather the following background information found on the various web pages.

- [the Epiville Chamber of Commerce web site](#)
- Information about [Superfit Fitness Center](#)
- Information about [Glop industries](#)
- Information about [Susser Syndrome at the Epiville Department of Health Web Page](#)

Listen to the WEPI1 which provides background to your investigation (text of the newscast is also available). Based on your own research and the newscast, you decide to investigate both the Superfit Fitness Center and Glop Industries.

Interview Transcript

Reporter

"Good evening. I am Lyle Regression and you are watching WEPI Channel 1 news. From our Health and Medicine Desk - doctors at the Epiville General Hospital report a dramatic rise in the number of patients suffering from Susser Syndrome, a rare and debilitating neurological disease characterized by dizziness, double-vision, fainting spells, and difficulty in concentration. Susser Syndrome was first characterized over a century ago in South Africa and came to prominence during an apparent outbreak in London immediately following World War 1 although the cause of the disease was never discovered. Up until this point, it has been seen very sporadically and in very few numbers throughout the United States.

We spoke with hospital officials who report a steady rise in new cases over the past two years with a rather dramatic upswing since March of this year. The cause of this increase is unknown and, because of its rarity, Susser Syndrome has been poorly characterized. Medical experts do believe that its occurrence may be linked to a possible environmental exposure.

The Epiville Health Department is aware of these new cases of Susser Syndrome and will investigate the matter fully. A team of public health officials consisting of medical epidemiologists, biostatisticians, and research assistants is being assembled to determine if there is in fact an increase in Susser Syndrome cases, the cause of this increase, and preventative measures that can be taken.

Doctors warn that all residents of Epiville may be at risk for developing the disease. However, Channel 1 has exclusively discovered that a significant number of diagnosed individuals are members of the Superfit Fitness Center, located in the Epiville industrial park. Superfit is owned and operated by Superclean Industries. When asked about this information, representatives from Superclean had no comment.

Hospital officials warn that those suffering from dizziness, double-vision, and fainting spells should immediately seek medical attention in the hospital emergency room. Stay tuned as Channel 1 News continues to investigate this Susser Syndrome outbreak. If you would like to obtain more information on the situation, go to Epiville's home page."

You enter the Superfit Fitness Center, flash the powerful Epiville Department of Health Identification Card (being sure to cover the word "intern" with your thumb), and ask to speak with the manager. You are immediately greeted by Mr. Abe Crunch who is very responsive to your questions.

Interview Transcript

Fitness Instructor

"I've been the manager here at Superfit since we opened. As you probably know, Superfit is actually owned by Superclean Industries. As you can see, we have nothing but state of the art facilities, state of the art equipment, and all of our trainers are certified. Frankly, this place is awesome. We even have a gift shop! Superclean Industries has a licensing agreement with Glop Industries and as a result we only carry products manufactured by Glop. In fact, we carry some things that you can't even get outside of here. For example, all of our members exclusively drink the sports drink Quench-It and eat the energy bar Endurobrick - those two products cannot be found anywhere else in retail stores. And rather than have them walking around with money while they're working the free weights, we issue each member a fitness credit card they use to keep track of their food and drink and other purchases. At the end of the day, we can see exactly how much Quench-it someone drank or EnduroBrick they ate and bill their account accordingly. The tap water is of course free. As for a number of members being sick, well, the only thing I can say is we all get sick from time to time. I mean, who hasn't been sick? You get sick, I get sick...actually, I don't get sick. But that's because I'm in perfect shape."

You gain access to Glop Industries (that ID Card sure comes in handy) and you meet with the production floor foreman, Mr. Hank Lockjaw.

Interview Transcript

Foreman

"My grand-daddy was a Glop man, my daddy was a Glop man, and I've been a Glop man my whole life. I was promoted to foreman a few years back, just before we started making Superclean. Anyway, behind you there is the production line of Quench-it. Those plastic bottles shoot down the conveyer belt and then are filled up with the drink. The hard part is keeping the bottles nice and clean. Just last week we installed a brand new sterilization system. Back in 2000 we used to rinse the empty the bottles with Superclean to sterilize them before adding Quench-it – before that we just used hot water. Now, we only use this gamma radiation trick to sterilize the bottles. I don't much understand it but it's supposed to be more efficient and cheaper in the long run than using the Superclean. Like I said, we only switched last week so time will tell. Let's see...over in the other corner is the Endurobrick line. It's a secret recipe, you know. Anyway, the bars ride on the conveyer belt through that big oven which serves to not only bake them but sterilize them as well. That oven is pretty old but she still purrs like a kitten. My job is to make sure everything runs nice and smooth and I'll tell you, there's been not a

single breakdown on my watch."

Questions in Steps 3 and 4 require you to demonstrate your knowledge of epidemiological terminology and concepts, including study design and data collection. In **Step 5 Data Analysis** you will perform calculations of the measures of effect and explain your findings. Select what you think is the best answer for each question. At the same time, read carefully through the explanations of both correct and incorrect answers. Finally, answer the discussion questions in Step 6 found at the end of the exercise. Bring your answers to your seminar section and be prepared to discuss them in class. Please proceed to Step 3. Good luck and have fun!

Step 4: Study Design

Thanks to all of the legwork, you now have enough information to generate a solid hypothesis or two. You report back to your supervisor and you both agree Quench-it and EnduroBrick are likely causes. You decide to design a case-control study so that you may look at these exposure variables. From all of your class work, you know that you want your hypotheses to be as explicit and detailed as possible.

Now you must decide upon who will be eligible for the study. You must determine the

1. Based on the above information, which of the following three hypotheses are the best to investigate in this case-control study?

- ☒ a. Individuals diagnosed with Susser Syndrome are more likely to have ingested Endurobrick than individuals without Susser Syndrome; individuals diagnosed with Susser Syndrome are more likely to have consumed Quench-it than individuals without Susser Syndrome.
- ☐ b. Those who ingest Endurobrick are more likely to be diagnosed with Susser Syndrome than those who do not ingest Endurobrick; those who consume Quench-it are more likely to be diagnosed with Susser Syndrome than those who do not consumer Quench-it.
- ☐ c. Individuals diagnosed with Susser Syndrome are more likely to have been members of Superfit Fitness Center than individuals without Susser Syndrome.

Correct

These clearly reflect our case-control design in which we begin with the disease status - cases and controls - and compare their exposure status.

Incorrect

These hypotheses are indicative of a cohort study design in which we begin with an exposure of interest and the endpoint is the disease outcome.

Incorrect

This hypothesis is not specific enough; we want to explore more precise exposure variables.

eligibility criteria for both your cases and controls. Remember, we are actually operating under 2 hypotheses here, each with their own unique exposure variable. Eligibility criteria should be as specific as possible in order to minimize the chance of spurious findings. You decide to start with defining the eligibility criteria for the cases.

After talking with medical experts, you believe that the physiological changes associated with Susser Syndrome take at least 6 months to develop. In other words, a period of at least 6 months needs to pass from the moment an individual is possibly exposed until the first symptoms of Susser Syndrome can plausibly occur. This, you recall, is termed the induction time.

For The Intellectually Curious

Two primary explanations exist to explain induction time. The suspected exposure may need to accumulate to a certain level and other factors have to be present before the disease can occur. This accumulation takes time. Alternatively, the suspected exposure may be the first event in a series of causal events that need to occur for the disease to develop. This sequence of events takes time. For example, we may believe that Susser Syndrome is the result of a) exposure of a certain susceptible individual to a necessary accumulation of manufacturing chemicals which leads to b)a genetic mutation which leads to c)a decrease in the production of a certain

neurotransmitter. Thus, Susser Syndrome cannot occur until a susceptible individual is exposed to enough chemical which triggers the casual sequence of events leading to disease. This process may take months or even years. Individual susceptibility varies based on specific biological/ physiological factors.

The exact process leading to Susser Syndrome is poorly understood. However, based on expert opinion, you are assuming a minimal induction period of 6 months for the primary environmental exposure. Therefore, exposure to either Endurobrick or Quench-it of less than 6 months is not sufficient to cause Susser Syndrome.

2. Which of the following do you think is the best eligibility criteria for the cases? [Gordis Ch.9, pg 143;Ch 12, pg 180-183]

- ☐ a. Cases should have been members of Superfit between September 2000 and September 2002 for at least 6 months and consumed either Endurobrick or Quench-it.

Incorrect

It may seem obvious but it is important to state that cases need to have been correctly diagnosed with Susser Syndrome; additionally, we are interested in determining the exposure status and thus should not require that they have been exposed.

- ☐ b. Cases should be correctly diagnosed with Susser Syndrome and be an employee of Glop Industries.

Incorrect

We are interested in possible exposures at Superfit Fitness Center and not at Glop Industries.

- ☒ c. Cases should be correctly diagnosed with Susser Syndrome and have been members of the Superfit Fitness Center for at least 6 months between September 2000 and September 2002.

Correct

We want our eligibility criteria to be as specific as possible; it is crucial to incorporate time elements in our study to ensure that our exposures of interest could be plausibly associated with the development of Susser Syndrome if our analysis statistically indicates an association.

Now you must decide who is eligible to be a control. The eligibility of controls is dependent on their "exchangeability" with cases. Controls should have the same opportunity of having been exposed and of developing the disease as cases, i.e., if they switched places with cases, they would have similar experiences. A control should come from the same underlying population as a case.

3. With this in mind, which of the following do you think is the best eligibility criteria for the controls? [Gordis Ch 9, pg 143-146]

- ☐ a. Controls should be residents of

Incorrect

	Epiville who have not been diagnosed with Susser Syndrome.	We would violate exchangeability as our fitness center cases would be more healthy than the general population controls; additionally, our cases would probably have greater opportunity of having been exposed than our controls due to the arrangement at the club.
<input type="checkbox"/>	b. Controls should be members of Superfit who have been diagnosed with Susser Syndrome but have not consumed either Endurobrick or Quench-it.	Incorrect Most importantly, controls should not be diagnosed with Susser Syndrome; additionally, we are interested in the exposure variables and thus should not place any requirements concerning the ingestion or consumption of Endurobrick and Quench-it.
<input checked="" type="checkbox"/>	c. Controls should be members of Superfit for at least 6 months between September 2000 and September 2002 and not be diagnosed with Susser Syndrome.	Correct An important point is that controls should be able to become cases if they develop Susser Syndrome; in other words, controls should meet the eligibility requirements of cases but for their disease status

Now that the eligibility criteria are set, you must determine the specifics of the case-control study design. How many cases should you recruit; how many controls; should you recruit all of your cases first and then your controls or should you recruit them simultaneously? All of these questions make your head hurt and you decide to take a nap.

Upon awakening 15 minutes later (remember, you've got a job to do!), you have a sudden and prolific brainstorm - some might say epiphany - and the answers to these questions are now clear. You go through them one by one:

How many cases and controls?

That obviously depends on your time and resources. However, an equally important consideration is how much power you want the study to have.

For The Intellectually Curious

Put simply, a study's power is the probability that you will correctly accept the alternative hypothesis when in fact the alternative hypothesis is true (or put in another way, power is the probability of obtaining a statistically significant result when the alternative hypothesis is true). This is a measure which is appropriate before the start of a study, but should not be considered after a study is completed when the p-value or confidence interval gives the more appropriate guide to the significance of the findings and to the possible contribution of random error.

The power of a study can be calculated and is dependent on a number of variables, including the type 1 error level (α), the type 2 error level (β), the proportion of the controls exposed (P_0), the ratio of controls to cases (R), the prevalence of disease in the underlying population, and the magnitude of the measure of association we are trying to estimate. The P_0 is fixed and depends on the underlying population and whether or not it was properly sampled. We can set R based on our resources and desired study efficiency. Finally, we can set the magnitude of the measure of association we are trying to estimate based on the literature describing Susser Syndrome. As epidemiologists, we prefer to draw conclusions of measures of association (e.g. OR) greater than or equal to 2.0. The larger we set this magnitude, the smaller our study size can be for a given power value; conversely, the smaller we set this magnitude, the larger our study size needs to be for a given power value.

This makes sense - for small magnitudes we are predicting that the cases and controls are similar and thus to see a subtle difference between the two groups we would need a large sample. Conventionally, we want a study's power to be at least 80 percent in being able to find a significant difference between the groups. If the study has less than 80 percent, we conclude that the study is underpowered. This does not mean our results are incorrect; rather we cannot draw any definitive conclusions about associations between cases and controls.

After crunching the numbers, you decide that the study should have the following size to achieve a desired power of 80 percent:

Number of cases: 112
Number of controls: 224
Total number of subjects (N): 336

One thing you want to remember is that the study is voluntary. This means that subjects, even when eligible, do not have to participate. You do a quick literature review and discover that study participation is never 100 percent and depends in large part on the survey method. In-person recruitment is the best, followed by telephone interviews, and then mail surveys. Case participation rates are almost always greater than controls. With this in mind, you realize you will have to contact and screen a significantly larger number of subjects as many will either not meet the eligibility requirements or will decide not to participate.

Should you recruit cases and controls simultaneously or an entire group first?

A number of sampling techniques come to mind, such as recruiting all of the controls at the beginning of the study, recruiting all of the controls following the accrual of all the cases, or recruiting each control at each time a case is ascertained. Each method has its pros and cons. Some are logistically more difficult and expensive but will allow you to better estimate the rate ratio or the risk ratio. Others are easier and more efficient but require important assumptions to estimate particular measures of association. After weighing all of the many factors, you decided to employ a method that epidemiologists term cumulative incidence sampling in which you select all of your controls after you have already selected all of your cases.

Now that you have the size of your study established and the basic method of recruitment, you need to start planning the actual data collection stage.

Step 5: Data Collection

With the design of the case-control study complete, you now begin planning the protocol for data collection.

4. What is the best source for gathering information on the disease (case) status? [See Gordis, Ch.3, pg. 35-36]



- a. diagnosis of Susser Syndrome identified from the hospital charts of the local hospital and based on the neurology consultation and supported by lab results.

Correct

We will not miss any cases as all subjects with the disorder will end up at the local hospital and all cases will be valid.



- b. complaints of neurological symptoms identified from the records of Superfit staff nurse

Incorrect

We might miss persons with the syndrome who never saw the staff nurse and might include persons whose symptoms are not actually full-blown Susser Syndrome.



- c. complaints of neurological symptoms based on information provided by Superfit Membership Directory Office about medical leaves of absence of club members

Incorrect

We might miss persons with the syndrome who never saw the staff nurse and might include persons whose symptoms are not actually full-blown Susser Syndrome.

5. From where should the disease status data be collected? [See Gordis, Ch.3, pg. 31-38]



- a. look through the records of the local hospital dated from September, 2000 to September, 2002 to identify those with the disorder and see if there is information in the chart about their membership to Superfit

Incorrect

Although plausible, this is not the best choice because subjects who had already terminated their club membership as a result of the illness would be missed.



- b. link a computer database containing the names of Superfit

Correct

Modern linkage techniques allow us to

members with the discharge database from the local hospital

identify approximately 95% of people based on their name and birth date. Because the local hospital treats all potential cases, the only cases you are likely to miss are those who moved out of the area before treatment or those patients discharged after the study end date.

You decide that cases will be recruited using the hospital discharge data cross-referenced with a membership directory provided by the Superfit Fitness Center. Cases meeting the eligibility criteria will then be telephoned and asked to participate.

6. What is the best way to accrue the controls? [See Gordis, Ch.9, pg 143-148]

- ☐ a. Using hospital discharge data, you will find subjects with a diagnosis of anything but Susser Syndrome. These subjects will then be cross-referenced with the Superfit membership directory and contacted via the telephone.

Incorrect

This method would be inefficient and time consuming as the majority of Superfit members would not be admitted to the hospital; additionally, the sole inclusion of controls with some sort of disease outcome may introduce potential bias.

- ☒ b. You will take a random sample from the complete list of all members listed in the Superfit directory and determine their eligibility criteria. Those eligible will be asked to participate by phone. If they agree to participate, an interview will be scheduled.

Correct

Because of the membership at the club, these controls will be exchangeable with the cases. Additionally, their selection must be random to insure that they are representative of the entire eligible population.

You must also decide how you will assess the exposure variable in this case-control study. The exposure variables of interest are the ingestion of Quench-it or the consumption of Endurobrick.

7. Given the study design, what is the best way to assess the exposure variable? [See Gordis, Ch.3, pg. 37; Ch.18, pg. 283-285]

- ☐ a. Directly observe the ingestion or consumption of Endurobrick and Quench-it at Superfit.

Incorrect

This is a case-control study and the exposure has already occurred - you're a very good Department of Health intern but you cannot time-travel.

<input type="checkbox"/>	b. Find and test for a biological marker, such as gut enzyme level, that would serve as a surrogate exposure variable, indicating the ingestion or consumption of Endurobrick and Quench-it.	<p>Incorrect</p> <p>Given the exposure variables, it seems highly implausible that a marker could even be identified; furthermore, this type of testing dramatically increases the time and cost of the study; finally, the sensitivity and specificity of such a test would be questionable.</p>
<input type="checkbox"/>	c. Question all of the subjects as to their own assessment of Endurobrick and Quench-it intake using a standardized survey tool.	<p>Incorrect</p> <p>This is commonly employed and it is probably the fastest and cheapest method; however, it is subject to recall bias as individuals may incorrectly remember the amounts they consumed, especially over a 2 year period, which can lead to spurious findings. A better method exists for this particular study.</p>
<input checked="" type="checkbox"/>	d. Use the tally employed by the fitness center credit card to bill the members for their consumption of Endurobrick and Quench-it.	<p>Correct</p> <p>This will provide the most accurate assessment. Furthermore, the two products are not available in retail stores and thus there is no possibility of subjects consuming more than is recorded by the fitness center.</p>

Your supervisor reads over your recommendations and agrees with your suggestions. Before the study can begin and the data can be collected, however, your supervisor instructs you of all the administrative work that must be in order. You must:

1. Get approval of your study from your Institutional Review Board (IRB) - this will ensure that the study adheres to the ethical principles of conducting public health research and that the rights of study participants are protected.
2. Prepare a budget and get funding.
3. Develop an operations manual to be used by all study personnel which will describe the standardized procedures for collecting data, managing data, etc. This is used to ensure quality control.
4. Design a consent form for study participants - it should clearly indicate your goals; it should also explain risks, benefits and expenses that participants might incur if they decide to participate in your study; it should also state how participants would benefit from their participation and how you plan to make use of the data once it is collected.
5. Design a questionnaire that will be used to collect data from the study participants.
6. Hire and train interviewers.

7. Design a data management plan (how and where paper forms will be stored, when and how they will be entered into computer database, when periodical checks of the data will be performed to spot possible problems in the study).
8. Design data analysis plan and think about publicizing your findings.

Having received the necessary IRB approval, the study starts. The data begin to file back to the Department of Health and must now be collated and carefully entered into the computer database. Despite your leadership role, you are still the intern and thus have the inglorious yet crucial responsibility of data entry. Once all of the data are entered, you can proceed to the analysis stage where the associations stated in your 2 hypotheses are characterized and tested.

Step 6: Data Analysis

The data collected yield the following counts:

Total number of Cases: **112**

Total number of Controls: **224**

Number of Cases who ingested Endurobrick: **28**

Number of Controls who ingested Endurobrick: **56**

Number of Cases who consumed Quench-it: **50**

Number of Controls who consumed Quench-it: **56**

You decide to test the hypothesis that cases are more likely to have ingested Endurobrick than controls. [See Gordis, pgs. 162-168]

8. How would you set up the classic 2x2 table using the above information to test this hypothesis?

	Case	Control	Total
Exposed (Endurobrick)	28	56	
Unexposed (No Endurobrick)	84	168	
Total	112	124	336

a. Calculate the odds of exposure among cases:	Odds E Cases = $28/84 = 0.333$
b. Calculate the odds of exposure among controls:	Odds E Cases = $56/168 = 0.333$
c. Calculate the exposure Odds Ratio (OR)	OR = Odds E Cases / Odds E Controls = $(28/84)/(56/168) = 1.0$
d. Calculate the odds of Susser Syndrome among the exposed:	Odds SS Exposed = $28/56 = .500$
e. Calculate the odds of Susser Syndrome among the unexposed:	Odds SS Unexposed = $84/168 = .500$
f. Calculate the disease Odds Ratio:	OR = Odds SS Exposed / Odds SS Unexposed = $(28/56)/(84/168) = 1.0$
g. Interpret your findings:	Individuals with Susser Syndrome have the same odds of having ingested Endurobrick as those without Susser Syndrome. Conversely, individuals who eat Endurobrick have the same odds of developing Susser Syndrome as those who do not eat Endurobrick. The OR=1 and thus there does not appear to be an association between Susser Syndrome and Endurobrick ingestion.

You now decide to test the hypothesis that cases are more likely to have consumed Quench-it than controls.

9. How would you set up the classic 2x2 table using the above information to test this hypothesis?

	Case	Control	Total
Exposed (Quench-It)	50	56	
Unexposed (No Quench-It)	62	168	

Total	112	224	336
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- a. Calculate the odds of exposure among cases: $50/62 = 0.806$
- b. Calculate the odds of exposure among controls: $\text{Odds } E|\text{Controls} = 56/168 = 0.333$
- c. Calculate the exposure Odds Ratio (OR) $\text{OR} = \text{Odds } E|\text{Cases} / \text{Odds } E|\text{Controls} = (50/62)/(56/168) = 2.4$
- d. Calculate the odds of Susser Syndrome among the exposed: $\text{Odds } SS|\text{Exposed} = 50/56 = 0.893$
- e. Calculate the odds of Susser Syndrome among the unexposed: $\text{Odds } SS|\text{Unexposed} = 62/168 = 0.369$
- f. Calculate the disease Odds Ratio: $\text{OR} = \text{Odds } SS|\text{Exposed} / \text{Odds } SS|\text{Unexposed} = (50/56)/(62/168) = 2.4$
- g. Interpret your findings: Individuals with Susser Syndrome have a 2.4 times higher odds of having consumed Quench-it than those without Susser Syndrome. Conversely, individuals who drink Quench-it have a 2.4 times higher odds of developing Susser Syndrome than those who do not eat Endurobrick. The OR = 2.4 and thus there does appear to be an association between Susser Syndrome and Quench-it consumption.

10. You wipe the sweat from your analytical brow and present your findings to your supervisor. What should you tell her?

- ☐ a. It looks as though we've ruled out both Endurobrick and Quench-it as possible exposures. In my opinion, neither appears to be related Susser Syndrome development. **Incorrect**
The one elevated OR supports the hypothesis that Quench-it consumption is associated with Susser Syndrome development.

- ☐ b. The data regarding both Endurobrick ingestion and Quench-it consumption are totally inconclusive. I think we should repeat the study with more participants.

Incorrect

The OR of 2,4 is not inconclusive and suggests an association between Susser Syndrome and Quench-it consumption. The OR of 1.0 is an actual finding and, rather than being inconclusive, it suggests no association between Susser Syndrome and Endurobrick ingestion.

- ☐ c. While ingestion of Endurobrick does not cause Susser Syndrome, the data do indicate that consumption of Quench-it does cause Susser Syndrome.

Incorrect

You must not confuse association with causation. The data suggest that Quench-it is associated with Susser Syndrome development whereas Endurobrick is not. However, as detailed in Gordis, to move from association to causation requires a substantial amount of epidemiological evidence as well as biological plausibility. At this stage in the investigation, we are far from having enough.

- ☒ d. The data clearly suggest that the consumption of Quench-it is associated with later development of Susser Syndrome whereas the ingestion of Endurobrick does not appear to be associated with Susser Syndrome. I think we might want to explore other potential exposure sources to be sure as well as to further characterize this association.

Correct

The data do suggest that Quench-it is associated and Endurobrick is not; however, we need to check the statistical significance of these findings as they may be due to chance. Furthermore, it is important to rule out other potential exposures that may confound the findings.

After reporting your results, you decided to do a little bit more detective work. You head over to the Public Health Laboratory records department and check the log file on Quench-it. Since its production, the Health and Food Safety Inspector has taken random samplings of Quench-it back to the lab to analyze it for any possible contamination. This is normal surveillance procedure. Looking the file you notice something interesting: during the time period between 2000 and 2002, a significant amount of Superclean was found in Quench-it, probably, you recall, a result of the old sterilization process. After 2002 when Glop Industries changed techniques, Quench-it was completely free of Superclean. Realizing the importance of this finding, you immediately report back to your supervisor.

Step 7: Seminar Discussion Questions

Carefully consider the following questions related to your work above. Write down your answers and be prepared to discuss them in seminar.

1. What are some of the advantages and limitations of doing a case-control study?
2. What would you have done differently in the design of this study?
3. Why is the selection of controls important? How else might you have selected controls?
4. Explain what is meant by "violation of exchangeability" and give examples?
5. What are the limitations of using surveys to assess exposure status in study subjects? What kind of bias is this? How might it affect our findings? Does our study design limit or avoid this bias?
6. What do your findings in question 10c and f and 11c and f tell you about the Odds Ratio?

Questions for the Intellectually Curious

1. When does OR approximate the Rate Ratio? When does it approximate the Risk Ratio?
2. What are some potential confounders in this study? How could we control for them?