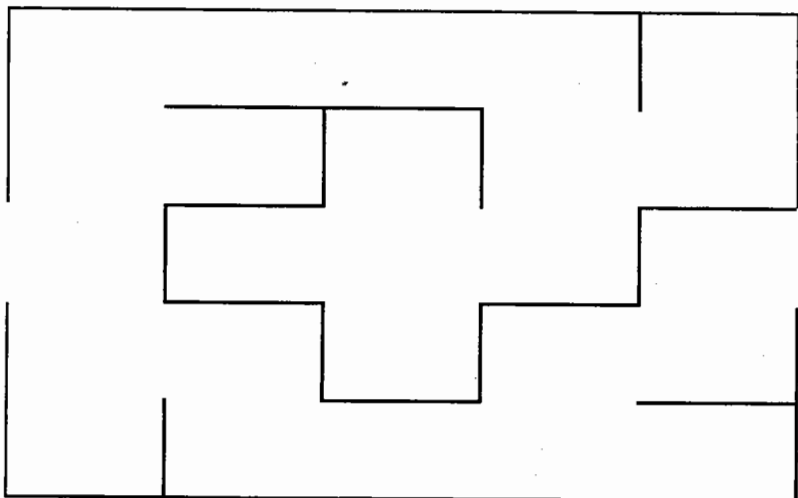# 12

Questions for Review

We have very little direct experience of risks or rates in our personal lives, and as a consequence, intuition about the right choices to make in designing a study often fails, even in persons who seem to have a grasp of epidemiologic theory. The questions that follow are intended to retrace the ground covered in such a way as to challenge the reader's grasp of the fundamentals and their implications.

Disease Frequency

When the size of the population under observation is one, what values of risk can be observed? What probabilities of disease might characterize the individual who constitutes the observed population?

The prevalence of a characteristic may change within a given population over time. Describe one way in which a population prevalence can change without any member changing with respect to the characteristic, and one in which the population does not change although many of the members change.

Can a person become an incident case of a disease while he has the disease? How does the foregoing answer help define the population that should be studied for an estimate of incidence?

The experience of even a single individual comprises many different periods with different time-bound characteristics. How can the experiences of many individuals be aggregated for study into pools within which there is a homogeneity of characteristics?

If a personal characteristic affects the mean duration of disease in individuals who have acquired the disease, but does not affect the incidence of disease, how will the characteristic affect prevalence?

Comparisons

The incidence rate of hepatic adenoma in oral contraceptive users is at least fifty times that in nonusers. Oral contraceptive use is common, yet the population rate difference for hepatic adenoma due to oral contraceptive use is tiny. As a consequence, what must be true of the incidence rate of hepatic adenoma?

The rate of subacute sclerosing panencephalitis (SSPE) in persons who have suffered measles 30 to 59 days previously is on the order of one per 6,000 person months (assume that one person month equals 30 person days), and is approximately zero at other times. Prior to the availability of measles immunization, the prevalence of persons who had measles among urban ten year olds in the United States was approximately 90 percent. In that pre-immunization era, approximately what was the cumulative incidence of SSPE from birth to age 10?

The rate of cataract formation among long-term users of high doses of systemic steroids is approximately five times that in otherwise comparable populations, yet the population rate difference for cataract due to systemic steroid use in the United States is small. What can you conclude about systemic steroid use?

"The incidence of myocardial infarction doubles with every five-year increase in age after age forty in smoking men." Write down a model of incidence that describes this relation, using the following terms: a, the age in years; I_a, the incidence at age a; and I_{40}, the incidence at age 40.

Study Types

Refer to Figure 3.1. Describe one causal hypothesis suggested by the data and suggest the design of a study that might test that hypothesis.

In order to assess the present need for services to residents of Massachusetts with Downs' Syndrome, would you need to conduct a survey, a cohort study, or a case-control study?

Working at the Massachusetts Cancer Registry, you notice a number of cases of Down's syndrome among newly diagnosed cases of acute lymphocytic leukemia of childhood. Assume that all cases of leukemia are notified to the Cancer Registry and that you can readily determine whether any notified case is also someone with Down's syndrome. How might you integrate the results of the previous study (given in the answer to the question above) with the Cancer Registry data in order to estimate the relative rate of leukemia as a function of the presence of Down's syndrome? What kind of study have you done?

Phenylpropanolamine (PPA) is a common over-the-counter decongestant, used by people with upper respiratory infections. You wish to examine the possibility that use of PPA increases the incidence of stroke within 24 hours of use. Describe the study subjects, the exposure and outcome data, and the comparisons that would be required for each of the following studies of this question: a closed cohort study, an open cohort study, a case-control study.

Time

Caffeine affects myocardial irritability for six hours following consumption of a cup of coffee. Would lifetime coffee consumption be a helpful measure of caffeine exposure for a study of the risk of disease events that are determined by myocardial irritability?

After infection with HIV, a period ensues during which the virus multiplies and progressively destroys immunocompetent cells. Early in this period, there is no alteration in any aspect of the victim's immunocompetence. Of what time-related phenomenon is the interval from infection to first symptom an example? If you were studying the effects of HIV, how would you interpret the person time and any disease events that accrue in this interval?

The incidence of adult onset asthma rises abruptly for workers who enter an occupational setting that requires contact with allergenic agents. The incidence then declines with progressive time since entry into the setting. Offer possible explanations for the decline that invoke the distinction between inception and survivor cohorts.

Are the results displayed in Figures 3.4 and 3.5 examples of period effects or cohort effects?

Cohort Studies

Refer to Example 5.1. In the context of that study, was a conventioneer who attended the luncheon but did not eat the chicken salad and was not exposed to group G streptococcus a member of a population "at risk"? Was a conventioneer who ate the chicken salad but did not furnish any information about his activities a member of a population at risk?

Some commentators on studies of the relation between alcohol and breast cancer have criticized cohort studies that did not include negative mammograms in the cohort definition. By what definition of breast cancer might women with occult neoplasms at the beginning of observation be considered to be at risk during observation? By what definition would they not be at risk?

Why does standardization of compared risks or rates by definition eliminate confounding by the factor over which risks or rates are standardized?

Must the time that an individual contributes to a single category of person time be continuous, or can it be disjoint? Give an example.

Can events that preceded the time of observation in an open cohort study affect the categorization of an individual's person time under observation? Can they affect the categorization of a disease event?

Case-Control Studies

What is the source population for a study of cases of myocardial infarction that are admitted to the emergency room of an urban hospital?

What is the source population for a study of deaths from myocardial infarction noted on death certificates held by the state of Massachusetts?

In Australia, persons eligible to vote are obliged by law to register with the election authorities, and the lists so created are a matter of public record. What is the importance of these lists for the conduct of case-control studies in Australia? Is there an argument for limiting the cases of case-control studies to eligible voters?

Under what circumstances might elderly nuns be an acceptable control series for a study in which the cases are sexually active young males?

Assume that case ascertainment involves a sophisticated diagnostic procedure that is not routinely available to persons who may have the disease under study. Describe the ways in which the results of a case-control study based on such ascertainment may be distorted. Would a cohort study using the same case ascertainment procedure be similarly affected?