Example 1: Oral Contraceptives and Thromboembolic Disease [...]

Example 2: Pedestrians Fatally Injured by Motor Vehicles

In their concern with learning about the diseases that present complex diagnostic or pathophysiologic problems, medical personnel are apt to forget that injuries and death due to gross physical trauma are major health problems in affluent industrialized societies as well as in "less-developed" areas. In particular, accidents are the leading cause of death in children and young adults in the United States. Automobile accidents lead all other types as a cause of death.

The word *accident* implies that physical injuries produced by automobiles and other energy sources are haphazard and uncontrollable. Among those arguing against this fatalistic concept, Haddon advocated the use of carefully designed and implemented epidemiologic studies as a means of identifying factors responsible for traumatic injuries, so that appropriate preventive measures can be instituted. His research group's interesting study of the characteristics of pedestrians fatally injured by motor vehicles in New York City is an example of the imaginative use of the case-control method to attack a serious and poorly understood problem (Haddon et al., 1961).

At the time of the study in 1959, little was known about pedestrian-associated, or *host,* factors related to being struck and killed by a car. Substantial funds were being expended for public education programs and other means of "pedestrian control," without much evidence that these were effective preventive measures. Previous findings that many fatally injured pedestrians had been drinking heavily had not been evaluated in comparison to the alcohol consumption of the population at risk or, more simply, to that of noninjured pedestrians. Likewise, the age distribution of killed pedestrians, with relatively high percentages of young children and elderly adults, had not been compared with the age distribution of all or of nonkilled pedestrians, to determine whether the *mortality rate,* or risk of being killed, is actually greater in very young and very old pedestrians. Thus, age and blood-alcohol concentration were included among several characteristics that were measured in fatally injured pedestrians and their matched controls in the study to be described.

Manhattan was an appropriate place for this investigation. Pedestrian deaths were relatively frequent, and they accounted for about 70 percent of all fatalities in motor vehicle accidents. The case series consisted of 50 adults (18 years of age or older) who were struck and killed by automobiles in Manhattan between May 3, 1959, and November 7, 1959. Autopsy confirmation of the cause of death was required. Of 57 cases initially considered, the 7 omissions consisted of 2 who were killed by bicycles, 1 who was purposely pushed into the path of a car, 1 with unknown site or time of the accident, 1 who died of a coronary occlusion while convalescing from the accident, and 2 who were omitted because of clerical errors.

Four matched controls were selected for each case by visiting each accident site at a later date but on the same day of the week and as close as possible to the time of day when the accident occurred. All but eight site visits for control selection were completed within 6 weeks of the accident. Thus, controls were matched to the cases for accident site and time. In addition, controls were matched to the accident cases for sex and were limited, as were the cases, to adults.

The practical problems involved in this form of "shoe-leather" epidemiology can best be communicated by the investigators' own description of the control selection and interview procedures.

The site visits were made by a team of two or three of the authors and one to four medical students working at each location with one or two uniformed members of the Police Department Accident Investigation Squad (A.I.S.).

In visiting each site one of three basic approaches was used. In the first type, that used in many busy neighborhoods, for example, opposite Grand Central Station on a weekday at 6:10 p.m., the entire team arrived and immediately stopped the *first 4* adult pedestrians of the same sex as the deceased. At such busy sites the group arrived and accomplished its purposes in 15 minutes or less from start to finish.

When the accident site was in a neighborhood in which it was suspected that the group might be seen and avoided, a second approach was used. Under such circumstances, for example, at sites in the Bowery, the group arrived and "swept the block" stopping successively the *first* 4 adult pedestrians of the required sex who were headed toward or away from the accident site. By pedestrian here and throughout this report is meant a person progressing by walking, not lounging stationary, sitting, or lying down.

In the third approach, used when pedestrian traffic was very light, for example at 108th Street and the East River (F.D.R.) Drive at 1:40 a.m., the group would lounge nearby or sit in a car at or near the site watching for approaching pedestrians, and as each of the *first* 4 of these came into view he, or, where appropriate, she, was quickly approached and stopped.

The site visited was the sidewalk point closest to the exact location of the accident as described on the police or medical examiner's report. For example, one report indicated that the deceased had been crossing the street 40 feet from a given corner. This was found to be

directly in front of a "rathskeller," and it was at that point that the first 4 pedestrians were stopped.

Great care was taken to avoid any attempt at matching for the characteristics of the deceased, except in so far as sex and adulthood were concerned. In addition, for methodologic uniformity, at all sites the same investigator pointed out to the accompanying police each individual to be stopped. Although the exact details varied with the circumstances, the person was immediately approached and told by the policeman, "Please step over for a minute while the doctors ask you a few questions." A nearby member of the team immediately stepped up and began talking uninterruptedly: "I don't want to know your name; I merely want to ask you a few questions. Do you live in Manhattan?" The interview was usually easily begun in this manner, although 12 refusals occurred (for each of which the next pedestrian was substituted)....

This investigation was carried out without publicity of any kind. With one exception it was invariably possible to stop the members of each pedestrian sample prior to the formation of the substantial group of watchers which sometimes formed thereafter. The exception, in a "tough" neighborhood at 2:30 a.m., involved the only site at which 2 persons had been fatally injured in the same accident. On arrival, it was possible to obtain quickly the first 7 but not the eighth interview and specimen of breath, a small, hostile crowd quickly forming from an adjacent bar. As a result, only the first 4 of the 7 interviews and specimens obtained at this site were used, being counted twice in the analysis of the data.

The interview included questions as to: place and length of residence; place of birth; age; present occupation; and marital status. Sex, apparent race, appearance and apparent sobriety, date, location, time of interview, and weather were also recorded.

Immediately on finishing the interview the interviewer stated approximately as follows, "I only have one more thing for you to do (and then you can go) and that is to blow up this bag for me." Simultaneously he removed a Saran bag from an envelope and showed the pedestrian how to place one of its two ends in his mouth and blow until told to stop. This finished, the pedestrian was thanked and told that the interview was over.

A large percentage of those interviewed were foreignborn, and many of these admitted to no knowledge of English. Rather than weaken the investigation by omitting these pedestrians when no member of the team knew a common language, passersby were stopped and asked to serve as interpreters. Apparently because those walking in the same neighborhoods or, in some cases, accompanying those stopped (many of the latter being interviewed themselves) tended to know the same languages, this procedure proved very satisfactory. With its use no one failed to be interviewed because of a language barrier and interviews were completed in Armenian, German, Greek, Spanish, and other languages and dialects (pp. 657-659).

As implied above, blood-alcohol concentrations were measured by analysis of breath specimens and the other data concerning the controls were recorded as described. Data concerning the cases were obtained chiefly from official records describing the accidents. Postmortem blood-alcohol measurements were studied in those cases who survived fewer than 6 hours after the accident.

Data analysis for the case-control comparison revealed that fatally injured pedestrians were indeed older than the controls, their mean ages being 58.8 years and 41.6 years, respectively. Additional data collected later showed nonfatally injured pedestrians to be intermediate in age, with a mean of 48.4 years. Thus, advancing age appeared to increase the pedestrian's risk both of being struck by a car and of dying once struck.

Regarding the effects of alcohol, significantly higher blood alcohol concentrations were found in cases than in controls. Appreciable increases in risk were noted even at the relatively low levels of 10 to 40 mg/100 mL. Putting together the age and alcohol data, it appeared that there were two relatively discrete high-risk groups: the elderly who had been drinking little if any alcohol and the middle-aged who had been drinking heavily.

It was also found that the case group was less often married and more often foreign-born and of lower socioeconomic status than were the controls. However, these differences could be explained by age differences between the case and control groups. Weather conditions, rain in particular, did not appear to be associated to any substantial degree with traffic deaths.

In addition to the case-control comparisons, information about the fatally injured group itself was of interest and importance. Only a small percentage lived outside Manhattan, either as commuters or out-of-town visitors. While the accidents were scattered about the city, most occurred outside of major business and shopping areas. The accidents occurred most frequently in the evening and night hours, suggesting the importance of having emergency care available during this time.

Example 3: Estrogens, Progestogens, and Endometrial Cancer

Estrogen preparations are commonly taken by women to treat menopausal symptoms and prevent complications of the menopause such as osteoporosis. Unfortunately, they also greatly increase the risk of endometrial cancer. It was proposed that if a ..