APPLYING THE M.A.A.R.I.E. FRAMEWORK

Population Comparisons

The unique feature of population comparisons or ecological studies is their ability to suggest relationship between risk factors and diseases or other outcomes without having information on any one individual. Population comparisons are designed to compare the rates of events in two or more populations or to investigate changes that have occurred in the same population over a period of time. Alternatively, population comparisons may examine differences between two or more populations at the same point in time (Fig. 1.2).

Population comparisons compare rates in two or more populations without having available information on particular individuals. Population comparisons typically observe the rates of a disease or other outcome and the rates of a risk factor or other characteristic. They often ask whether populations with higher rates of the risk factor also have higher rates of the disease.

To examine the relationship between the use of birth control pills and stroke in young women, the investigator using a population comparison might proceed as follows:

Assignment: Select a study population and measure its rate of strokes among young women and a similar comparison control population and measure its rate of strokes among young women

Assessment: Determine the rate of use of birth control pills among young women in the study population and in the control population

Results: Compare the rates of use of birth control pills with the rates of strokes among young women in the study population and in the control population

Interpretation: Draw conclusions about the meaning of birth control pill use for women included in the investigation

Extrapolation: Draw conclusions about the meaning of birth control pill use for women not like those included in the investigation, such as women who have the option to use newer low-dose birth control pills.

When populations of young women with high rates of strokes also have high rates of use of birth control pills compared with populations of young women with low rates of strokes we say that a *group association* exists. That is, even though we do not know whether the particular women who developed stroke actually used birth control pills, we can conclude that an association exists at the group or population level. Identifying group associations are often the first step in demonstrating a cause and effect relationship, but as we will see group associations often merely suggest hypotheses for further investigation.

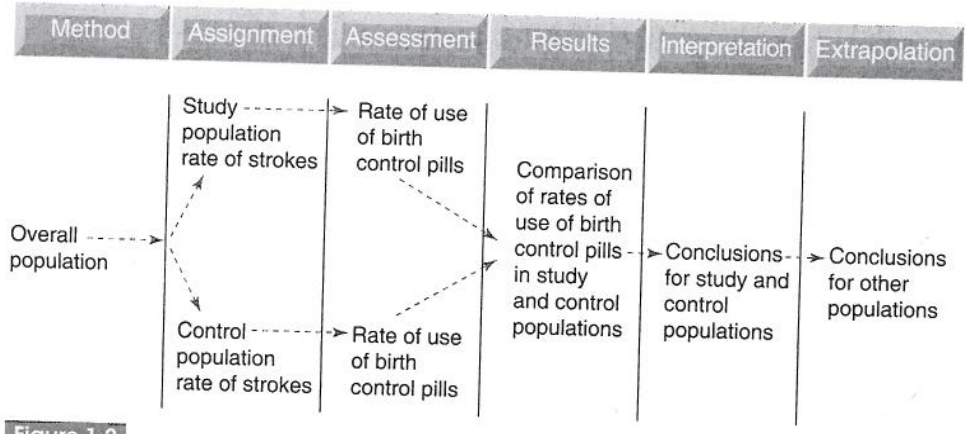

Figure 1.2 M.A.A.R.I.E. framework for a population comparison.

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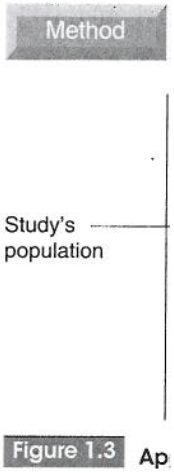

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Case-Control Study

The unique feature of case-control studies of disease is that they begin by identifying individuals who have developed or failed to develop the disease or condition being investigated. After identifying those with and without the disease, they look back in time to determine the characteristics of individuals before the onset of disease. In case-control studies, the *cases* are the individuals who have developed the disease, and the *controls* are the individuals who have not developed the disease. To use a case-control study to examine the relationship between birth control pill use and stroke in young women, an investigator might proceed as follows:

Assignment: Select a study group of young women who have had a stroke (cases) and a group of otherwise similar young women who have not had a stroke (controls). Because the development of the disease has occurred without the investigator's intervention, this process can be called *observed assignment*.

Assessment: Determine whether each woman in the case or study group and also in the control group previously took birth control pills. The previous presence or absence of the use of birth control pills is the outcome in a case-control study.

Results: Calculate the chances that the group of women with a stroke had used birth control pills versus the chances that the group of women without stroke had used birth control pills.

Interpretation: Draw conclusions about the meaning of birth control pill use for women included in the investigation.

Extrapolation: Draw conclusions about the meaning of birth control pill use for categories of women not like those included in the investigation, such as women on newer low-dose birth control pills.

Figure 1.3 illustrates the application of the M.A.A.R.I.E. framework to this investigation. Notice that case-control studies unlike population comparisons identify individuals and ask whether there is an association at the individual level between young women with strokes and the use of birth control pills. Thus case-control studies are capable of establishing what we will call an *individual association*.

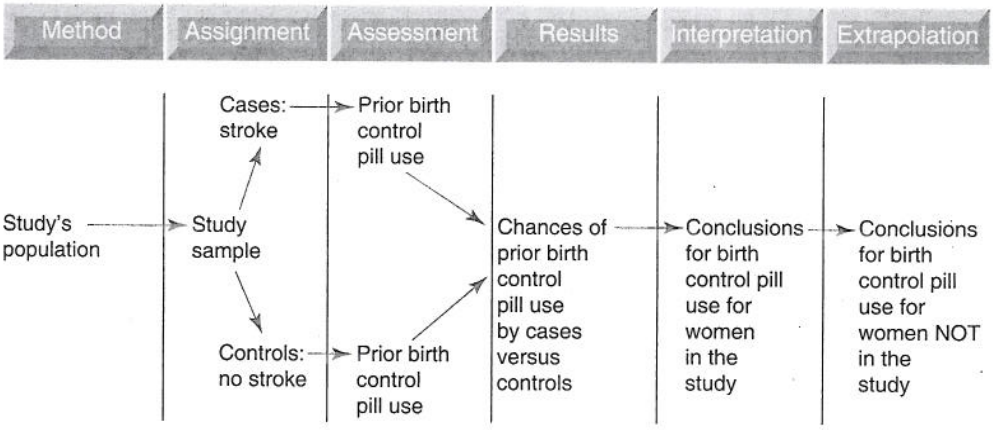

Figure 1.3 Application of the M.A.A.R.I.E. framework to a case-control study.

Cohort Study

Cohort studies of disease differ from case-control studies in that they begin by identifying individuals for study and control groups before the investigator is aware of whether they have developed the disease or other outcome. A *cohort* is a group of individuals who share a common experience. A cohort study begins by identifying a cohort that possesses the characteristics under study as well as

a cohort that does not possess those characteristics. Then the frequency of developing the disease in each of the cohorts is obtained and compared. To use a cohort study to examine the relationship between birth control pill use and stroke, an investigator might proceed as follows:

Assignment: Select a study group of women who are using birth control pills and an otherwise similar control group of women who have never used birth control pills. Because the use of birth control pills is observed to occur without the investigator's intervention, this process is also called *observed assignment*.

Assessment: Determine who in the study group and the control group develops strokes. As opposed to a case-control study, the outcome for a cohort study is the subsequent presence or absence of a stroke.

Results: Calculate the chances of developing a stroke for women using birth control pills versus women not using birth control pills.

Interpretation: Draw conclusions about the meaning of birth control pill use for women included in the study.

Extrapolation: Draw conclusions about the meaning of birth control pill use for women not included in the study, such as women on newer low-dose birth control pills.

Figure 1.4 illustrates the application of the M.A.A.R.I.E. framework to a cohort study.

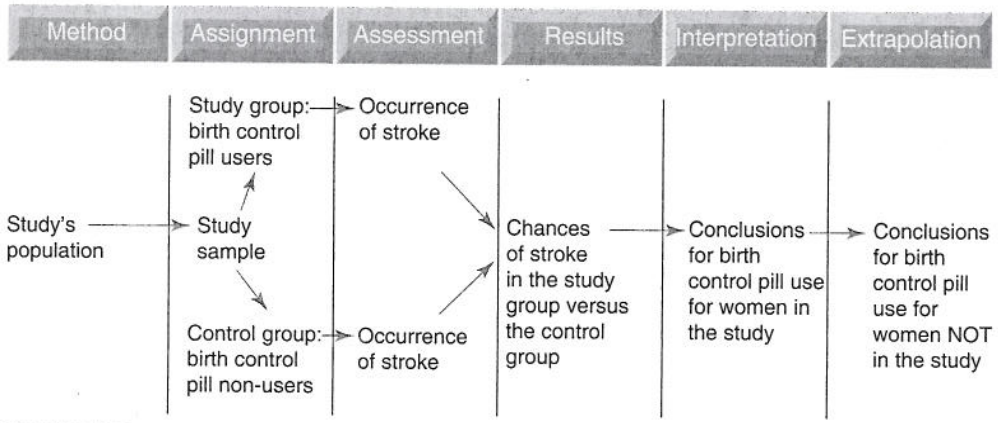

Figure 1.4 **Application of the M.A.A.R.I.E. framework to a cohort study.**

Randomized Controlled Trial

Randomized controlled trials are also called randomized clinical trials. They are a form of experimental study. As in cohort studies, individuals are assigned to study and control groups before determining who develops the disease or other outcome. The unique feature of randomized controlled trials, however, is the process for assigning individuals to study and control groups. In a randomized controlled trial, participants are randomized either to a study group or to a control group.

Randomization means that chance is used to assign a person to either the study or the control group. This is done so that any one individual has a known, but not necessarily equal, probability of being assigned to the study group or the control group. Ideally, the study participants as well as the investigators are not aware of which participants are in which group. *Double-blind* assignment means that neither the participant nor the investigators know whether the participant has been assigned to the study group or the control group. Single blinding implies that the participants are unaware of their group assignments.

To use a randomized controlled trial to examine the relationship between birth control pill use and stroke, an investigator might proceed as follows:

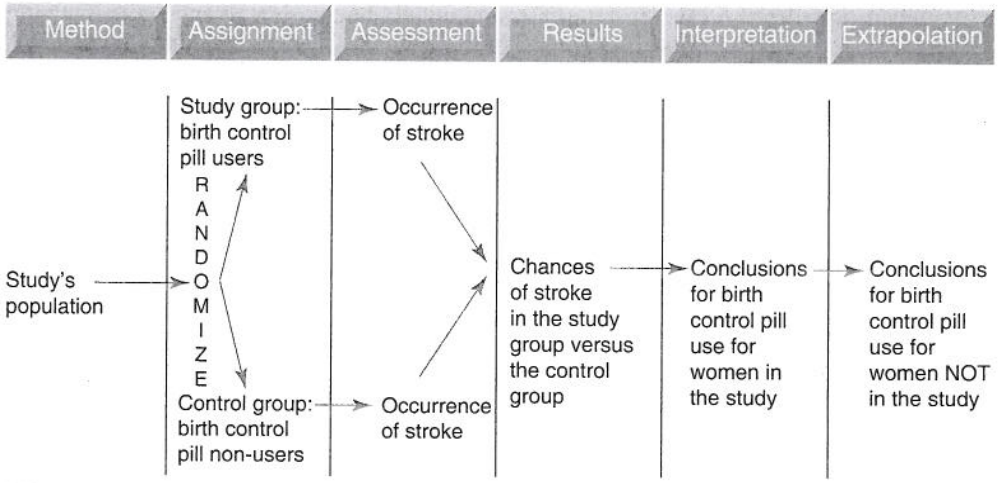

Figure 1.5 **Application of the M.A.A.R.I.E. framework to a randomized controlled trial.**

Assignment: Using randomization, women are assigned in a double-blind fashion to a study group that will be prescribed birth control pills or to a control group that will not be prescribed birth control pills.

Assessment: Observe these women to determine who subsequently develops stroke. As in a cohort study, in a randomized controlled trial the outcome is the presence or absence of stroke.

Results: Calculate the chances that women using birth control pills will develop a stroke versus women not using birth control pills.

Interpretation: Draw conclusions about the meaning of birth control pill use for women included in the study.

Extrapolation: Draw conclusions about the meaning of birth control pill use for women not included in the study, such as women on new low-dose birth control pills.

Figure 1.5 illustrates the application of the M.A.A.R.I.E. framework to a randomized controlled trial.

ADVANTAGES AND DISADVANTAGES OF THE BASIC STUDY TYPES (3,4,5)

The basic components and key questions we have outlined are common to the four basic types of investigations, the population comparison (or ecological study), case-control (or retrospective study), cohort (or prospective study), and randomized controlled trial (or experimental study). Each type, however, has its own strengths, weaknesses, and roles to play in health research.

Population comparisons have the advantage of not requiring information on specific individuals. They can often be conducted using routinely collected data that may permit the use of large data sets. This makes them relatively inexpensive to perform and rapid to conduct. They often provide a starting point for investigating relationships and generating hypotheses. In addition, once a cause and effect relationship and/or the efficacy of an intervention has been established, population comparisons can often be helpful in determining whether the intervention has effectiveness, that is it works in practice.

Case-control studies have the distinct advantage of being useful for studying rare conditions or diseases. If a condition is rare, case-control studies can detect differences between groups using far fewer individuals than other study designs. Often, much less time is needed to perform a case-control study because the disease has already developed. This method also allows