The outcomes and costs associated with medical care are critical issues for society. Interventions, treatments, and health care providers are required to be both effective and cost-effective. More and more the cumulative effects of disease, treatment, and outcome are becoming the standard for evaluation of effectiveness and cost-effectiveness. Although randomized clinical trials are the “gold standard” for comparing alternative treatments, results may not be generalizable to usual clinical care nor reflect treatment effectiveness in community practice. The discrepancy between clinical trials and studies of actual effectiveness has been pointed out a number of times over more than 30 years (1–4). Key design elements of clinical trials, such as strict selection criteria, double blinding of patients and providers, and treatment protocols, are specified to isolate differences resulting from treatment. As a result, other sources of variability, including practice heterogeneity, patient heterogeneity, comorbid illness, and imperfect adherence to treatment regimens, limit the generalizability of results to usual clinical care.

There are several alternatives to the conventional randomized clinical trial that may yield results more generalizable to clinical practice, but that still provide rigorous measurement of outcomes. These include pragmatic clinical studies that randomize patients to usual care, retrospective cohort studies, and prospective multicenter cohort studies (4–6). These studies measure outcome over time and can capture the impact of long-term
illness and evaluate the role concomitant disease or treatment play in long-term effectiveness and are a sensitive indicator of treatment effect and have been shown to have similar results to clinical trials (7–9). This chapter will discuss the design of observational studies.

1. WHAT ARE LONGITUDINAL OBSERVATIONAL STUDIES?

Observational, prospective cohort studies, also called registries, evaluate the actual experience of persons after the identification of a specific event, such as a disease diagnosis, clinical milestone, or initiation of medical or surgical treatment. Sequential measurement of clinical and patient-reported outcomes, obtained at regular intervals, is an essential component of these studies. Longitudinal, observational studies are useful in evaluating a breadth of data in a timely fashion; especially patient reported outcomes, resource utilization, costs, and clinical outcomes in community settings because there is no assignment of patients to specific treatment protocols.

Although the term registry is used widely to describe longitudinal studies, it is most often used to describe prospective cohort studies and not registries as defined in epidemiologic studies. The true registry, exemplified by the Surveillance Epidemiology and End Results (SEER) registry for cancer, is population based and records incident events. SEER provides basic information on multiple cancers from various geographically diverse areas of the United States (10).

There are several successful observational databases in chronic disease that have yielded significant research findings. ARAMIS (Arthritis, Rheumatism and Aging Medical Information System) is now more than 25 years old and includes patients with rheumatologic conditions and community populations followed through patient self-report. ARAMIS investigators have published hundreds of peer-reviewed articles in the areas of treatment strategies, health status assessment, costs of care, and radiologic outcomes (11).

Observational databases also have been used extensively in clinical research. This chapter will focus on use of observational studies in prostate cancer to evaluate the longitudinal outcomes associated with surgical and radiation therapy. There are three prostate cancer databases, the Prostate Cancer Outcomes Study, the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) database (12), and the Department of Defense Center for Prostate Disease Research. The CaPSURE database was established in 1995 and includes both clinical variables and patient-reported outcomes. Patients are recruited from community sites and three academic medical centers throughout the United States (12). Evidence from CaPSURE suggests that the results of the diagnostic biopsy contribute significantly to accurate risk assessment among patients with newly diagnosed prostate cancer and that the incidence of positive surgical margins after prostatectomy is associated with adverse outcomes (13,14).

2. WHAT ARE THE OBJECTIVES OF OBSERVATIONAL DATABASES?

There are multiple objectives for observational databases. The first goal is to accumulate and document a large, heterogeneous patient experience over time. These studies allow access to large samples of patients treated by a broad base of community practitioners. Clinical data, outcomes, survival, resource utilization, workforce participation, health-related quality of life, and patient satisfaction with care and treatment may all be collected over time.

Another goal of observational studies is to use this experience to identify and prioritize the key issues for medical effectiveness research, including aiding in development of