resource consumption for renal replacement therapy may be delayed but not avoided. If the time horizon of a study is too short, there may not be sufficient information to assess whether resource consumption is avoided or delayed.

Trial endpoints in phase III treatment protocols are usually cure, progression or improvement, failure, and other adverse endpoints. Economic analysis usually relies on final endpoints such as survival or quality-adjusted survival. Thus, economic protocols may have a duration that is different from that for the clinical endpoint. Often, economic trials continue to follow patients when they have stopped the active treatment phase of the protocol. This is because patients often become most important from an economic perspective when they progress in their disease from a clinical perspective.

Because the ratio of the difference in the effect size to the variance is usually smaller for economic data than for clinical data, economic studies generally require a larger sample size than do clinical studies. Budget and time constraints often will limit the sample size of phase III studies, and thus limit the statistical power of economic evaluations. Early communication would allow calculation of sample size requirements for the economic portion of the study based on the phase II economic data, or could allow the development of economic evaluation as a primary study endpoint with an appropriate sample size calculation. Sample size calculations may be performed using pilot data from phase II studies, but the limited number of centers in phase II studies may result in misleading estimates of variances for sample size calculation for multinational phase III studies.

In phase III studies, resource-utilization information is often collected within the clinical protocol. In many trials, the costs of these resources will be assessed through a separate data-collection exercise. Quality of life and utility information can be collected periodically in the trial from study patients (patient assessment), or health states of study patients can be collected periodically within the trial to be valued later from a population sample (societal assessment).

Possible audiences for economic data from phase III trials include government, politicians, physicians, the public, patients, and formulary committees (in hospitals or within government organizations, for example). However, seldom can a single study provide appropriate data for all of these groups.[37] Various decision makers will use economic data in order to determine if they will approve the service or product, if they will use it in practice, if they find it valuable as taxpayers, or if they want to use it themselves.

Phase IV: Clinical economics studies in phase IV consist of efficiency trials and post marketing surveillance studies. These studies are conducted after the product is licensed and marketed and collect data that can be used to perform post-marketing validation of data collected in phase III studies and to look for uncommon effects of treatment. Economic evaluation within phase IV studies are important because of the potential for increased generalizability (the results of phase IV studies may be closer to actual results of future patients in a community) and are conducted to validate in a real-world setting the results of clinical economics studies in phase III clinical trials, or to compare a new drug with other conventional drugs or therapies, or to assess the use of the agent in a special population.

In post-marketing settings, economic data can be collected using prospective and retrospective analysis of clinical trials, retrospective analysis of specific patient populations, analysis of administrative data bases that describe the experience of a specific patient population defined by the type of health care payer, or decision-analytic models that predict the effectiveness of therapies using existing clinical data.

Generalizability of Clinical Economics Data Collected Alongside a Clinical Efficacy Study

Both clinical investigators and health care purchasers have concerns about the external validity (generalizability) of both clinical and economic data from clinical trials. Since many clinical trials are performed in teaching hospitals using patients mainly of university hospitals and public hospitals, the clinical results and resource consumption may not be generalizable to all primary care practices. Teaching hospitals, in general, consume more resources than non-teaching hospitals, because teaching hospitals must spend time and money for education of medical students and residents and for better patients' care expected by society. Patients in clinical trials frequently have better survival and better response to therapy than non-trial patients,[48,49] irrespective of whether they receive the control or the experimental therapy. The closer monitoring of patients in a trial of an antibiotic drug resulted in economic findings different from those that would be observed in normal practice.[10]

There are limitations in economic analysis incorporated into phase III trials. External validity may be limited because the number of patients participating in the trial is relatively small and those patients may lack variability compared to the patients using the product once it has been approved and marketed. Budget issues may restrict sample size and time horizon. Generalizability to the health system of decision-makers may be limited by differences in cultures and health care sys-