Epidemiological Activities in the Countries

Establishment of the National Epidemiology Commission of Argentina

The Secretariat of Health in the Ministry of Health and Social Action of Argentina has decided to establish a National Epidemiology Commission (CONEP), which will be chaired by the Undersecretary for Health Programs and administered by a professional in epidemiology from the Health Promotion and Protection Directorate.

The Commission’s honorary advisory board will be formed by professionals from the National Health Promotion and Protection Directorate, the Dr. Juan H. Jara National Institute of Epidemiology, the Dr. Emilio Coni National Institute of Epidemiology, the School of Public Health of the Medical School of Buenos Aires University, the School of Public Health of the Medical School of Córdoba National University, and the Pan American Sanitary Bureau.

The Commission will function in an advisory capacity on all aspects related to the development of epidemiology and the implementation of the recommendations originated at the Seminar on Epidemiology of Argentina, whose final report is part of Resolution (SS) No. 275 of 7 July 1986, establishing the National Epidemiology Commission.

Scientific Challenges in the Application of Randomized Trials

In recent years, scientific challenges in the application of randomized trials have become more apparent, especially with the extension of such trials to the assessment of nondrug treatments, such as health education, psychotherapy, and health care provision. Six issues (individual versus group randomization, blinding and unblinding, the effect of trial participation on outcome, selective subject participation, treatment compliance, and standardized versus individualized treatment) are discussed in terms of their impact on internal validity, generalizability (external validity), and clinical relevance. Specific design strategies may be necessary to enhance these methodological and clinical desiderata. Attention to these challenges should lead to improvements in future randomized trials.

The randomized controlled trial (RCT) is generally regarded as the most potent scientific tool for evaluating medical treatments. Its appeal stems from its apparent similarity to the laboratory experimental setting, where two or more groups of genetically identical animals (or tissue cultures, cells, or cellular extracts) are subjected to different maneuvers or manipulations, and some outcome of interest is then measured. Although human beings do not share the homogeneity usually achievable with mice or fibroblasts, randomization into treatment groups is generally relied on to account for known or unknown baseline attributes, also called confounding factors, which might otherwise predispose to or protect from the outcome of interest, independent of treatment.

Randomized trials have contributed greatly to the evolution of more effective treatments and preventive measures for a variety of medical conditions. Randomized controlled trials represent an increasing proportion of the articles published in leading medical journals and have become the sine qua non for the proof of efficacy the U.S. Food and Drug Administration requires for marketing new drugs. Despite the obvious advantages and impressive track record of RCTs, clinical investigators have become increasingly aware of certain difficulties in their interpretation, feasibility, and ethics. Some of these difficulties have been overcome; others await resolution. None, however, has challenged the scientific validity of the method itself. In recent years, especially with the extension of RCT methodology to assessments of nondrug treatments, including health education, psycho-
therapy, and health care provision, new concerns have emerged that challenge an uncritical reliance upon the RCT as an automatic scientific "gold standard" in clinical research.

It seems timely, therefore, to consider a critical reappraisal of some of the scientific issues involved in randomized trials. The purpose of this paper is not to discredit the method but rather to emphasize difficulties and challenges inherent in its application, especially in studying behavioral outcomes or outcomes that might be influenced by behavior (e.g., cardiovascular mortality). When such difficulties arise, specific design strategies may be necessary to enhance scientific validity and clinical relevance. Some of the issues being raised have already surfaced in previous clinical trials; others remain theoretical and await empirical demonstration. The authors focus on six aspects of RCT design: (1) individual versus group randomization, (2) blinding and unblinding, (3) the effect of trial participation on outcome, (4) selective subject participation, (5) treatment compliance, and (6) standardized versus individualized treatment.

The first two of these issues threaten the internal validity of a trial, i.e., the extent to which the treatment comparison is unbiased. The next three affect the generalizability, or external validity, of the trial's findings. The last issue concerns the clinical relevance and utility of the treatment comparison.

After discussing each of the six issues the authors summarize their conclusions as follows:

Although the RCT design appears to come closest to approximating the laboratory experiment, the complexities of the human psyche can affect participation, compliance, blinding, and outcome in a trial. This is especially true when the outcome is either itself an observed behavior (e.g., maternal-infant bonding) or an event that is known to be etiologically linked to behavior (e.g., cardiovascular mortality). These human psychological factors can affect the internal validity of the treatment comparison, the generalizability (external validity) of the results to a larger population, or the clinical relevance of the conclusions.

These same factors also operate in observational, nonexperimental research studies. In fact, they can also influence treatment selection, and thus lead to selection bias in such studies. In an RCT, randomization usually occurs after the decision to participate, and selection bias is thereby eliminated. This is a strong argument in favor of the RCT, since selection bias affects the internal validity of a treatment comparison. Internal validity is a necessary prerequisite for external validity and should always, therefore, receive highest methodological priority.

When selective participation seriously threatens external validity, trade-offs will occur between higher participation and a risk of selection bias in observational studies, compared with an unbiased (internally valid), but possibly less generally applicable, result in randomized trials. This kind of trade-off arises, for example, in studying putative health effects of breastfeeding. If an RCT were attempted, women agreeing to be randomly assigned to breast-feed or formula-feed their infant would be so few and so atypical that the results would have little meaning for mothers and infants in general.

For most questions involving treatment efficacy, the RCT remains the research methodology of choice whenever randomization is feasible, but a study's use of this methodology does not necessarily confer certainty on its conclusions. In the majority of cases in which scientific challenges arise, implementation of specific design strategies should enhance internal and external validity. In other cases, a trial's conclusions may have to be tempered by inescapable methodological limitations.

The purpose here has not been to denigrate the value of the RCT, but rather to discuss some scientific difficulties and challenges inherent in its application. As has been noted, the model of methodological rigor represented by the RCT invites close scrutiny for any departures from the ideal. It is hoped that a critical reappraisal of some of the scientific underpinnings of the randomized trial may help bring about changes in attitudes and practice. The interests of medical research and the public it is intended to benefit may not be best served by an unquestioning acceptance of the results of a study merely because it uses an RCT design that can, in certain circumstances, lead to scientifically invalid or clinically irrelevant inferences. Most importantly, the authors hope that attention to these challenges may facilitate improvements in future RCTs.

(Source: Based on: Kramer, M. S. and Shapiro, S. H. Scientific challenges in the application of randomized trials. JAMA 252:2739-2745, 1984. ©American Medical Association. The complete article as well as its bibliographical references can be obtained from the Health Situation and Trend Assessment Program, PAHO.)

Editorial Comment

This article describes one of today's most potent tools for evaluating the efficacy and safety of a medical treatment. All existing methods for evaluating treatments and programs implemented at the community level are more or less rigorous adaptations of this procedure. Therefore, it has been considered of interest to publish those parts of the discussion that describe the main challenges resulting from the application of this instrument.