Revisions to Instructions to JASN Authors Regarding Articles Reporting Studies Using DNA Arrays, DNA Polymorphisms, and Randomized Controlled Clinical Trials

WILLIAM G. COUSER, MD
Editor-in-Chief, Journal of the American Society of Nephrology

The science of nephrology, both basic and clinical, has advanced dramatically in the past decade alone. The molecular revolution is readily visible in most basic research papers published now in JASN. Clinical research has also seen a marked increase in the rigor with which studies are designed and results analyzed as the tools of modern epidemiology are more universally applied.

JASN is committed to providing our readers with not only the best of such articles related to the kidney but also articles that contain significant new insights that can be readily interpreted. Beginning with this issue, we will request that authors submitting three types of articles adhere to the principles outlined below. These three areas illustrate the application of modern science to the study of renal disease. Paragraphs summarizing these requirements have been added to the Instructions to Authors, which can be found at the back of each issue of the Journal and on our web site at http://jasn.manuscriptcentral.com/.

DNA Arrays

The development of chip technology and the widespread availability of DNA arrays that allow analysis of thousands of genes to be studied simultaneously in experimental and control samples has now become a routine tool for many laboratories studying the regulation of gene expression in the kidney. While extremely powerful, the results of array analysis alone represent only preliminary data regarding which genes are overexpressed under the study conditions, which are downregulated, and which are not changed. These results alone do not provide information on whether any change in gene product occurs or whether any changes that do occur are of biologic or functional significance. Now that this new technology has become established in renal research, JASN will review only papers in which the initial results of array analysis have been extended to either identify and characterize a new gene of interest or to analyze the functional significance of known genes observed to be dysregulated. Papers reporting the results of array analysis alone without further follow-up will not be considered for publication except under unusual circumstances.

Studies of DNA Polymorphisms

The sequencing of the human genome and identification of many variants and single-nucleotide polymorphisms (SNPs) in genes of interest, some associated with disease processes, has led to a marked increase in studies of the relationship between these polymorphisms and clinical disease. As in all human studies in which cause and effect are difficult to determine, the possibility of spurious associations in studies of SNPs is significant, particularly if appropriate consideration is not given to adequate sample size and control for population stratification.

For population-based case-control studies describing an association between a DNA polymorphism and renal disease, in addition to ensuring adequate sample size, appropriate correction of \( P \) values for multiple comparisons, and findings that “make sense” biologically, JASN will usually require one of the following for papers to be considered for publication:

- Data showing an effect of the polymorphism on protein function or gene expression
- Confirmation of the association using a family-based method, e.g., transmission-disequilibrium test (TDT)
- Replication of the association in an independent sample
- Measurement of and correction for population stratification in the samples
- Moreover, recent studies indicate that the haplotype structure of the human genome is relatively limited. The genome has been depicted as a series of regions of high linkage disequilibrium (haplotype blocks), each with limited diversity, separated by sites of recombination. A particular SNP may be shared by several common haplotypes, of which only one is associated with a disease. It is not possible to identify this “risk haplotype” by genotyping a single SNP. Therefore, special consideration will be given to studies in which haplotype analysis is used to identify the “risk haplotype” associated with a renal disease.

Randomized Controlled Trials

The randomized controlled trial is the gold standard that is used in evidence-based medicine to assess the validity of therapeutic claims. To properly interpret the results and validity of randomized controlled trials, readers must be able to understand the trial design, methodology, conduct, and interpretation of the results. During the last decade, clinical trialists,
methodologists, statisticians, epidemiologists, and journal editors have become increasingly aware of the limitations in the methods employed by authors when reporting the results of otherwise carefully designed and conducted trials (1). This concern has led to the Consolidated Standards of Reporting Trials (CONSORT) Statement, which is a set of recommendations for improving the quality of reports of parallel-group randomized trials. The results of this collaborative effort, the Revised CONSORT Statement, is free from copyright restrictions and may be published and used with the sole restriction that modifications to the checklist or flow diagram, made by authors to suit specialized needs, not be published without first obtaining permission.

The CONSORT Statement includes 22 recommendations for details that should be included in the complete reporting of a randomized controlled trial. The CONSORT recommendations are not departures from information routinely included by authors reporting randomized clinical trials. Rather they are a list of the elements requisite for a complete description of the trial that will enable the reader to assess the validity of the trial’s results, make comparisons of results across trials, and determine the applicability of a trial’s results to a particular patient population.

The Journal now encourages authors submitting reports of randomized controlled trials to review the CONSORT Statement (http://www.consort-statement.org/). The CONSORT Statement includes recommendations and a checklist of items that should be included in a comprehensive report and a participant-flow diagram. Reports of randomized controlled trials that do not conform to the CONSORT guidelines may be returned to authors for revision prior to formal review.

It is hoped that adoption of the above policies will help to make articles in JASN of even higher quality, more easily compared to articles in other top-quality journals, and of more value to our readers and the scientific community.

References