The Number, Quality, and Coverage of Randomized Controlled Trials in Nephrology

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Abstract. Randomized controlled trials (RCT) are the optimal study design to answer intervention questions. The authors evaluated the number, quality, and coverage of RCT in nephrology. MEDLINE was searched using the relevant medical subject headings for nephrology and 12 major specialties in internal medicine, limited by "randomized controlled trial" as a publication type. A random selection of 160 RCT in nephrology (40 for each decade) published since 1966 and an additional 270 RCT from ongoing or published Cochrane systematic reviews in various areas of nephrology, dialysis, and transplantation were evaluated for quality of reporting using standard criteria. The number of RCT published in nephrology from 1966 to 2002 (2779) is fewer than all other specialties of internal medicine (range: 5335 in hematology to 27109 in cardiology) with the proportion of all citations which are RCT being the third lowest (1.15%). There has been an increase in both indices from 1966 to 1996, but not at a greater rate than other specialties, and there has been no increase over the past 5 yr. Some areas of nephrology, in particular glomerulonephritis, are clear outliers with very low numbers of RCT to guide clinical decision-making. Overall the quality of RCT reporting in nephrology is low and has not improved over the past 30 yr with unclear allocation concealment (89%), lack of reported blinding of outcome assessors (92%), and failure to perform "intention-to-treat analysis" (50%) particularly frequent. The challenges of improving the quality and quantity of trials in nephrology are substantial, but they can be overcome by using standard guidelines and checklists for trial reporting, greater attention to the trial methods and not just the results, involving experts in trial design and reporting, multicenter collaboration, and larger and simpler trials.

Because randomized controlled trials (RCT) are designed to provide unconfounded estimates of intervention effects, they are the ideal study type to answer intervention questions. However, not all RCT provide valid results. Validity of RCT depends on the underlying methodological quality (1). Allocation concealment, blinding, intention-to-treat analysis, and loss to follow-up are the critical items in the design and conduct of RCT, and inadequately conceived and conducted RCT, like observational studies, may overestimate or underestimate true effects of interventions (2–11).

To our knowledge, there has never been a systematic evaluation of the number, coverage, and quality of RCT in nephrology. This was the aim of our study. If problems were identified, we also sought to propose feasible solutions.

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Materials and Methods

Number and Proportion of RCT in Nephrology Compared with Other Specialties

The medical subject heading (MESH) tree structure in MEDLINE (2002) was used to identify all major headings relevant to the primary specialties of internal medicine. Specifically, eight areas of internal medicine were searched by using the single broadest heading in the MeSH structure (cardiology-"cardiovascular diseases"; endocrinology-"endocrine diseases"; immunology-"immunologic diseases"; nephrology-"kidney diseases"; rheumatology-"musculoskeletal diseases"; oncology-"neoplasms"; neurology-"nervous system diseases"; respiratory medicine -"respiratory tract diseases"), whereas five were searched by two or more major relevant headings (infectious diseases-"bacterial infections", "mycoses", "virus diseases", "parasitic diseases"; gastroenterology-"digestive system diseases" and "gastrointestinal diseases"; hematology-"hematologic diseases" and "lymphatic diseases"; dermatology-"skin diseases" and "connective tissue diseases"; nutrition-"metabolic diseases" and "nutrition disorders").

These MeSH headings for each specialty were "exploded" to capture all of the relevant subheadings within these major headings, and the total number of publications in that area was identified. The results of these MEDLINE searches were limited by "randomized controlled trial" as a publication type to estimate the total number of RCT published in each specialty and ordered by year of publication. From these data, the proportions of citations that were coded as RCT were also calculated.

Coverage of RCT within Nephrology

To assess coverage within nephrology, the major content areas were identified by consulting the index pages of three major nephrology and internal medicine textbooks (12–14). Ten major areas of nephrology were identified, and MEDLINE was searched by using the following relevant textwords for these areas: “acid-base imbalance”, “acute renal failure”, “chronic renal failure”, “diabetic nephropathy”, “glomerulonephritis”, “hemodialysis”, “peritoneal dialysis”, “transplantation”, “urinary calculi”, “urinary tract infections”. The number of citations was found, and the proportion of citations that were RCT were subsequently identified by limiting the results of these searches by “randomized controlled trial” as a publication type.

Quality of RCT in Nephrology

Sample Selection. Evaluating all RCT was not feasible, so a representative sample was selected by two methods. First, the Cochrane Renal Group specialized register of RCT was used to randomly select 40 RCT for every 10-yr period from 1966 to 2002 (160 in total). This is the most complete register of nephrology RCT, listing over 4000 RCT, and was used to select trials for quality assessment because MEDLINE only indexes 20–25% of published RCT. The Cochrane Renal Group specialized register is developed by thorough multi-database electronic searches and by hand-searching of medical journals and conference proceedings (15). A list of all RCT included in this registry was obtained and sorted by year; using a computer-generated sequence of random numbers, four RCT per year were selected, for a total of 40 RCT in every decade. Second, data on quality of trial reporting were extracted from RCT included in Cochrane meta-analyses that the authors have published or are currently conducting, one from dialysis (16 RCT), one from transplant (61 RCT), and three from general nephrology (193 RCT) (16).

Quality Assessment. The methodological quality of all these RCT was assessed by two independent assessors (GFMS, JC) using standard accepted quality of trial reporting indicators (allocation concealment, blinding, “intention-to-treat” analysis, completeness to follow-up). These were chosen because there is now strong empirical data showing that these items, if poorly reported, are generally associated with an over-estimation of treatment effect (2–11). Disagreements in the quality assessment for these RCT were resolved by discussion and consensus among the two investigators (GS, JC). Where duplicate publication of a trial existed, only the main publication was included in this analysis.

Allocation concealment was recorded as adequate when sequentially labeled, sealed, opaque envelopes or a central or pharmacy randomization were used and reported. It was considered unclear when the methods used to allocate the randomized intervention were not provided (*e.g.* “patients were randomized to. . .”; “treatment was assigned in random order. . .”; “patients were randomly allocated to. . .”). Allocation concealment was rated as inadequate when methods of randomization such as alternation, number of medical record, date of birth (odd or even years), or unsealed envelopes were used or where any information in the study indicated that investigators or participants could influence the assignment to treatment groups. Blinding of participants, investigators, and outcome assessors was recorded as “not stated” when there was no report of any blinding procedure. When the RCT was reported as “double blinded” but clear indication existed that this was not the case (*e.g.*, a RCT that was reported as double-blinded when there was an obvious difference in route or frequency of administration of the two interventions), the item was recorded as “no blinding” of participants, or investigators, or outcome assessors (17,18). “Intention-to-treat” analysis was rated as adequate when sufficient data were included to confirm that the analysis was undertaken according to the treatment assignment, irrespective of whether “intention-to-treat” was stated or not. Completeness at follow-up was calculated from the number of patients for which at least one outcome measure was obtained divided by the total number randomized. Possible predictors of trial quality were explored: content area (*e.g.*, glomerulonephritis), year of study publication, and industry support.

Frequency of Intervention Questions in Nephrology Journals

To determine whether the expected low number of RCT in nephrology journals was because few intervention questions were asked or

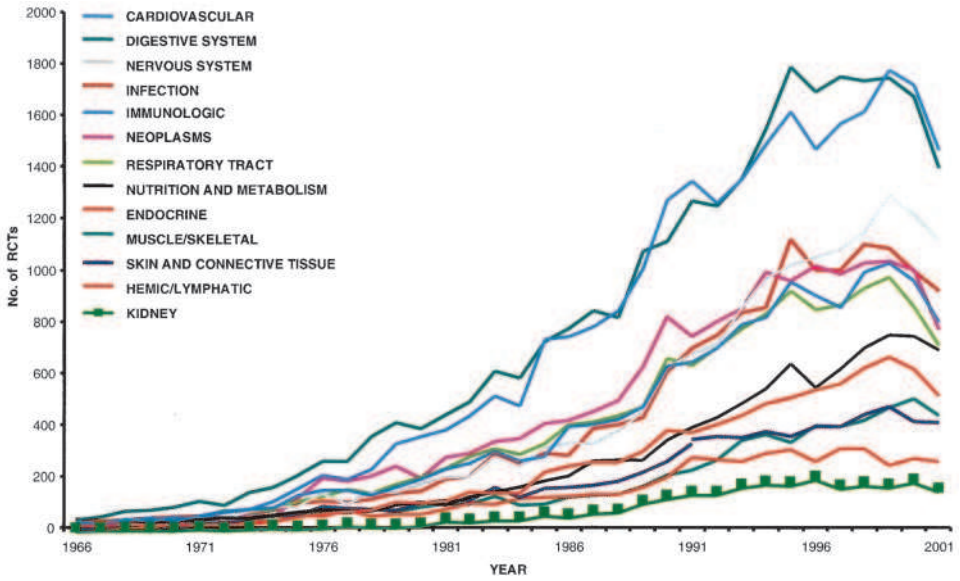

Figure 1. Number of randomized controlled trials (RCT) published in nephrology and 12 other specialties of internal medicine from 1966 to 2002.

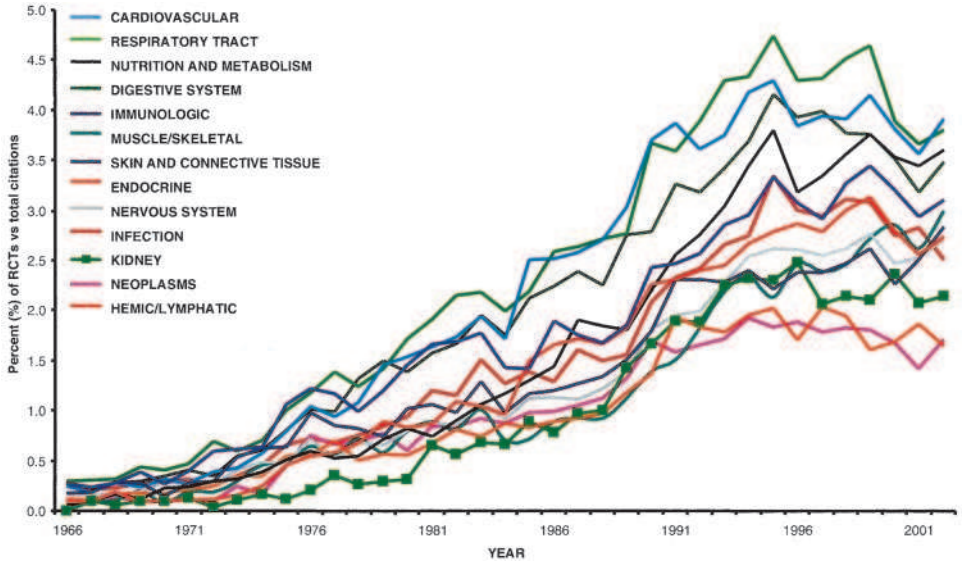

Figure 2. Percentage of RCT *versus* total citations in nephrology and 12 other specialties of internal medicine from 1966 to 2002.

because non-RCT study designs were used to answer intervention questions, all issues of the three nephrology journals with the highest impact factor (*Journal of the American Society of Nephrology*, *Kidney International*, *American Journal of Kidney Diseases*) published in 2001 were hand-searched by two independent investigators (GFMS, JC). This analysis was limited to one year and only the three major nephrology journals because we wanted to evaluate the current status of published nephrology research. Every publication was classified into four categories (basic research, intervention questions, reviews, editorials and other type of study). Publications addressing an intervention question were broadly defined as any study that evaluated the association between a group of patients and an intervention and classified into the following study designs: RCT, cohort studies, case series, cross-sectional analytical studies, and historical control studies. Disagreement between the two investigators were resolved by consensus, and a third investigator was involved in discussing disagreement on quality assessment for RCT included in the systematic reviews.

Statistical Analyses

The precision of point estimates of the frequency of trials in each specialty per year was given as 95% CI calculated using Poisson distributions (19), and the precision of point estimates for proportion of citations that were trials given as 95% CI calculated using the exact method. Differences in the frequency of reporting of quality items were compared across groups using the exact χ^2 statistic, and variation over time was assessed with the Mantel-Haenszel χ^2 statistic for trend. Data were computed and analyzed by SAS V8.2 (SAS Institute, Inc.).

Results

RCT in Nephrology and Other Specialties of Internal Medicine

Figure 1 shows the trend in publication of RCT by specialty of internal medicine. The total of 2779 (95% CI, 2677 to 2885) RCT published in nephrology from 1966 to 2002 is lower than that of any other specialty of internal medicine, whereas the number of RCT in other specialties in the same time period varied from 5335 (95% CI, 5256 to 5546) RCT in hematology to 27109 (95% CI, 26778 to 27425) RCT published in cardiology. A common ascending trend from 1966 to 2001 is observed in the publication of RCT in all specialties of internal medicine, but there has been a fall from 1998 to 2002. In nephrology, this ascending trend has been slower than in the other specialties.

Proportion of Citations that are RCT

Figure 2 shows the proportion of citations that are RCT, grouped by specialty and by year, from 1966 to 2002. A total of 240789 studies were published on kidney diseases from 1966 to 2002, 2779 of which (1.15%) were RCT (95% CI, 1.11 to 1.20%). Like other specialties, this proportion has risen over time, and there is evidence of improvement relative to other specialties, but nephrology remains with the third lowest proportion of citations that are RCT of the 13 specialties evaluated.

Coverage of RCT within Nephrology

Figure 3 is a plot of the number of RCT *versus* the total number of publications in ten major areas of nephrology, with

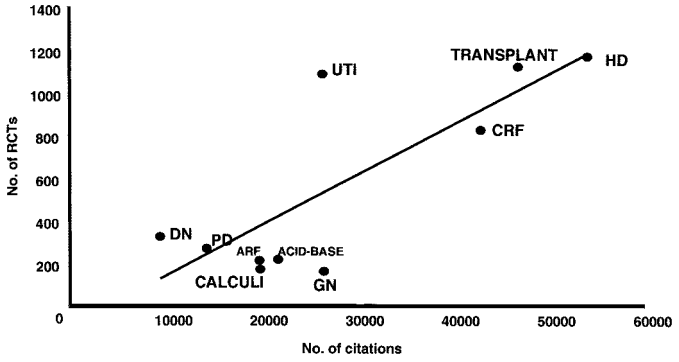

Figure 3. Percentage of RCT *versus* total citations published in ten specific areas of nephrology (1966 to 2002).

Table 1. Quality assessment of a selection of 430 randomized controlled trials (RCT) in nephrology, dialysis, and transplantation

Quality Item	Random Sample (n = 160) % (95% CI)	Diabetic Nephropathy Prevention (n = 156) % (95% CI)	Primary and Secondary Glomerulonephritis[a] (n = 37) % (95% CI)	Hemoglobin Targets Adequacy (n = 16) % (95% CI)	Transplant[b] (n = 61) % (95% CI)	Total (n = 430) % (95% CI)	P Value[c]
Allocation concealment							
adequate	4.3 (1.7 to 8.8)	7.7 (3.5 to 11.9)	7.9 (1.6 to 21.3)	0.0 (0.0 to 20.5)	16.4 (8.1 to 28.0)	7.4 (4.9 to 9.8)	0.07
unclear	92.6 (87.2 to 96.0)	89.7 (84.9 to 94.4)	84.3 (68.7 to 93.9)	100.0 (79.4 to 100.0)	80.4 (68.1 to 89.4)	89.4 (86.4 to 92.2)	
inadequate	3.1 (1.0 to 7.1)	2.6 (0.1 to 5.1)	7.8 (1.6 to 21.3)	0.0 (0.0 to 20.5)	3.2 (0.0 to 11.3)	3.2 (1.5 to 4.9)	
Blinding							
participants	37.5 (29.9 to 45.4)	60.2 (52.5 to 67.8)	18.4 (7.7 to 14.3)	43.7 (19.7 to 70.1)	27.8 (17.1 to 40.8)	43.0 (38.3 to 47.7)	<0.05
investigators	32.5 (25.3 to 40.3)	52.5 (44.6 to 60.3)	13.1 (4.4 to 28.0)	25.0 (7.2 to 5.2)	14.7 (6.9 to 26.1)	35.3 (30.8 to 39.9)	
outcome assessors	1.8 (0.3 to 5.3)	12.1 (6.9 to 17.2)	2.6 (0.6 to 13.8)	0.0 (0.0 to 20.5)	14.7 (6.9 to 26.1)	7.4 (4.9 to 9.9)	
Intention-to-treat							
yes	33.7 (26.4 to 41.6)	25.1 (18.3 to 31.9)	42.1 (26.3 to 59.1)	12.5 (1.5 to 38.3)	26.3 (15.7 to 39.0)	29.7 (25.1 to 33.8)	<0.01
no	53.2 (45.0 to 61.0)	58.3 (44.6 to 60.3)	44.8 (28.6 to 61.6)	87.5 (61.6 to 98.4)	19.7 (10.5 to 31.8)	51.0 (46.1 to 55.6)	
unclear	13.1 (8.3 to 19.3)	16.6 (10.7 to 22.4)	13.1 (4.4 to 28.0)	0.0 (0.0 to 20.5)	54.0 (40.8 to 66.9)	19.3 (15.3 to 22.7)	
Lost to follow-up (%)[d]							
0–20	86.8 (81.5 to 92.0)	85.5 (79.9 to 91.0)	92.1 (78.6 to 98.3)	68.7 (41.3 to 88.9)	100 (94.1 to 100.0)	86.7 (74.7 to 89.5)	0.28
20–40	9.5 (5.3 to 14.9)	12.4 (7.2 to 17.5)	5.3 (0.6 to 17.7)	25.1 (7.2 to 52.3)	0.0 (0.0 to 5.78)	10.2 (6.5 to 12.0)	
>40	3.7 (1.4 to 8.0)	2.1 (1.1 to 8.2)	2.6 (0.0 to 13.8)	6.2 (0.1 to 30.2)	0.0 (0.0 to 5.78)	3.1 (0.9 to 3.7)	

[a] Including ten trials from an ongoing Cochrane systematic review on immunosuppressive and non-immunosuppressive agents for IgA nephropathy and 27 trials from an ongoing Cochrane systematic review on treatment for lupus nephritis.

[b] Including 32 trials from an ongoing Cochrane systematic review on tacrolimus *versus* cyclosporin for renal transplant recipients and 29 trials from an ongoing Cochrane systematic review on interleukin-2 for renal transplant recipients.

[c] χ^2 test for difference in proportions, 8 degrees of freedom.

[d] Excluding trials where assessment of number of patients lost to follow-up was not possible or unclear.

the slope of the line corresponding to the average proportion of citations that are RCT across all areas of nephrology. Diseases with proportions of RCT well above average were urinary tract infections (UTI) (4.0%), diabetic nephropathy (DN) (3.2%), and kidney transplantation (TRANSPLANT) (2.4%). Diseases with proportions of RCT well below average were acid-base imbalance (ACID-BASE) (0.9%) and glomerulonephritis (GN) (0.89%, CI 0.78% to 1.00%).

Quality of Randomized Trial Reporting

Although there was significant variability across the 430 trials sampled, it is clear that the many nephrology trials are suboptimal in their reporting practices (Table 1). Reports of adequate allocation concealment were very uncommon (7.4%), with the majority of trials not reporting the methods by which patients were allocated to the randomized intervention. In 3.2% of RCT, the methods of allocation were clearly inadequate (alternation, date of birth, alternate medical records) so that investigators could predict with certainty what the next patient would be allocated to.

Blinding of participants and investigators (often termed "double-blinding") was more common but was not reported in the majority of trials, and blinding of outcome assessors was rarely reported (7.4%). "Intention-to-treat" analysis was performed in 29.7% of RCT and was not reported in 51.0%. It was not possible to assess "intention-to-treat" analysis in 19.3% because of insufficient data on the number of randomized and analyzed patients and whether analysis was by allocated intervention or "per protocol" (*i.e.*, what the patient actually received). Unlike all other quality domains, completeness of follow-up was high, with more than 80% of trials having fewer than 20% of randomized patients "lost" during the study, with no outcomes evaluated.

Figure 4 presents an evaluation of quality of nephrology RCT over time. There has been little variation over the past 30 yr in the quality domains of blinding, "intention-to-treat" analysis and loss to follow-up. There has been a small but statistically significant decrease in the proportion of trials with unclear allocation concealment. Reported industry involvement was not associated with the quality of reporting (Table 2), but there was no mention of industry funding in 29.1% of trials evaluated.

Intervention Questions in Nephrology Journals

Table 3 shows that the major reason why so few RCT were done and published in nephrology journals was because rela-

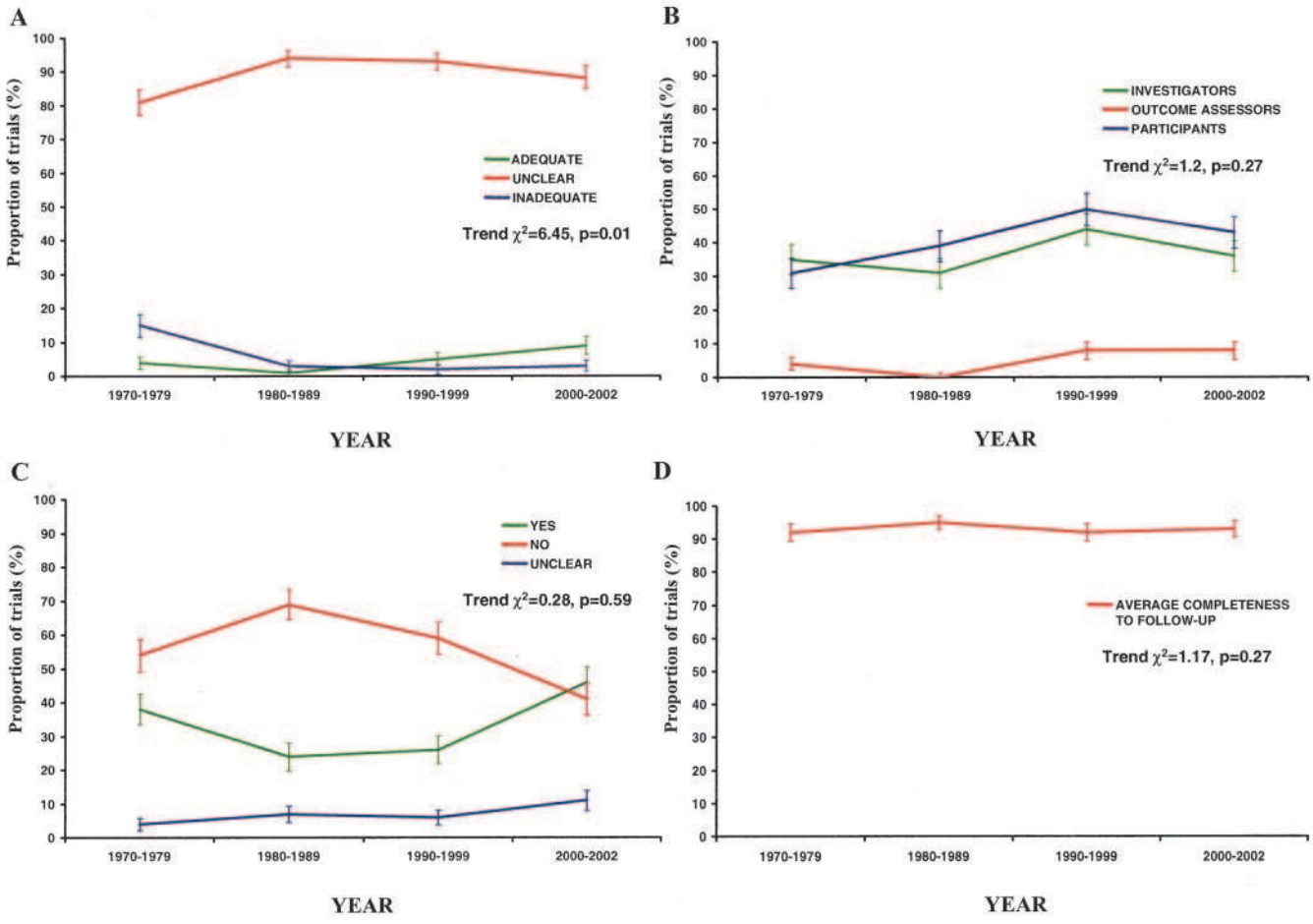

Figure 4. Allocation concealment (A), blinding (B), use of "intention-to-treat" analysis (C) and percentage of patients lost to follow-up (D) in 430 nephrology randomized controlled trials. Trend from 1966 to 2002.

Table 2. Comparison of the quality of 209[a] RCT from ongoing or published Cochrane systematic reviews on major topics in nephrology and dialysis according to whether or not the pharmaceutical industry was involved in the trial

Quality Item	Industry Involved (%) (95% CI) (n = 96)	Industry Not Involved (%) (95% CI) (n = 44)	Industry Involvement Uncertain (%) (95% CI) (n = 69)	P Value[b]
Allocation concealment				
adequate	8.3 (2.6 to 13.4)	11.4 (3.8 to 24.5)	2.9 (1.0 to 6.8)	0.08
unclear	90.6 (80.3 to 93.8)	86.3 (75.4 to 96.2)	89.9 (82.7 to 97.0)	
inadequate	1.1 (0.0 to 5.7)	2.3 (0.1 to 12.0)	7.2 (1.1 to 13.3)	
Blinding				
participants	71.9 (59.7 to 78.2)	27.3 (14.9 to 42.9)	36.2 (24.8 to 47.5)	0.95
investigators	61.5 (49.1 to 8.4)	18.2 (8.2 to 32.7)	34.8 (23.5 to 43.0)	
outcome assessors	12.5 (5.5 to 18.5)	4.5 (0.7 to 20.8)	8.7 (2.0 to 15.3)	
Intention-to-treat analysis				
yes	33.3 (21.7 to 40.2)	29.5 (23.5 to 61.0)	27.6 (17.0 to 38.1)	0.26
no	51.1 (39.0 to 59.0)	65.9 (50.1 to 79.5)	63.2 (50.8 to 73.7)	
unclear	15.6 (7.8 to 22.1)	4.6 (0.5 to 15.4)	10.1 (2.9 to 17.2)	
Lost to follow-up				
0–20	84.5 (67.2 to 84.7)	88.4 (74.9 to 96.1)	87.7 (79.9 to 95.4)	0.58
20–40	14.3 (6.1 to 19.9)	9.3 (2.5 to 22.1)	9.2 (2.3 to 16.0)	
>40	1.2 (0.0 to 5.9)	2.3 (0.1 to 13.8)	3.1 (0.9 to 7.1)	

[a] This analysis excludes data of 61 trials from two ongoing Cochrane systematic reviews on transplant immunosuppression because information regarding funding of trials was not available.
[b] χ^2 test for difference in proportion, 6 degrees of freedom.

tively few intervention questions were asked, rather than intervention questions being addressed by non-RCT study designs. Of the three highest-ranking specialist nephrology journals, each journal contributed about 10 RCT from 20 to 30 publications addressing intervention questions. This represented about one third of the number of editorials or review articles. The largest single category of publications was basic science.

Discussion

We have found that the number of RCT published in nephrology, and the proportion of citations that are RCT, is very low compared with other internal medicine specialties. Our data suggest that this is primarily because few intervention questions are asked, rather than because intervention questions are not investigated with the appropriate study design (RCT). We have also shown that the number of RCT to inform clinical decision making is very low in some areas of nephrology, particularly glomerulonephritis, that the quality for reporting nephrology RCT is generally suboptimal, and that there has been little improvement over time.

Our study was not designed to determine whether the methodological deficiencies in the reports of RCT also represent problems in design. However, previous studies have shown that poor-quality reports are associated with biased estimates of intervention effects; importantly, on average this leads to overestimating the true effects of interventions (2,11,20). These data imply that reporting problems are proxies of design issues.

Studies similar to ours have been conducted in other specialties (3,21–24). These also show problems in the conduct and design of trials in other specialties.

Our data on the quantity and quality of trials in nephrology is of major concern and suggests that clinical research in nephrology, and trials in particular, is in crisis. This is not a new idea, but this study is the first to provide empiric evidence for this observation. It should be emphasized that this problem is not unique to clinical research in nephrology, but is representative of clinical research in medicine in general (25–28). The Clinical Research Roundtable at the Institute of Medicine was established to address these problems and recently reported. One of the major findings was the block in the translation of basic science to human studies (as well as a block in the translation of new knowledge into clinical practice and health decision making) (25).

Our study does have important limitations. It was designed to evaluate the quality and quantity of trials in nephrology, rather than to identify the mechanisms for a relatively low number of published trials in nephrology compared with other internal medicine specialties. The findings that the quality of trial reporting is suboptimal and that many areas of nephrology are not supported by RCT would not be surprising to many observers. Our analysis of nephrology journals suggests that this is primarily because non-intervention questions are asked by nephrology researchers rather than non-RCT designs being used to address intervention questions. Why nephrology researchers address fewer intervention questions than researchers in other internal medicine specialties is open for speculation. Clearly adjusting only for the number of citations does not

Table 3. Number and types of publications in major nephrology journals in 2001

Journal	Total Number of Publications	Basic Research Articles (%)	Reviews and Editorials (%)	Other[a] (%)	Publications Dealing with Intervention Questions[b] (%)	Number of RCT[c] (%)	Proportion of Intervention Questions[b] Addressed by RCT *n* (%)
Journal of the American Society of Nephrology	291	204 (70.1)	13 (4.4)	57 (19.5)	17 (5.8)	9 (3.0)	9/12 (75.0)
Kidney International	429	294 (68.5)	34 (7.9)	79 (18.4)	22 (5.1)	12 (2.7)	12/22 (54.5)
American Journal of Kidney Diseases	238	51 (21.4)	26 (10.9)	117 (49.1)	34 (14.2)	11 (4.6)	11/34 (32.3)

[a] Case reports, non-experimental pathology, clinical research not dealing with intervention questions.
[b] Publications whereby a question is formulated in terms of a relationship between the patient, some "exposure" to a treatment, and one or more specific outcomes of interest.

address inequalities across specialties, which may explain these differences, such as number of patients eligible for trial participation, funding (both by the pharmaceutical industry and governmental and other granting bodies), and the number of new pharmaceuticals and devices. It may well be that "adjustment" for these inequalities may mean that nephrology as a community is doing comparatively well. However, the question is, compared with what. Compared with other specialties, perhaps; but if the comparator is the ideal of a firm basis for clinical decision making across all areas of nephrology by well-designed, conducted, and reported trials, there is clear room for improvement. It is likely that the reasons identified for blocks in the translation of basic science to human studies by the Clinical Research Roundtable—lack of willing participants, regulatory burden, fragmented infrastructure, incompatible databases, lack of qualified investigators, career disincentives, practice limitations, high research costs, and lack of funding—are equally true for nephrology as they are for the rest of the medical research community (25,29,30).

Given the findings of our study, what can be done to improve the quality of reporting of RCT in nephrology? This is a problem for triallists, reviewers, and editors of journals, and is clearly not just a problem for nephrology RCT.

Editors from most major biomedical journals have collaborated since 1984 to develop a set of guidelines for the reporting of RCT (31). These Consolidated Standards of Reporting Trials (CONSORT) were revised and published widely in 2001 and provide comprehensive checklists for triallists to ensure that RCT are reported accurately and comprehensively (32,33). Adoption of these guidelines has resulted in some improvement in the quality of trial reporting (34). It would be feasible for triallists, reviewers, and editors involved in nephrology trials to accept and use these CONSORT guidelines, which to date have been endorsed by 152 major biomedical journals, an exponentially growing list which still does not include nephrology journals (http://www.consort-statement.org/journals.htm).

Other initiatives include the "Protocol Reviews" from *The Lancet*, which aim to assesses protocols of randomized trials from a clinical and statistical point of view, to encourage good principles in design of clinical research, publicize a list of accepted protocols and make a provisional commitment to publication of the main clinical endpoints of studies (http://www.thelancet.com/info/info.isa?n1=authorinfo&n2=Protocol+reviews).

What can be done to improve the number of trials in nephrology? Does a relatively small specialty with relatively rare diseases mean that trials are impractical? Groups such as the European Vasculitis Study Group and the North American Pediatric Transplant Collaborative Study Group (NAPRTCS; http://spitfire.emmes.com/study/ped/index.htm) have overcome the small-numbers barrier by multicenter collaboration. Another advance in trial design has been the large, simple trial that has been strongly advocated by Peto *et al.* (35). Costs can be limited and trial design strengthened by only assessing outcomes that are clinically important and that are routinely

collected rather than adding in laboratory expensive tests of uncertain clinical significance.

Finally, and perhaps most importantly, there may need to be a cultural change in nephrology toward RCT and the value of medical "evidence," a change which may already be starting to occur. The importance of RCT in nephrology is widely accepted, but there is some way to go before the majority of kidney patients are entered in RCT when it is unclear what the best intervention is. Any additional improvements will be driven by a well-trained workforce available in nephrology clinical research, which will only occur when a track record in trials and clinical research is regarded as equal to a track record in basic science for trainee nephrologists seeking a faculty position and for the promotion of senior nephrologists (25,36).

An important agency in the identification, evaluation, and synthesis of available RCT and the promotion of clinical research and research training is the Cochrane Collaboration (37). The Cochrane Renal Group (http://www.cochrane-renal.org/) is specifically responsible for coordinating the production of systematic reviews relating to topics in nephrology, dialysis, and renal transplantation. In addition, this group coordinates and updates the specialist registry of nephrology RCT, which contributes to the Cochrane Central register of Controlled Trials (CENTRAL). Both the production of systematic reviews and the thorough search for RCT to hold and update the renal registry, help to identify those areas where RCT are lacking (both in number and in quality). This ensures further improvement in clinical research and development of a solid base of evidence for decision making.

In conclusion, we have shown that RCT in nephrology are relatively few and the quality of reporting has substantial room for improvement. These observations should be regarded as challenges, not as a blame, for all sectors of the nephrological community: patients, clinicians, triallists, reviewers, and editors. The dual problems of number and quality are both remediable. We would hope that being aware of the problems would prompt improvements by better adherence to the CONSORT guidelines, greater attention to the trial methods and not just the results, involving experts in trial design and reporting, multicenter collaboration, and larger and simpler trials.

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