SPECIAL ARTICLE www.jasn.org

Quantity and Reporting Quality of Kidney Research

Markos Kyriakos Tomidis Chatzimanouil, Louise Wilkens, and Hans-Joachim Anders

Division of Nephrology, Medizinische Klinik and Poliklinik IV, Klinikum der Universität München, Ludwig Maximilians University München, Munich, Germany

ABSTRACT

Background In 2004, researchers reported that the number of nephrology clinical trials was low and that the reporting quality of such trials was suboptimal. Furthermore, the number or quality of preclinical kidney-related studies has not been systematically evaluated.

Methods We performed a systematic review of randomized clinical trials published in 1966–2017 (listed in the Cochrane Library) and preclinical studies published in 1945–2017 (listed in PubMed). For reporting quality analysis, we evaluated the final main paper of 118 clinical trial reports and 135 preclinical studies published in leading journals in 1996, 2006, and 2016 on the basis of criteria from the widely used CONSORT and ARRIVE guidelines.

Results The annual number of reports of clinical kidney-related trials more than doubled between 2004 and 2014 along with reports in other medical disciplines. Hypertension remains the dominant focus of study, but ongoing trials also center on CKD, ESRD, and AKI. The reporting quality analysis revealed improvements, but deficits in reporting of clinical trial design, mode of randomization, and intention-to-treat analysis remain. Annual numbers of kidney-related preclinical studies remained low between 1945 and 2017 compared with other disciplines. Reporting quality analysis of preclinical studies revealed substantial reporting deficits across all leading journals, with little improvement over the last 20 years, especially for group size calculations, defining primary versus secondary outcomes, and blinded analysis.

Conclusions Nephrology studies keep increasing in number but still lag behind other medical disciplines, and the quality of data reporting in kidney research can be further improved.

J Am Soc Nephrol 30: 13–22, 2019. doi: https://doi.org/10.1681/ASN.2018050515

In 2004, Strippoli *et al.*[1] presented quantitative and qualitative analyses of the clinical trials performed in the field of nephrology. As a disappointing finding, kidney-related clinical trials were not only low in number compared with other medical disciplines but also of poor quality, either as conducted or reported.[1] The authors concluded: "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."[1]

Increasing abstract submissions to international kidney conferences, a substantial increase in nephrology journals, and increased scientific productivity of evolving countries give the impression that the number of kidney-related clinical trials may have substantially increased compared with 15 years ago. In addition, guidelines for the conduct and reporting of clinical trials and preclinical studies have become available, and adherence is requested by the leading journals in internal medicine and nephrology.[2,3] Thus, we speculated on an increasing quantity and reporting quality of kidney-related clinical trials within the last 15 years as well as preclinical studies, the latter not being systematically evaluated before.

METHODS

The study is composed of two parts. One is the quantitative analysis regarding the numbers (both total and per year) of randomized, controlled trials (RCTs) and preclinical studies in the field of nephrology compared with other specialties of internal medicine as well as the distribution of nephrology studies inside the field. The second part is a qualitative analysis of a sample of papers (RCTs and preclinical studies) on the basis of criteria for trial reporting using established guidelines, such as the CONSORT Statement and the ARRIVE guidelines. A test analysis using ten RCTs and ten preclinical studies was performed by two investigators (M.K.T.C. and L.W.), and

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Hans-Joachim Anders, Medizinische Klinik and Poliklinik IV, Klinikum der Universität München—Innenstadt, Ziemssenstrasse 1, 80336 Munich, Germany. Email: hjanders@med.uni-muenchen.de

it defined an interobserver analytical coherence of 90.3%.

Quantitative Analyses of Clinical RCTs

Databases were selected for the RCTs as well as the preclinical analyses from which the data were extracted. For the RCTs, the database selected was the Cochrane Library, mainly because it uses an integrated system of trees and subtrees for each MeSH term, which provided a better overview of the research process compared with other databases. Because the Cochrane Library is limited to clinical trials, PubMed was used for the preclinical studies.

Number and Proportion of RCTs in Nephrology Compared with Other Specialties

For the question on the number of RCTs in nephrology in comparison with other specialties, an MeSH term, thought to most accurately summarize the data in question, or a combination of two or more relevant MeSH Terms was used for each specialty as listed in Supplemental Material.

Coverage of RCTs within Nephrology

RCTs from nine areas were retrieved for the years 1966–2016 using the following MeSH terms: "Renal Insufficiency, Chronic," "Kidney Transplantation," "Diabetic Nephropathies," "AKI," "Peritoneal Dialysis," "GN," "Hypertension, Renal," "Kidney Calculi," and "Hypertension." Because "Renal Dialysis," "Peritoneal Dialysis," and "Kidney Transplantation" were subterms of the more general MeSH term "RRT," we created another term, named "Kidney Exp.," to include all of them.

Quantitative Analyses of Preclinical Studies

A similar search regarding the preclinical studies was conducted using PubMed by applying the same MeSH terms (before the conversion to match the Cochrane System) used for the RCT search. To limit the results specifically to animal trials, the limit "Animals" in the PubMed interface was used, and the results were extracted for the timeline 1945–2016. A per year categorization was applied for the construction of the per year diagrams.

Qualitative Analyses

Paper Selection Criteria

We searched the PubMed database. As representative RCT sample periods, we selected the years 1996, 2006, and 2016 and identified all kidney-related RCTs from the top five journals as assessed by impact factor and the number of kidney-related RCTs per year: *The New England Journal of Medicine* (NEJM) *The Lancet*, *Kidney International*, *Journal of American Society of Nephrology* (JASN), and *American Journal of Kidney Diseases* (AJKD). For the qualitative analysis of preclinical studies, we used the same years (1996, 2006, and 2016) but limited sample collection to January to March of each year from the journals JASN, *Kidney International*, *Nephrology Dialysis Transplantation* (NDT; selected by impact factor and tendency to publish preclinical studies in the kidney domain) using the PubMed database. The search for the RCTs was conducted using the MeSH term "kidney diseases" and the limits "Randomized Controlled Trial" and "Humans," limited each time by the specific journal of publication and the appropriate year. For the animal trials, the same MeSH term "kidney diseases" was used and limited by "Animals," and the search was conducted per year for each of the three journals. Only results published inside the first 3 months of each year were included. Inclusion criteria for both the RCTs and the preclinical studies were that the papers were original articles, in English, and published online. Review articles, editorials, special articles, and commentaries were excluded. From the RCT analysis, observational, prospective, and nonrandomized trials were excluded. Because the ARRIVE criteria apply to *in vivo* animal experiments, preclinical studies exclusively mechanistic or only *in vitro* studies were excluded.

Quality Assessment

The methodological quality of all of these studies was assessed by one independent investigator (M.K.T.C.) using the criteria mainly on the basis of the original CONSORT 2010 checklist for RCTs[2] and the ARRIVE guidelines for the preclinical studies.[3] Only the main body of the final paper was analyzed, and supplementary information and previously published study protocols were not analyzed. For the RCT analysis, we extracted data by allocating points (zero for insufficient, one for unclear or insufficiently reported, and two for adequate reporting) to each of the 19 core items of the CONSORT Statement regarding "Title and Abstract," "Introduction, " "Methods," and "Results" and each of the subitems. In addition, to match the previous analyses from Strippoli *et al.*[1] and Deo *et al.*,[4] two extra items were added (*i.e.*, "Intention-to-treat analysis" and "Loss-to-analysis"). "Intention-to-treat analysis" was rated as adequate when sufficient data were included to confirm that the analysis regarding the primary end point was undertaken according to the treatment assignment and that the numbers of participants randomly assigned were identical to the numbers of participants analyzed, irrespective of whether "intention-to-treat" was stated or not. We also tried to calculate the "Loss-to-analysis" for each trial included so as to try to determine what percentage of participants

Significance Statement

Turning the research lens inward to assess the state of nephrology research, this systematic review assesses the quantity of clinical trials and preclinical studies reported over the past five to seven decades, finding that, although the numbers of clinical and preclinical studies have substantially increased with time, nephrology still lags behind other medical disciplines. In addition, the authors' quality analysis of nephrology research reports published by leading journals in the past two decades (on the basis of applying criteria from the widely used CONSORT and ARRIVE research guidelines to assess the main body of the final paper) reveals that, although deficits remain, clinical trial reporting quality has improved. However, many gaps persist in reporting quality of preclinical studies. Identifying deficits may help improve quantity and quality of kidney research and accelerate advancement.

randomly assigned was not included in the analysis. In total, 35 items regarding trial reporting for RCTs were graded.

For the analysis of the preclinical studies, the 15 core items of the ARRIVE guidelines regarding "Introduction," "Methods," and "Results" were included. In addition, we added to the core items 3, 6 (subitem "d: A time line diagram or flow chart" was included by initiative of the researchers), 10, and 13. The subitems were assessed separately; otherwise, they were included in the grading method of the core item (zero for insufficient, one for unclear or insufficiently reported, and two for adequate reporting) for a total of 23 graded items regarding trial reporting for animal trials. A more detailed view of the criteria used to assess the quality of the trials and the grading system used to evaluate each item separately can be found in Supplemental Tables 1–3.

Statistical Analyses

Data are presented as mean±SD. Comparison of groups was performed using ANOVA, and *post hoc* Bonferroni correction was used for multiple comparisons. A value of $P<0.05$ was considered to indicate statistical significance.

RESULTS

Number and Trends of Clinical Trials in Nephrology Compared with Other Medical Disciplines

Our Cochrane MeSH tree analysis displayed the reported clinical trials across medical disciplines (Figure 1A). Neurology and cardiology kept reporting the most clinical trials since the early 1990s, whereas both MeSH term "kidney diseases" and its definition extended by RRTs ("Kidney Exp.") remained at the lowest ranks of medical disciplines (Figure 1A). The average slope of additional clinical trials reported each year from 1966 to 2003 was 27.7±14.6 for all disciplines, and slopes were 7.5 and 11.0 for kidney diseases and expanded kidney diseases, respectively (both *P* values versus all disciplines <0.001). Since the last evaluation in 2003 (years 2004–2014), the slope has increased to 68.4±42.2 for all disciplines, indicating a profound increase in number and spread among the disciplines in annual clinical trial reporting. In the same period, kidney diseases and their expanded definition increased to 23.3 and 31.2, respectively (both *P* values versus all disciplines <0.001). The years 2015 and 2016 were excluded from this analysis, because delays in MeSH term indexing within the PubMed database led to declining curves for all disciplines (M. Collins, United States National Library of Medicine, personal communication). Over the entire period, all disciplines displayed an annual increase of reported clinical trials of 38.4±21.2, whereas kidney diseases displayed an annual increase of reported clinical trials of 11.3 and expanded kidney diseases displayed an annual increase of reported clinical trials of 15.8 (both *P* values versus all disciplines <0.001). Together, the number of kidney-related clinical trials has increased but less so compared with other disciplines.

Clinical Trial Coverage of Different Kidney Disease Entities

Cochrane database MeSH tree analysis for trial coverage of different disease entities within the field of nephrology showed that clinical trials addressing hypertension have been the highest in number starting from the 1970s and that they continue to predominate (Figure 1B). RRT-related trials were already much lower in number, and disease entities, such as GN, AKI, or kidney calculi, although all being prevalent, contribute only a few papers to clinical trial activity (Figure 1B).

Number of Preclinical Studies in Nephrology Compared with Other Medical Specialties

Preclinical research activity was analyzed using PubMed from 1945 to 2017. Oncology, infectious diseases, and neurology have reported the most studies since the 1990s, whereas kidney disease–related studies, in narrow and expanded definitions, remain at the low end among the medical disciplines since 1945 (Figure 2A). The average slope of additional preclinical studies reported each year from 1945 to 2003 was 95.0± 60.2 for all disciplines, and the average slopes were 26.7 and 30.5 for kidney diseases and expanded kidney diseases, respectively (both *P* values versus all disciplines <0.001). Since the last evaluation in 2003 (years 2004–2014), the slope has increased to 313.8±217.0 for all disciplines, indicating a profound increase in number and spread among the disciplines in annual preclinical study reporting. In the same period, studies on kidney diseases and their expanded definition increased to 88.5 and 89.3, respectively (both *P* values versus all disciplines <0.001). Over the entire period, all disciplines display an annual increase of reported clinical trials of 133.6±85.1, whereas kidney diseases display an annual increase of reported clinical trials of 37.8 and expanded kidney diseases display an annual increase of reported clinical trials of 40.5 (both *P* values versus all disciplines <0.001). Thus, although increasing in number, the count of kidney-related preclinical studies is lagging behind other disciplines.

Preclinical Trial Coverage of Different Kidney Disease Entities

Studies focusing on hypertension by far outweigh all other kidney disease entities and preclinical research as well (Supplemental Figure 1), but preclinical kidney research topics covered a broader range of topics than seen in clinical trials (Figure 2B). Whereas studies on kidney transplantation revealed an early peak in the mid-1960s, preclinical research activity on GN substantially increased starting from the early 1980s (Figure 2B). As a more recent trend, studies addressing AKI, CKD, and diabetic nephropathy have become the most popular preclinical research topics within the last decade (Figure 2B).

Quality of Clinical Trial Reporting

To assess the quality of trial reporting, we selected 125 publications from top medical and nephrology journals as listed in Supplemental Figure 2. Seven had to be

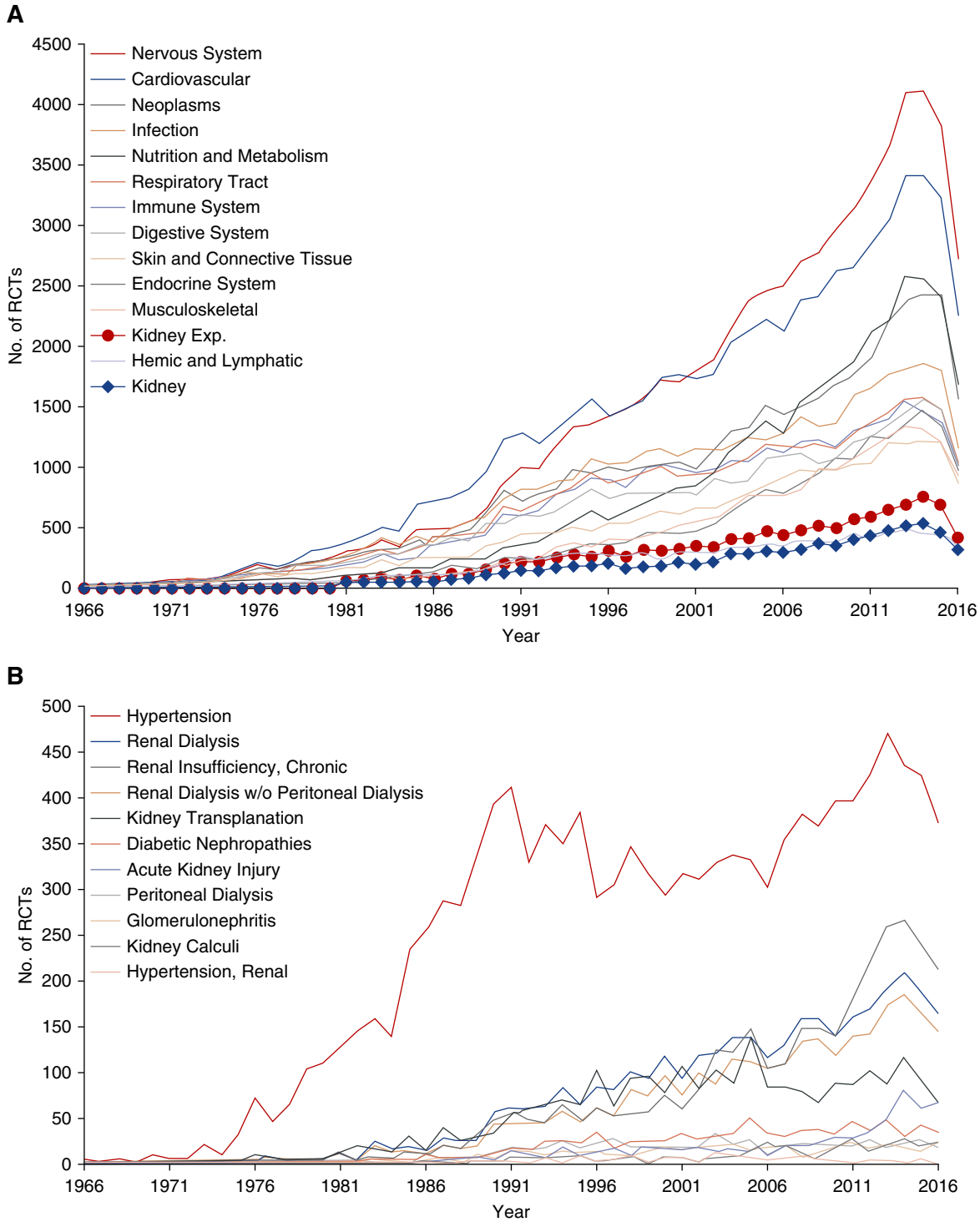

Figure 1. Quantitative analysis and topic coverage of clinical trials in medical disciplines identified from the Cochrane database. Several MeSH terms were applied to best cover each discipline as described in Methods. Nephrology ("Kidney") is represented by the MeSH term "kidney diseases." Expanded (Exp.) nephrology ("Kidney Exp.") also covers the MeSH term "RRT" (subterms included "renal dialysis," "peritoneal dialysis," and "kidney transplantation"). (A) Annual number of clinical trials per discipline from 1966 to 2016. The sudden decline in numbers in the years 2015–2016 should relate to delays in data inclusion. (B) Disease entities as defined by the available MeSH terms were quantified as described in Methods. Annual number of clinical trials per kidney disease entity from 1966 to 2016. The sudden decline in numbers in the years 2015–2016 should relate to delays in data inclusion. RCT, randomized, controlled trial; MeSH, medical subject heading.

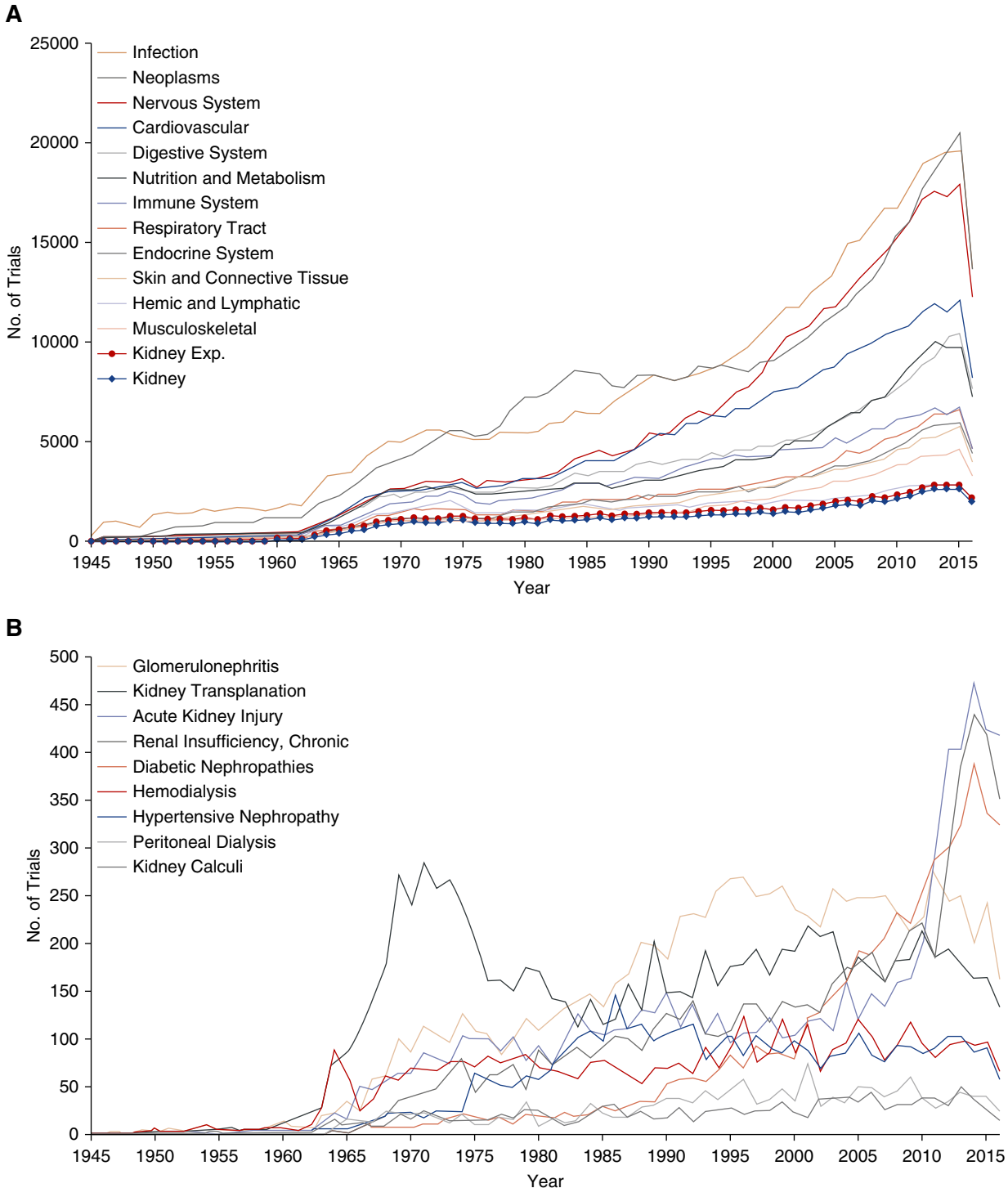

Figure 2. Quantitative analysis of preclinical studies identified from PubMed. Several MeSH terms were applied to best cover each discipline as described in Methods. Nephrology ("Kidney") is represented by the MeSH term "kidney diseases." Expanded (Exp.) nephrology ("Kidney Exp.") also covers the MeSH term "RRT." (A) Annual number of preclinical studies per discipline from 1945 to 2016 and (B) topic coverage among the preclinical studies trials of the nephrology domain (B). The sudden decline in numbers in the years 2015–2016 should relate to delays in data inclusion. MeSH, medical subject heading.

deleted for invalidity criteria (two prospective trials, one observational trial, one nonrandomized trial, and three nonoriginal articles). The main bodies of the remaining 118 papers were scored for the CONSORT criteria as not reported, insufficiently reported, or sufficiently reported as listed in Supplemental Table 1.[2] The title identified studies as RCTs in only 23.7%. Abstracts provided a structured summary of the trial design in 51.7% (Supplemental Table 2). The introduction named the objectives and a clear hypothesis in 82.2%. The method sections specify the precise trial design, including allocation ratio, in only 17.8% and any changes to trial design and the respective reasons after trial commencement in ≤1.7%. A precise description of how and when the intervention was administered was reported in 66.9% of the studies. A precise definition of the prespecified primary and secondary outcomes was reported in ≤60.2% of the trials. Information about sample size calculation was lacking in 52.5% of trials. The modes of randomization, such as sequence generation, the mechanisms of allocation concealment, and implementation, were reported only in 35.6%, 19.5%, and 14.4%, respectively. Modes of blinding were reported in <15% of trials, whereas the statistical methods used for group comparisons on primary and secondary outcomes were reported in 90.7%. However, only 77.1% of studies report the numbers of participants included in each analysis. An intention-to-treat analysis regarding the primary end point was performed in only less than one half (45.8%) of the studies. Adverse events of the intervention were reported in only 55.9.%.

Analyzing trends over time revealed linear improvements from 1996 to 2016 in reporting trial nature in the title, structuring abstracts, reporting trial design, prespecifying primary and secondary outcomes, sample size calculations, analysis adjustments, presenting flow diagrams, defining periods of recruitment and follow-up, baseline data, providing denominators (number of participants) for each analysis, and side effects (Figure 3A, Supplemental Table 2). Reverse trends were found for describing precisely how and when the interventions were performed.

Among the leading journals reporting kidney-related clinical trials, a great diversity of matching CONSORT quality criteria was found. Only *The Lancet*, NEJM, and AJKD provided structured abstracts, whereas *Kidney International* and JASN did not (Figure 3B, Supplemental Table 2). Trial design was insufficiently described in all aforementioned journals. In JASN, proper descriptions of sample size calculations and the randomization procedures were less frequent than in the other journals. Clinical trials reported in JASN also more frequently lacked an intention-to-treat analysis compared with those in the other journals. Unlike NEJM, the other journals insufficiently reported the statistical methods. Finally, we checked the frequency of kidney trial registration before enrolment of the first participant, a request by the International Committee of Medical Journal Editors since 2005.[5] Of 100 randomly picked human kidney RCTs from PubMed (years 2008–2018), 93 were registered in a public database, one was an observational trial that did not need registration, and the other six had been concluded before the recommendation had been published.

Quality of Preclinical Trial Reporting

For quality assessment of preclinical studies, we selected 209 publications from JASN, *Kidney International*, and NDT. Seventy-four had to be deleted for invalidity criteria (Supplemental Figure 3). The remaining 135 papers were graded for the ARRIVE criteria as specified in Methods and Supplemental Table 3.[3] Objectives or a hypothesis were specified in the introduction in 73% (Supplemental Table 4). The methods specify a detailed ethical statement in 81% and the number or type of experimental groups in 65%. However, details on randomization, details on blinding, and a timeline diagram were provided in only 17%, 1%, and 12%, respectively. Experimental procedures and type of animals were generally well described (98% and 84%, respectively), although information on housing and husbandry were largely lacking (34%). Information on sample size calculation was always absent (0%), and also, numbers of independent replications were rare (19%). Only a minority of studies (13%) specified the primary and secondary outcomes. Regarding statistical methods, the types of tests were almost always reported (95%), but the unit of analysis for each dataset and whether the data met the prespecified assumptions of the statistical approach were not reported (0%). Baseline data were reported in only 12% of the studies, and the numbers analyzed for each test were reported in only 33%. Adverse events were hardly ever reported (2%).

Analyzing trends over time revealed improvements from 1996 to 2016 in reporting ethical statements, blinding, and timeline diagrams (Figure 4A, Supplemental Table 4). Reverse trends were found for describing the primary and secondary objectives or a research hypothesis and defining primary or secondary outcomes. Completely neglected across the entire study period was reporting details on group size calculations and whether the data obtained met the assumptions of the statistical approach. Instead, rationale, experimental procedures, statistical methods, and outcomes were generally well reported.

Among the evaluated journals (JASN, *Kidney International*, and NDT), reporting of preclinical studies according to the ARRIVE quality criteria revealed some but no profound differences (Figure 4B, Supplemental Table 4). JASN scored higher on ethics statement reporting. NDT reported group allocation methods better. All journals rarely reported details on group size calculations, whether the data obtained met the assumptions of the statistical approach, blinding, and adverse events.

DISCUSSION

We had hypothesized that the numbers of kidney-related clinical trials would have increased within the last 15 years, maybe also compared with other medical disciplines. We had further speculated that reporting quality improved and that both assumptions also apply

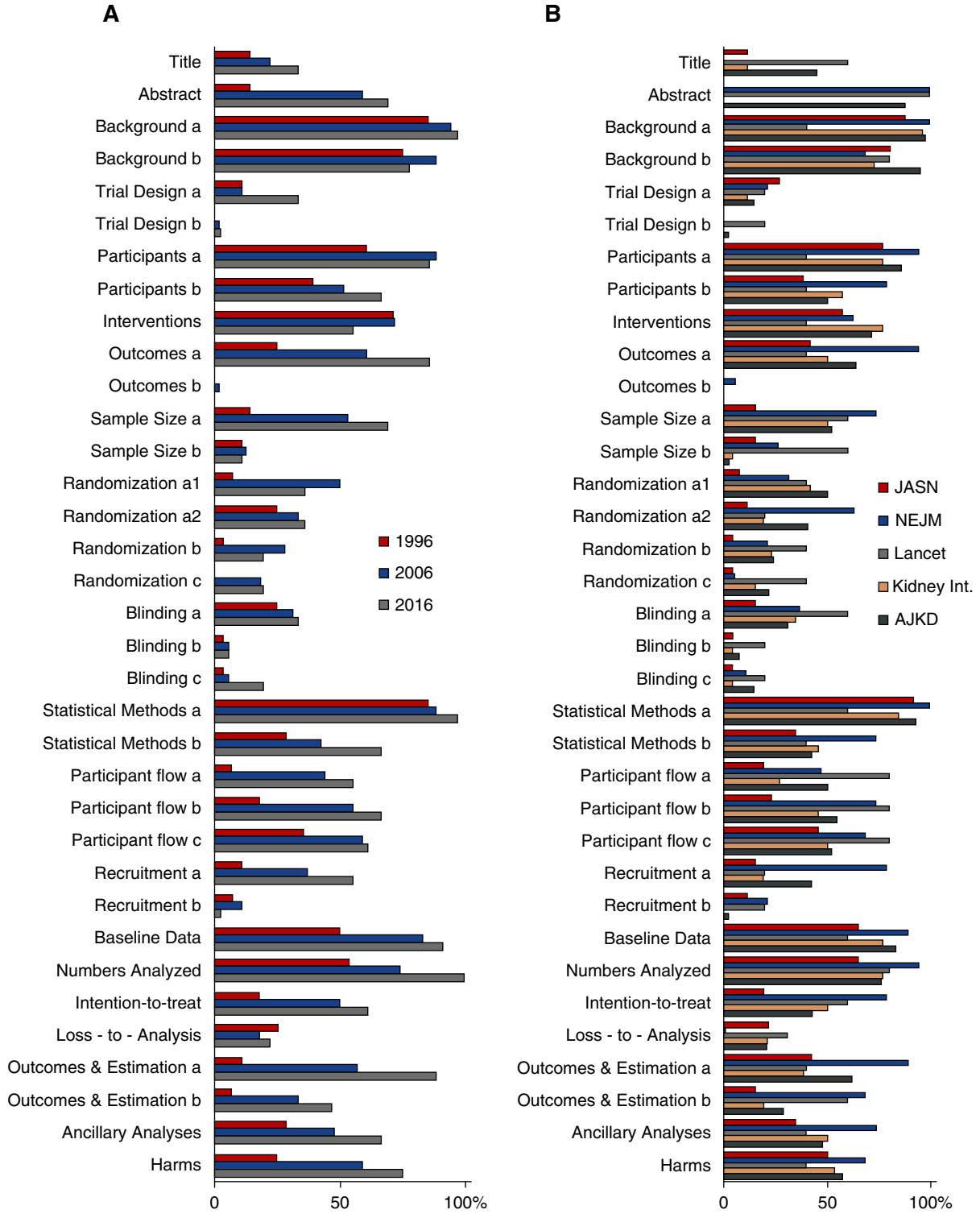

Figure 3. Quality assessment of reporting clinical trials in the main final paper according to the Consolidated Standards of Reporting Trials (CONSORT) criteria reveals improvements with time. Each of the CONSORT criteria was assessed as nonreported, unclear/insufficiently reported, or sufficiently reported in representative samples selected from *The New England Journal of Medicine* (NEJM), *The Lancet* (Lancet), *Journal of the American Society of Nephrology* (JASN), *American Journal of Kidney Disease* (AJKD), and *Kidney International* (Kidney Int.) of the years 1996, 2006, and 2016. Shown are the percentages of papers fulfilling the criterion "sufficiently reported" for (A) all journals in each of the 3 years to detect changes over time or (B) each of the journals across all time points. The selected number of papers was too small to also analyze trends over time for each journal.

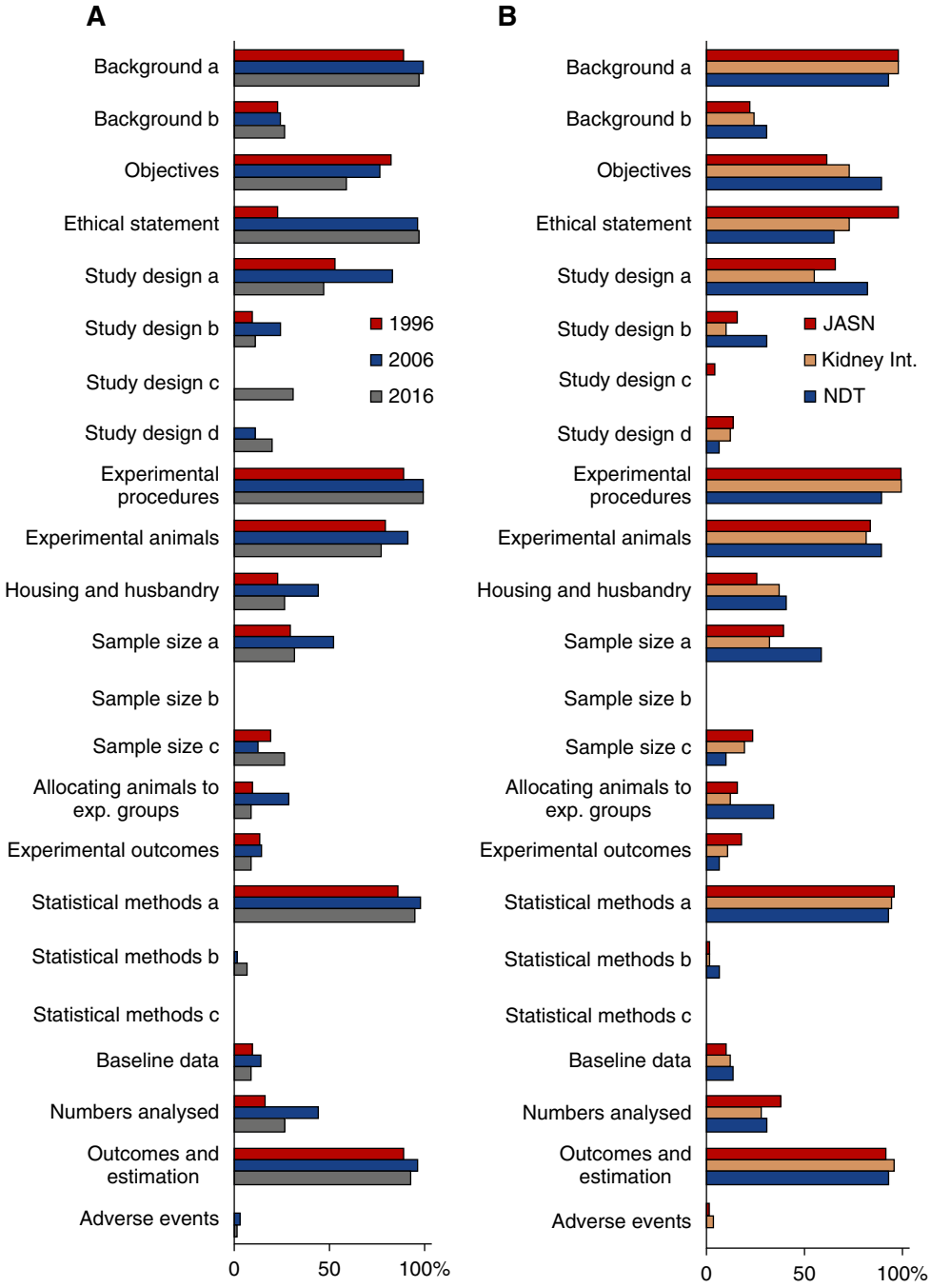

Figure 4. Quality assessment of reporting preclinical studies in the main paper according to the Animal Research: Reporting *In Vivo* Experiments (ARRIVE) criteria does not reveal improvements with time. Each of the ARRIVE criteria (except for title and abstract criteria) was assessed as nonreported, unclear/insufficiently reported, or sufficiently reported in representative samples selected from *Journal of the American Society of Nephrology* (JASN), *Kidney International* (Kidney Int.), and *Nephrology Dialysis and Transplantation* (NDT) of the years 1996, 2006, and 2016. Shown are the percentages of papers fulfilling the criterion "sufficiently reported" for (A) all journals in each of the 3 years to detect changes over time or (B) each of the journals across all time points. The selected number of papers was too small to also analyze trends over time for each journal.

to preclinical studies, which had not been assessed before. In contrast, nephrology takes last rank among the disciplines regarding clinical trial and preclinical study numbers. Analysis of reporting quality of clinical trials has improved over time, whereas for preclinical studies, numerous reporting deficits persist across leading kidney journals.

In 2004, Strippoli *et al.*[1] first documented the low quantity of kidney

disease–related clinical trials among the other medical disciplines, which raised some disappointment in the field. To exclude that this could have been a false negative result due to omitting trials on RRTs, we introduced an "expanded nephrology" definition; however, this did not substantially change the result. Among the kidney trials, topic coverage remains biased toward hypertension and RRTs, probably because these entities allow for shorter trials for outcome evaluation. In contrast, trials addressing the progression of CKD face the problem of primary outcomes that sufficiently predict ESRD. Another factor may be industry activity. Disciplines with strong publication output may benefit from strong industrial involvement (*e.g.*, funding support), which may be also a factor favoring publications in the areas of hypertension and RRTs in contrast to CKD prevention or GN.

The reporting quality of clinical trials remains a concern. It is of note that our analysis did not include supplementary information or previously published study protocols; hence, our results do not necessarily question the quality of trial design but mostly, question underreporting in the main body of the final paper, which may be hampered by space limitations. However, precise definitions of prespecified end points and performing an intention-to-treat analysis are essential to avoid erroneous conclusions, and these important aspects should be reported in main body of the final paper. Indeed, most journals now routinely request the trial design to be registered before enrolment of the first participant (http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/) and provision of CONSORT criteria checklists on submission, which may help to improve this aspect. Analyzing clinical trial reporting over time revealed significant improvements for some but not all criteria. Interestingly, reporting quality of how and when the intervention was performed showed even a reverse trend. These data imply that defining standards and assuring them during the review process and at the level of the editorial processing are both needed to further improve trial reporting. This is supported by comparing reporting quality in different journals. NEJM seems to request more accuracy of statistical methods reporting than other journals. However, none of the journals scored high for all criteria. As one limitation, seven of 125 studies (5.6%) during our quality analysis did not match the "interventional clinical trial" nature. It is likely that there is a similar rate of misclassified articles in the quantitative analysis. However, this rate should be distributed equally among all the disciplines or kidney disease entities, and therefore, it should not affect the conclusions.

An identical quantitative analysis for preclinical studies revealed similar findings. Expanding the nephrology-related MeSH term also did not result in a relevant increase in study numbers. Nephrology completely lacks the profound increases in published preclinical studies reported from other medical disciplines in the given timeframe. The reasons for this remain uncertain but may include structural problems in fundraising or number of related institutions. The coverage of research topics varied over time, mimicking major trends in nephrology, such as the implementation of kidney transplantation in the 1960s, novel classifications for AKI and CKD, and the evolving global epidemic of type 2 diabetes.

The increasing awareness of the lack of proper reporting and reproducibility of preclinical studies[6–10] fueled concerns about the reliability of preclinical research as a predictor of human outcomes as a whole.[11,12] To this aim, the ARRIVE guidelines on reporting of preclinical studies were published in 2010.[3] Our quality analysis revealed significant deficiencies in adhering to these guidelines before and after this date. In particular, providing precise information on animal substrains and housing conditions, naming the assumptions for group size calculations, randomization, and defining primary end points that are also relevant for human disease in animal studies are important deficits.[13] Over time, only the reporting of ethical statements, blinding, and timeline diagrams improved, whereas many other criteria did not. No major differences in strengths and deficiencies between JASN, *Kidney International*, and NDT were found. Enforcing adherence to the ARRIVE standards and reporting results accordingly may help to improve what has been called the "reproducibility crisis" in preclinical research.[6,8,9,12] Assuring proper group size calculations and a blinded analysis and considering sex disparities in experimental animals should be important in this context.[12,14,15] It would have been interesting to also analyze other important journals, such as *Journal of Clinical Investigation*, *Nature Medicine*, *Nature*, *Science*, *JCI Insight*, *etc.*, but these multidisciplinary journals publish kidney-related preclinical studies less frequently and only in low numbers within the set time periods.

In summary, clinical and preclinical research papers in nephrology have remained low in number compared with those of other medical disciplines. The quality of data reporting in the main body of papers presenting clinical trials keeps improving but is still suboptimal in many ways. The quality of data reporting of preclinical studies is still in its infancy and may contribute to reproducibility problems. Efforts at all levels are needed to overcome these deficits in the future. Given the central role of kidney disease–related morbidity and mortality, as well as health care costs, greater investments in kidney research are needed.

ACKNOWLEDGMENTS

H.-J.A. was supported by Deutsche Forschungsgemeinschaft grant AN372/24-1.

This project was prepared as a doctoral thesis at the Faculty of Medicine, Ludwig Maximilians University Munich by M.K.T.C.

DISCLOSURES

None.

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2018050515/-/DCSupplemental.

SUPPLEMENTAL MATERIAL

Supplemental Figure 1. Quantitative analysis of preclinical studies identified from PubMed.

Supplemental Figure 2. Flow chart illustrating the identification and selection of clinical trial reports papers for the quality analysis.

Supplemental Figure 3. Flow chart illustrating the identification and selection of preclinical study reports papers for the quality analysis.

Supplemental Material. Supplementary methods.

Supplemental Table 1. Criteria for assessment of CONSORT recommendations.

Supplemental Table 2. Quality assessment of clinical trials according to the CONSORT criteria.

Supplemental Table 3. Assessment criteria for ARRIVE recommendations.

Supplemental Table 4. Quality assessment of preclinical studies according to the ARRIVE criteria.

REFERENCES

1. Strippoli GF, Craig JC, Schena FP: The number, quality, and coverage of randomized controlled trials in nephrology. *J Am Soc Nephrol* 15: 411–419, 2004
2. CONSORT. Available at: http://www.consort-statement.org/. Accessed September 9, 2017
3. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG: Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol* 8: e1000412, 2010
4. Deo A, Schmid CH, Earley A, Lau J, Uhlig K: Loss to analysis in randomized controlled trials in CKD. *Am J Kidney Dis* 58: 349–355, 2011
5. International Committee of Medical Journal Editors: Clinical Trials. Available at: http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html. Accessed September 22, 2018
6. Braybrook J: Reproducibility: Developing standard measures for biology. *Nature* 551: 168, 2017
7. Hsieh T, Vaickus MH, Remick DG: Enhancing scientific foundations to ensure reproducibility: A new paradigm. *Am J Pathol* 188: 6–10, 2018
8. Vasilevsky NA, Brush MH, Paddock H, Ponting L, Tripathy SJ, Larocca GM, et al.: On the reproducibility of science: Unique identification of research resources in the biomedical literature. *PeerJ* 1: e148, 2013
9. Begley CG, Ellis LM: Drug development: Raise standards for preclinical cancer research. *Nature* 483: 531–533, 2012
10. Kilkenny C, Parsons N, Kadyszewski E, Festing MF, Cuthill IC, Fry D, et al.: Survey of the quality of experimental design, statistical analysis and reporting of research using animals. *PLoS One* 4: e7824, 2009
11. van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, et al.: Can animal models of disease reliably inform human studies? *PLoS Med* 7: e1000245, 2010
12. Anders HJ, Jayne DR, Rovin BH: Hurdles to the introduction of new therapies for immune-mediated kidney diseases. *Nat Rev Nephrol* 12: 205–216, 2016
13. Hirst JA, Howick J, Aronson JK, Roberts N, Perera R, Koshiaris C, et al.: The need for randomization in animal trials: An overview of systematic reviews. *PLoS One* 9: e98856, 2014
14. Miller LR, Marks C, Becker JB, Hurn PD, Chen WJ, Woodruff T, et al.: Considering sex as a biological variable in preclinical research. *FASEB J* 31: 29–34, 2017
15. Shah K, McCormack CE, Bradbury NA: Do you know the sex of your cells? *Am J Physiol Cell Physiol* 306: C3–C18, 2014

See related editorial, "The Quality of Reporting of Kidney Research: A Challenge to JASN," on pages 1–2.