The Conduct and Reporting of Child Health Research: An Analysis of Randomized Controlled Trials Published in 2012 and Evaluation of Change over 5 Years

Allison Gates, PhD[1], Lisa Hartling, PhD[1], Ben Vandermeer, MSc[1], Patrina Caldwell, PhD[2], Despina G. Contopoulos-Ioannidis, MD[3], Sarah Curtis, MD[4], Ricardo M. Fernandes, MD, PhD[5,6], Terry P. Klassen, MD[7], Katrina Williams, PhD[8], and Michele P. Dyson, PhD[1]

Objectives For child health randomized controlled trials (RCTs) published in 2012, we aimed to describe design and reporting characteristics and evaluate changes since 2007; assess the association between trial design and registration and risk of bias (RoB); and assess the association between RoB and effect size.

Study design For 300 RCTs, we extracted design and reporting characteristics and assessed RoB. We assessed 5-year changes in design and reporting (based on 300 RCTs we had previously analyzed) using the Fisher exact test. We tested for associations between design and reporting characteristics and overall RoB and registration using the Fisher exact, Cochran-Armitage, Kruskal-Wallis, and Jonckheere-Terpstra tests. We pooled effect sizes and tested for differences by RoB using the χ^2 test for subgroups in meta-analysis.

Results The 2012 and 2007 RCTs differed with respect to many design and reporting characteristics. From 2007 to 2012, RoB did not change for random sequence generation and improved for allocation concealment ($P < .001$). Fewer 2012 RCTs were rated high overall RoB and more were rated unclear ($P = .03$). Only 7.3% of 2012 RCTs were rated low overall RoB. Trial registration doubled from 2007 to 2012 (23% to 46%) ($P < .001$) and was associated with lower RoB ($P = .009$). Effect size did not differ by RoB ($P = .43$)

Conclusions Random sequence generation and allocation concealment were not often reported, and selective reporting was prevalent. Measures to increase trialists' awareness and application of existing reporting guidance, and the prospective registration of RCTs is needed to improve the trustworthiness of findings from this field. *(J Pediatr 2017;■■:■■-■■).*

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Randomized controlled trials (RCTs) provide the best evidence to guide clinical practice when carried out appropriately.[1] Conversely, RCTs that are poorly conducted may yield biased estimates of treatment effects,[1,2] potentially leading to misinformed clinical decisions that could pose harm.[3] Especially for pediatric populations, where the quantity of relevant data lags behind that of adults,[4] there exists a need for well-conducted and reported RCTs. A review of a random sample (n = 300) of child health RCTs published in 2007 by our group[5] revealed that 92% were rated high or unclear risk of bias (RoB) based on Cochrane standards.[6] Though registered RCTs yielded superior Jadad scores[7] and lower RoB compared with those that were not registered, registration was declared in only 12% of publications.[5]

Since the time of our review, substantial effort has been applied to improving the conduct and reporting of health research. For example, the Cochrane RoB tool, which facilitates the appraisal of systematic error in RCTs based on their conduct and reporting qualities, was only in its infancy at that time.[6] The Enhancing the Quality and Transparency of Health Research Network,[8] which supports the development, dissemination, and implementation of robust reporting guidelines

CONSORT	Consolidated Standards of Reporting Trials
DMC	Data monitoring committee
RCTs	Randomized controlled trials
RoB	Risk of bias
SMD	Standardized mean difference

From the [1]Department of Pediatrics and the Alberta Research Centre for Health Evidence (ARCHE), University of Alberta, Edmonton, Alberta, Canada; [2]Center for Kidney Research and Discipline of Pediatrics and Child Health, University of Sydney, Sydney, New South Wales, Australia; [3]Department of Pediatrics, Division of Infectious Diseases, Stanford University School of Medicine and Meta Research Innovation Center at Stanford (METRICS), Stanford, CA; [4]Department of Pediatrics and Emergency Medicine, Women and Children's Health Research Institute, University of Alberta, Edmonton, Alberta, Canada; [5]Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; [6]Department of Pediatrics, Hospital de Santa Maria, Centro Hospitalar Lisboa Norte, Lisbon, Portugal; [7]Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, Manitoba, Canada; and [8]Department of Pediatrics, Royal Children's Hospital and Murdoch Childrens Research Institute, University of Melbourne, Victoria, Australia

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including the Consolidated Standards of Reporting Trials (CONSORT)[1,2] and Standard Protocol Items: Recommendations for Intervention Trials[9,10] statements, was launched in 2009. In response to a call for reduced research waste,[11-15] adherence to the CONSORT checklist as a condition of publication is being adopted by an increasing number of journals.[16]

Specific to pediatric health research, Standards for Research in Child Health was founded in 2009 with the mission of improving the design, conduct, and reporting of RCTs through the development and dissemination of evidence-based standards.[3,17-22] Moreover, a number of international pediatric trial networks have been established since the early 2000s to improve infrastructure and research capacity.[23] In light of these developments, we sought to investigate the conduct and reporting of child health RCTs published in 2012, 5 years following our 2007 analysis.[5] Specifically, for a random sample of 300 child health RCTs, we aimed to describe their design and reporting characteristics, including RoB; evaluate changes in trial design and reporting characteristics from 2007 to 2012; assess the association between trial design and reporting characteristics, and trial registration and RoB, respectively; and assess the association between RoB and magnitude of effect for the primary outcome.

Methods

On November 4, 2013, we searched the Cochrane Central Register of Controlled Trials for RCTs published in 2012 using pediatric subject headings and keywords (**Appendix 1**; available at www.jpeds.com). The search was modeled from that used to identify the 2007 sample (searched October 7, 2009).[5] Cochrane Central Register of Controlled Trials includes randomized and quasi-randomized controlled trials indexed in MEDLINE and EMBASE, hand-searched results, gray literature sources, and Cochrane Review Groups Specialized Registers of trials.[24]

The search yielded 2296 unique records, which we uploaded to EndNote (Clarivate Analytics, Philadelphia, Pennsylvania) reference management software. From EndNote, we transferred the records (ordered alphabetically by author) to a Microsoft Office Excel (IBM Corporation, Armonk, New York) workbook, with each record allocated to an individual row. To order the records randomly, we allocated a number to each record using Excel's random number generator (ie, the RAND function), which returns a random number between 0 and 1. We then reordered the records from smallest to largest to yield a randomly ordered list.

To ensure comparability to our 2007 findings,[5] we employed identical selection criteria. A single researcher screened the records by title and abstract and selected RCTs that reported on outcomes of participants ≤21 years of age. We did not restrict the sample by language, condition, intervention, nature of the comparator, nor outcome type. To be consistent with the 2007 sample size, we included the first 300 (13%) eligible records from the randomly ordered list (**Appendix 2**; available at www.jpeds.com).

We used the data extraction form from our 2007 study,[5] with additional items added following consultation with clinical and methodological experts (**Appendix 3**; available at www.jpeds.com). From each record we extracted characteristics of the publication, study design, intervention, trial conduct, study sample, sample size, data monitoring committee (DMC) and follow-up, outcomes and conclusions, methodological quality, and registration and protocol. We extracted data for the primary outcome. When not specified, we inferred the primary outcome as the (1) objective outcome, (2) outcome used to calculate the sample size, or (3) first outcome reported in the results. All extracted data were verified by a second researcher to identify and resolve errors.

When available, we used the trial register, published protocol, and/or companion article(s) to supplement data extraction. If not cited in the publication, we searched for trial registers in the International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/), the ISRCTN Registry (http://www.isrctn.com/), and via Google (https://www.google.ca/). We used protocols or companion articles only when cited in the publications.

We used the 2010 Cochrane RoB tool[25] to assess RoB for the primary outcome among 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias. We assessed each domain as low, unclear, or high risk following Cochrane procedures[6] and internal decision rules (**Appendix 4**; available at www.jpeds.com). Overall RoB was determined as follows: low when all domains were assessed as low; unclear when at least 1 domain was assessed as unclear and no domains were assessed as high; and high if any domain was assessed as high.[6] Two reviewers assessed each record and discussed the judgments until consensus was reached or a third party provided arbitration.

Statistical Analyses

We analyzed the data using StatXact (*v* 10.0; Cytel, Cambridge, Massachusetts) and Stata (v 11.2; StataCorp, College Station, Texas). We analyzed trial characteristics descriptively. To assess for 5- year changes in trial design, reporting, and RoB, we compared the 2012 sample with 300 RCTs published in 2007 on which we had previously extracted comparable data.[5] We assessed differences in trial design and reporting using the Fisher exact test. We assessed differences in RoB using the Cochran-Armitage test.

For the 2012 sample, we tested for associations between both registration status and overall RoB, and the following: continent of the corresponding author, funding source, sample size calculation, presence of a DMC, outcomes, adverse events, and conclusions. We assessed differences using the Fisher exact test for registration status and Cochrane-Armitage test for overall RoB, when appropriate. Otherwise, we used the Kruskal-Wallis or Jonckheere-Terpstra test.

We calculated pooled effect sizes across 203 RCTs with adequate data to test for an association between overall RoB and the magnitude of effect for the primary outcome. We

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