Assessment of Publication Trends of Systematic Reviews and Randomized Clinical Trials, 1995 to 2017

Systematic reviews and meta-analyses (SRMAs) and randomized clinical trials (RCTs) are considered the most robust and reliable forms of evidence to guide clinical practice. Previous research has demonstrated year-over-year increases in the number of published RCTs between 1950 and 2007[1] as well as increases in the number of published SRMAs through 2016.[2,3] The increase in SRMAs is needed to update cumulative evidence,[2] although some investigators speculate that SRMAs may also serve as "easily publishable units or marketing tools."[2,3] Given this context, we sought to compare publication trends overall and across clinical topic areas among SRMAs and RCTs over the past 22 years.

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Methods | We conducted a cross-sectional study of PubMed-indexed SRMAs and RCTs published from 1995 to 2017 using the UNIX terminal window Entrez Direct (EDirect). EDirect is the primary text search and retrieval system of the National Center for Biotechnology Information. The inclusion start period was set to 1995 to account for previous systematic errors in PubMed's categorization of SRMAs prior to this time period.[3] Systematic reviews and meta-analyses were searched as a single category because PubMed indexes meta-analyses within systematic reviews, and up to 60% of systematic reviews include meta-analyses (**Figure 1**).[4]

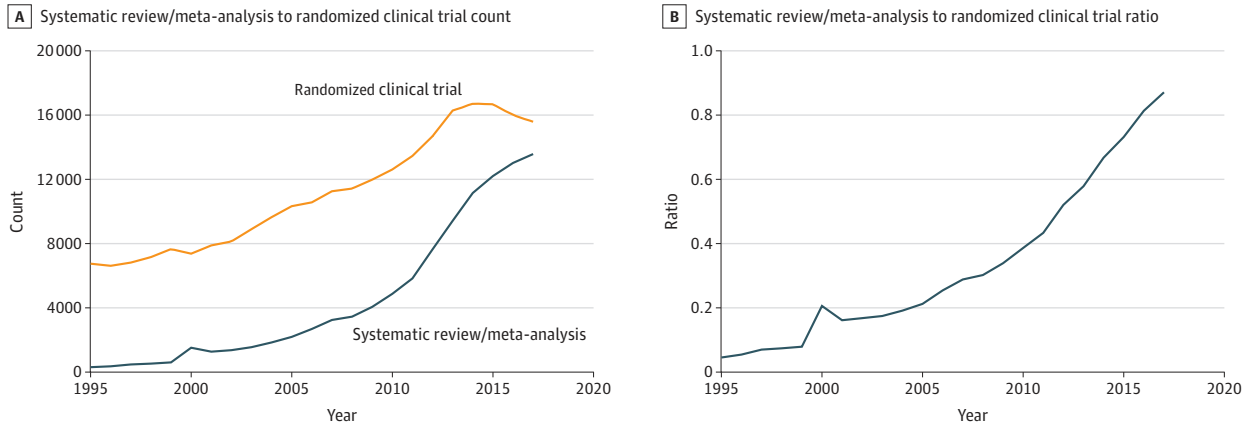
Medical subject headings (MeSH) were used to define clinical topic areas when the term was a major topic of an article using the following heuristic for MeSH categories: medical specialty, surgical specialty, surgical procedure, disease, and anatomic system where applicable. Searches for SRMAs used the terms Systematic Review[Ptyp] OR Meta-Analysis[Ptyp], whereas RCT searches used Randomized Controlled Trial[Ptyp]. The 18 medical and surgical topic areas included in this study are noted in **Figure 2**, with an example of a search strategy noted in the legend. Standard identifiers (PubMed identification numbers) indexed across more than 1 specialty were only counted once. The ratio of SRMAs to RCTs was calculated for each year. A ratio greater than 1 indicates that more SRMAs than RCTs were published, whereas a ratio less than 1 indicates that more RCTs than SRMAs were published. Data analysis was performed from February 1 to February 12, 2018, and Stata version 15 (StataCorp) was used for all analyses.

Results | From 1995 to 2017, increases were observed in the absolute number of published SRMAs (435 in 1995 vs 20 774 in 2017) and RCTs (9486 in 1995 vs 22 560 in 2017); however, the rate of growth was significantly greater for SRMAs vs RCTs at 4676% and 138%, respectively (Figure 1). In 1995, the overall ratio (SD) of SRMAs to RCTs was 0.045 (0.02), whereas in 2017 it was 0.871 (0.26). Increases in published SRMAs and RCTs were observed for all 18 clinical topic areas (Figure 2). In 1995, the lowest ratio of SRMAs to RCTs was observed for anesthesiology (0.005) and the highest was observed for hematology/oncology (0.083); in 2017, the lowest ratio was observed for anesthesiology (0.317) and the highest was observed for hematology/oncology (1.443).

Discussion | The number of published SRMAs and RCTs has substantially increased over the last 22 years, although the rate of growth was notably greater for SRMAs. These findings update those of previous studies and are consistent with earlier studies estimating an approximately 2700% increase of SRMA indexed in PubMed.[2,3] This increase may be secondary to the incorporation of the larger numbers of RCTs into SRMAs, incorporation of nonrandomized studies in SRMAs,[5] and/or the proliferation of SRMAs conducted by researchers in China, who now account for production of more than one-third of all published meta-analyses.[3]

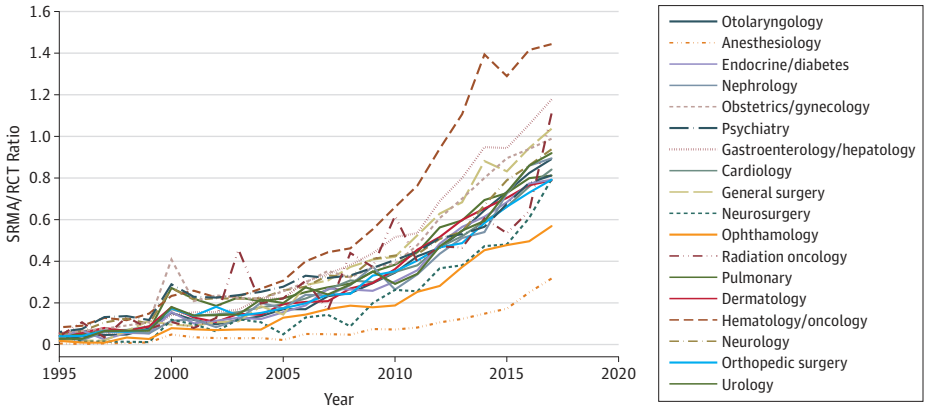
This study was limited by the use of PubMed, which may not be representative of overall trends in the literature.[3]

Figure 1. Published Systematic Reviews vs Randomized Clinical Trials, 1995-2017



The graphs show the total count of systematic reviews and meta-analyses (SRMAs) and randomized clinical trials (RCTs) per year (A) and the ratio of SRMAs to RCTs per year from 1995 to 2017 (B). A ratio greater than 1 means more SRMAs than RCTs were published, whereas a ratio less than 1 means more RCTs than SRMAs were published.

Figure 2. Trends for Publications in Selected Medical and Surgical Specialties, 1995-2017



The graph shows the ratio of systematic reviews and meta-analyses (SRMAs) to randomized clinical trials (RCTs) per specialty over time. A ratio of greater than 1 means that more SRMAs than RCTs were published, and a ratio less than 1 means that more RCTs than SRMAs were published. Searches for each specialty used the National Library of Medicine's medical subject headings for each specialty; for example, obstetrics and gynecology was searched the following phraseology ("Female Urogenital Diseases and Pregnancy Complications"[Majr] OR ("Obstetrics"[Majr] OR "Gynecology"[Majr]) OR ("Obstetric Surgical Procedures"[Majr] OR "Gynecologic Surgical Procedures"[Majr]) OR "Genitalia, Female"[Majr]).

Additionally, our search criteria relied on the National Library of Medicine's controlled vocabulary thesaurus, MeSH, instead of keywords to extract indexed papers.

Systematic reviews and meta-analyses help to synthesize and update the literature using valuable methods for evidence-based medicine. However, an estimated 3% of SRMAs are methodologically sound, nonredundant, and provide useful clinical information.[3] Although the optimal SRMA/RCT ratio has yet to be determined, an ever increasing proportion of this literature may provide minimal value, which should precipitate a reappraisal of the foundations, production, and reporting of SRMAs.[6]

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Invited Commentary

Meta-analysis Metastasis

In 2016, following an evaluation of publication trends over the last few decades, Ioannidis[1] declared that "the production of systematic reviews and meta-analyses has reached epidemic proportions." In particular, he estimated that the annual number of published systematic reviews and meta-analyses increased approximately 2700% from 1991 to 2014.[1] Systematic reviews and meta-analyses, which are fundamental tools of evidence-based medicine, aim to accumulate, synthesize, and evaluate evidence across individual studies, with the goal of resolving uncertainties, reducing biases, and informing practice. However, the production of reviews has far outpaced the 150% increase in annual publications across all PubMed–indexed article types between 1991 and 2014.[1] These recent trends have led to questions about the purpose, quality, and credibility of most reviews as well as calls to abandon systematic reviews and meta-analyses altogether.

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Articles combining the results from multiple studies have been published for over a century. However, the term *meta-analysis* and many of the fundamental principles of standardizing and synthesizing effect estimates were first introduced in the late 1970s. Over the next 2 decades, as the methodology was further formalized and adopted, there was a linear increase in the number of published health-related meta-analyses.[2] However, since 2000, exponential growth rates have been observed, raising concerns about the number of overlapping, conflicted, and misleading meta-analyses.[1] These findings led Ioannidis[1] to hypothesize that it is likely that "more systematic reviews of trials than new randomized trials are published annually."

In this issue of *JAMA Internal Medicine*, Niforatos and colleagues[3] evaluated a similar hypothesis by comparing the ratio of published systematic reviews and meta-analyses to randomized clinical trials (RCTs) available on PubMed from 1995 to 2017.[3] The authors reported that the ratio of systematic reviews and meta-analyses to RCTs increased from 0.045 in 1995 to 0.871 in 2017, suggesting that nearly 1 review is now published for every RCT. Although the results differed across clinical topic areas, they support previous concerns about the mass production of systematic reviews and meta-analyses.[1]

There are a number of factors that can explain these trends. Recent technological advances, including easily searchable databases and digital software for screening and synthesizing evidence, have enabled the rapid production of reviews that can be conducted with or without meta-analytical expertise.[4] Furthermore, reviews involve fewer barriers (ie, institutional review board requirements) and are less expensive to conduct than trials. On average, reviews receive more citations than all other study designs,[5] and given the academic incentive structure, which is often focused on citations and H-indices, researchers, editors, and journals may be preferentially pursuing and publishing review articles. It is also possible that there is a perceived demand for review articles that provide up-to-date summaries of rapidly evolving fields.[6] For example, Niforatos et al[3] found that in hematology/oncology, one specialty with an overwhelming number of new studies published each year, the ratio of published reviews to trials was 1.443.

Although these and other research practices can explain the growth in the number of published reviews, it is also worth noting that the true ratio of systematic reviews and meta-analyses to RCTs is difficult to measure. As the authors outline, they relied on PubMed classifications,[3] and previous studies have suggested that fewer than one-third of studies tagged in PubMed as a "systematic review" actually meet the stringent criteria of this study design.[1,7] Furthermore, the number of articles indexed as RCTs in PubMed has been increasing over time. Little is known about their purpose, size, quality, and how many of these are actually secondary analyses of existing trials. Although Niforatos et al[3] provided an estimate of the number of studies classified as systematic reviews/meta-analyses and RCTs, the ratio of reviews containing only RCTs to new RCTs is unknown and is more difficult to establish without manual screening of articles.

Although these trends indicate an alarming growth in the popularity of reviews across different specialties, rigorous systematic reviews and meta-analyses are still among the most informative research studies. The findings reported by Niforatos et al[3] do not suggest that reviews should be abandoned or that more trials are necessary. Instead, they support efforts to prioritize more robust trials and reviews, including living reviews in which meta-analyses are available online and continuously updated as additional studies are identified, as well as prospective and individual patient-level meta-analyses. Priority should be given to reviews that are conducted by nonconflicted investigators, including meta-analytical experts and research librarians, who help formulate search terms, identify relevant databases, and minimize any search inadequacies. To help curtail the production (and publication) of redundant, biased, and conflicted reviews, peer reviewers and editors may need additional training to assess the quality of submitted manuscripts. Together, these efforts can help slow the meta-analysis metastasis.

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Industry Payments to Physician Directors of National Cancer Institute–Designated Cancer Centers, 2015-2017

National Cancer Institute (NCI)–designated cancer centers shape cancer care in the United States and are supported by substantial public funds (in fiscal year 2018, $330 million in core funding for 70 cancer centers).[1] Cancer care is also shaped by industry, because developing new cancer therapeutics represents a major market opportunity. Industry payments to aca-