Systematic reviews and meta-analyses are valuable tools for understanding existing—and shaping future—medical research. The concepts of systematic reviews and meta-analysis were introduced more than 40 years ago and adopted into mainstream medical research shortly thereafter.\textsuperscript{1,2} When well performed, including the choice of a relevant topic, systematic reviews and meta-analyses can provide useful insights into disease diagnosis, epidemiology, treatment effects (including benefits and harms), and aspects of study design or populations that might be associated with (and possibly influence) treatment effectiveness or other outcomes, including adverse events. These effects may become apparent in a meta-analysis when not readily evident from individual small studies. Nearly half a century later, these objectives remain central, although additional applications and more rigorous methods have been developed.\textsuperscript{3}

However, as noted in a commentary by Berlin et al,\textsuperscript{4} there is great variability in the quality of published meta-analyses, particularly with regard to whether they were conducted in a transparent, reproducible, and valid manner. In this vein, there are numerous existing guidance documents relating to the conduct or reporting of systematic reviews and meta-analyses, eg, the Cochrane Handbook and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.\textsuperscript{5,6}

Another issue is the massive increase in meta-analyses and systematic reviews published during the past 3 decades, many of which are likely redundant or misleading.\textsuperscript{7} This trend presents a challenge for the editors of JAMA Network Open in terms of the volume of systematic reviews and meta-analyses, including network meta-analyses, that are routinely submitted. In 2021, there were 655 meta-analyses and 175 systematic reviews submitted, with 56 (9%) and 29 (17%) accepted, respectively. Although we have not established explicit standards for determining whether a submitted systematic review or meta-analysis should be accepted, the editors of JAMA Network Open have implicitly developed criteria by which to judge these submissions. The issues extend beyond methodological rigor, which is a fundamental requirement, to include the crucial questions of what makes the meta-analysis important and interesting. To clarify our expectations, and in the process, improve the chance that a manuscript might be considered further, we ask that authors of meta-analyses and systematic reviews to address a series of key questions in their cover letter:

- Why is a new meta-analysis or network meta-analysis needed? What do we not already know that the current analysis can address? A meta-analysis that addresses an egregious error in a prior analysis and makes this correction the focus of the report may be appropriate for JAMA Network Open, particularly if it relates to an important clinical question with public health implications.
- What meta-analyses on this topic have been conducted during the last 5 years, and how do the studies included in the current submission compare with those included in prior meta-analyses and/or network meta-analyses? There must be a compelling rationale to publish this type of replicative research in JAMA Network Open. An incremental update of existing meta-analyses would receive a lower priority and probably is better suited to other venues for living and dynamic reviews.\textsuperscript{8}
- Does the meta-analysis address a secondary question (eg, using metaregression to evaluate factors that might modify treatment effectiveness, risk factors in a subgroup of special interest)? These often represent novel questions and are a higher priority for JAMA Network Open.
- Is the systematic review or meta-analysis unique? The first meta-analysis on a topic, even if the results merely show that there is very little literature on a given topic, can be of some value and interesting.
Point to areas of future research. For example, JAMA Network Open has published a systematic review that examined the literature on communication between anesthesiologists and patients beyond simply the process for informed consent for the anesthetic. The main finding was that the literature on this topic was scant, which we believe to be an important finding and worthy of publication. JAMA published a network meta-analysis on types of noninvasive ventilation in adults with acute hypoxic respiratory failure. It was the first analysis of the question, and it was timely because it was COVID-19–related. At the same time, it is essential that meta-analyses fairly consider all potentially eligible studies and clearly document why a particular study may have been disqualified from inclusion. All too often, external reviews identify relevant studies that were missed or excluded for unclear reasons from a meta-analysis submitted for review.

- Does the systematic review or meta-analysis adequately address the heterogeneity and diversity of the populations studied among the included studies? JAMA Network Open is dedicated to promoting health equity by seeking inclusion of different groups in the population and analysis of variation in effects across groups.

Researchers who design systematic reviews and meta-analyses must make decisions about study inclusion and exclusion, so it is not surprising that other groups might make different choices. Because the data set of published studies is available, it is also not surprising that others may produce a different meta-analysis making different choices with different results. As noted previously, if there was a serious error in the prior analysis, and the clinical question is important, such submissions will be considered on a case-by-case basis.

When authors do not address these questions in their manuscript or cover letter, we may return the manuscript and ask them to do so before further consideration. Nonetheless, these are not necessarily hard and fast rules. There will always be exceptions, and we recognize the need to remain flexible. We continue to be committed to publishing high-quality systematic reviews and meta-analyses that address clinically relevant topics in unique ways. We set forth these questions to guide authors as to the kinds of submissions that might have a relatively higher chance of being accepted for publication and that will make a meaningful contribution to science and patient care.

ARTICLE INFORMATION

Published: August 24, 2022. doi:10.1001/jamanetworkopen.2022.28541

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Conflict of Interest Disclosures: Dr Berlin reported formerly being employed by Johnson & Johnson outside the submitted work. Dr O'Cearbhaill reported receiving personal fees from GlaxoSmithKline, Regeneron, Seagen/Seattle Genetics, Immunogen, the GOG Foundation, Genentech, R-Pharm, Bayer/Atara, Fresenius Kabi, and MJH/Curio/Onclive; receiving travel funds from Hitech Health; serving as an unpaid steering committee member for the PRIMA, Moonstone (Tesaro/GSK), and DUO-O (AstraZeneca) studies; serving as an unpaid advisor for Carina Biotech; receiving funding from the National Cancer Center; and that her institute receives funding for clinical research from Bayer/Celgene/Juno, Tesaro/GlaxoSmithKline, Merck, Ludwig Cancer Institute, Abbvie/StemCentRx, Regeneron, TCR2 Therapeutics, Atara Biotherapeutics, MarkerTherapeutics, Syndax Pharmaceuticals, Genmab/Seagen Therapeutics, Sellas Therapeutics, Genentech, Kite Pharma, and the Gynecologic Oncology Foundation. No other disclosures were reported.
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