Preclinical Evidence Synthesis Facilitates Open Science

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Executive Summary: Evidence synthesis methodology, particularly preclinical evidence synthesis reviews, provides substantial benefits by reducing research waste, enhancing the quality of research, and providing comprehensive and objective overviews of specific fields. These reviews also allow for the contribution of citizen scientists, who represent an important facet of open science. Recent policy changes by the Biden-Harris Administration require that researchers receiving federal funding immediately make their publications and data available to the public without an embargo, highlighting the importance placed upon the open science principles of transparency, reproducibility, and accessibility. Despite this, the following assessment highlights two challenges for evidence synthesis reviews that are at odds with open science principles: (1) the lack of funding available for evidence synthesis reviews, particularly preclinical reviews, despite their demonstrated value and (2) the slow and expensive traditional publication model. I recommend allocating funding for preclinical evidence synthesis reviews as they are beneficial to both the researchers conducting the review and the field that is being reviewed. I also recommend supporting publication platforms that employ the quick release of preprints with a transparent peer review process and/or creating a federally funded and run publication platform characterized by open access and minimal publication costs.

I. Introduction
Open science and citizen science go hand in hand, fostering the idea that scientific knowledge should be accessible and inclusive. In 2015, the ECSA (European Citizen Science Association) developed the Ten Principles of Citizen Science. These principles underscored the importance of engaging citizens in research endeavors and ensuring the widespread accessibility of research outcomes (Robinson et al. 2018). One of the ways in which citizens can be involved in scientific research is through evidence synthesis. Evidence synthesis provides a structured framework for researchers to collate findings from disparate studies, employing the scientific method in the synthesis process. However, owing to their methodical nature, these reviews are often time-intensive, prompting the exploration of crowdsourcing strategies to expedite the screening and synthesis phases (Strang and Simmons 2018). Evidence synthesis reviews have consistently demonstrated a positive impact on research and evidence-based medicine, but despite these positives, funding for evidence syntheses, particularly preclinical ones, remains sparse (Menon et al. 2021; MacEntee 2019).

The goal of this technology assessment is to demonstrate the symbiotic relationship between systematic reviews and the principles of open science. This will include a review of open science policy within the United States before presenting an overview of the evidence synthesis landscape. This assessment will then highlight the distinctions between clinical and preclinical evidence synthesis,
discussing their roles in curtailing research redundancy and inefficiency, before specifically outlining the advantages of preclinical evidence synthesis. Lastly, this paper will propose policy options focused on promoting open science and systematic reviews. This includes increasing funding for evidence synthesis and supporting open access publication platforms with minimal fees for authors.

II. History of open science: Charting a path toward research collaboration and transparency

Open science as a concept emerged as a way of addressing the large societal challenges of the 21st century, including climate change, public health problems, global hunger, sustainable energy, and better “smart” transport (Vicente-Saez and Martinez-Fuentes 2018). Researchers have advocated for expanding public access to scholarly literature beginning as early as the 1950s, but the idea gained more traction in the last 20 years as open science began to emerge as a term (Holbrook 2019) (Figure 1). At first open science did not have a clear definition, but a systematic review of seventy-five studies consolidated definitions of open science to arrive at the following description: “transparent and accessible knowledge that is shared and developed through collaborative networks” (Vicente-Saez and Martinez-Fuentes 2018). Arguments in support of open science include the notion that taxpayers, as funders of research, have a right to access the results of research funded by their taxes (Suber 2003). Additionally, open science has been shown to accelerate the pace of research (Woelfle, Olliaro, and Todd 2011). The importance of being able to quickly and freely access research became evident during the COVID-19 pandemic, when academic institutions frequently released preprints and genomic sequences before full peer review to expedite related research (Jialu Chen 2022).
However, even with a consensus among researchers on the benefits of open science, achieving universal adoption of its principles and practices remains a challenge. If a solitary researcher undertakes the effort to make their research ideas and data public while their colleagues do not follow suit, the lone researcher may not fully reap the benefits (Nielsen 2012). Universal and simultaneous adoption is essential to realize the true potential of open science, but the implementation of open science practices currently remains fragmented and organization-dependent (Adimoelja and Athreya 2022). Nielsen (2012) likened this to switching the side of the road on which one drives. It is unfeasible to make this switch one individual at a time; however, Sweden was able to make the switch through an extended campaign and a change in the law (Nielsen 2012).

The United States made this type of switch in support of open science when the National Institutes of Health (NIH) required that researchers make their papers publicly available on PubMed Central within twelve months of publication if they receive NIH funding (“Revised Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research” 2008). By 2013, this mandate extended beyond the NIH, with the White House issuing a memorandum stating that all federal agencies distributing research funding must establish policies to increase public access to research results, data, and publications (Holdren 2013). The Biden-Harris Administration expanded on this policy, advocating for no twelve-month embargo between publication and public access to research articles and the free availability of data within peer-reviewed publications (Nelson 2022). The administration also declared 2023 as the "Year of Open Science," accompanied by a comprehensive action plan aimed at promoting open and equitable research (The White House Office of Science and Technology Policy 2023).

In the present landscape, libraries play a pivotal role in implementing open science. They host Open Access Repositories, publish theses and dissertations, and offer guidance on adhering to institutional or governmental open access policies. Libraries and their librarians are instrumental in equipping researchers with the resources and knowledge needed to embrace open science (Horstmann 2017). Some universities have specialized library departments dedicated to implementing open science policies, such as Carnegie Mellon University, while others, like the University of California Los Angeles, offer modules that enable librarians to learn about the principles and practices of open science (Hamblett et al. 2023).

### i. Citizen science: A vital component of open science

Citizen science represents an integral facet of open science, aligning with the public school of thought within open science. This school of thought assumes that science must be made accessible to the public, engaging them in research through collaborative efforts (i.e., citizen science) and promoting understanding through lay summaries and less formal science communication (Ross-Hellauer 2017). Open science has always been a way of fostering innovation, and citizen science is itself an innovation. A citizen scientist can be defined as a community member who does not necessarily have formal scientific training or an active research position, but engages with researchers or works on research projects to answer scientific questions (National Park Service 2021). Large collaborative projects that require extensive manpower to collect or classify data would be impossible, or at least extremely difficult, without these volunteers or citizen scientists (Bonn et al. 2018).

Kullenberg and Kasperowski (2016) conducted a scientometric meta-analysis of citizen science projects. They found that the main focal point of citizen science is related to biology, conservation, and ecology, which all use citizen scientists as a way of collecting and classifying data (Kullenberg and Kasperowski 2016). Using crowdsourcing as a way of facilitating evidence synthesis, as will be discussed in Section III, would be an example of this. Within health research, this is sometimes called “popular epidemiology” (Kullenberg and Kasperowski 2016). During the COVID-19 pandemic, some researchers relied on crowdsourcing to complete projects like simulating proteins and collecting data on symptoms (Jialu Chen 2022). Crowdsourcing also played a key role in the development of a different formulation of the drug.
praziquantel. Researchers initiated the project with a request posted to a chemistry group on LinkedIn. Simultaneously, a contract research organization tackled the same problem. While both groups arrived at similar solutions, the open project was completed more swiftly with the added benefit of being entirely transparent (Woelle, Olliaro, and Todd 2011). The US government has also recognized the potential of crowdsourcing and established CitizenScience.gov, whose express purpose is to “accelerate the use of crowdsourcing and citizen science across the US government.”

III. Systematic evidence synthesis
In biomedical research, a spectrum of review methodologies exists, each varying in terms of rigor and purpose. Among these, narrative reviews, where an expert or a group of experts will summarize the literature on a specific topic, are more common (Faggion, Bakas, and Wasiak 2017). However, there are limitations to narrative reviews, as they typically draw from a selective subset of available literature without clear criteria and often fail to include the underlying data upon which their conclusions are based (Russell et al. 2022).

To address these limitations and enhance the scientific rigor and transparency of literature reviews, systematic evidence synthesis methodology emerged as a robust alternative. Evidence synthesis methodology involves researchers meticulously collecting and synthesizing research from diverse sources using systematic and transparent procedures (Gough et al. 2020). Evidence synthesis methodology has a set of best practices that are
predominantly determined by a few major sources in order to ensure the quality of the review. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) offers checklists that are specific to the type of review (Figure 2). Publishers often require that authors of evidence synthesis reviews submit a PRISMA checklist with their article to ensure transparency and evaluate the rigor of their methodology. The Cochrane Database of Systematic Reviews (CDSR) is the prominent database for systematic reviews in health care and publishes instructions on how best to conduct evidence synthesis reviews for health care (Higgins et al. 2023). Lastly, the Campbell Collaboration publishes the Campbell Systematic Reviews, a journal that focuses on evidence synthesis for social science topics and that also provides guidance on the best practices for evidence synthesis in the social sciences.

i. Benefits of clinical and preclinical evidence synthesis

The advent of evidence-based practice (EBP) in medicine during the 1990s ushered in an era where healthcare professionals relied on the extensive body of medical literature to inform their clinical decisions (Grant and Booth 2009). However, with the increased rate of research being published, it would be almost impossible for clinicians to absorb all this information in addition to actually treating patients. To address this challenge, systematic evidence syntheses, particularly meta-analyses, have emerged as essential tools for reviewing literature within a specific field.

The need to synthesize clinical data has been unmistakably established in the biomedical domain, both to inform medical decisions and to shape health policies (MacEntee 2019). This is especially true for meta-analysis studies, where the methodological protocols and meta-analysis classification criterion are specifically geared towards clinical data synthesis (MacEntee 2019; Grant and Booth 2009; Haidich 2010; Clarke 2018; Uman 2011). Systematic reviews and meta-analysis are the backbone of EBP, as evidenced by their widespread adoption in clinical research. As of 2014, it was estimated that over one million clinical systematic reviews had been published (Menon et al. 2021).

In stark contrast, preclinical evidence synthesis reviews have not enjoyed the same level of prevalence. Basic biology research has a very high rate of irreproducibility, between 60% and 100% (Ioannidis 2023). The lack of consistency between experimental groups is the central argument used against attempting evidence synthesis in the preclinical and basic science fields. However, this heterogeneity presents the strongest argument for needing systematic evidence synthesis within the field. The first preclinical evidence synthesis reviews began to emerge approximately a decade after the establishment of methodologies and standards for clinical evidence synthesis (Menon et al. 2021).

Despite their lower prevalence, preclinical evidence synthesis reviews provide an important value to the biomedical field. Evidence synthesis reviews can perform tests to reveal bias due to “p-hacking” (repeated analysis until a statistically significant one is found) or selection for the most impressive results. By looking at these studies as a whole, an evidence synthesis review can analyze the potential bias within the field (Ioannidis 2023).

Systematic evidence synthesis plays a pivotal role in translational studies, aiding in the assessment of whether a treatment under investigation is ready to transition to clinical trials (Russell et al. 2022). Furthermore, preclinical evidence synthesis reviews are helpful in evaluating the various animal models used to study different diseases and can expose the potential issues within these animal models (Basilious, Yager, and Fehlings 2015; Bansal et al. 2017; Brown et al. 2016; Hooijmans et al. 2012). This highlights ways that quality could and should be improved so that animals are not wasted (Pound and Ritskes-Hoitinga 2020; Ritskes-Hoitinga et al. 2014). These ways include improving the methodological quality of the animal studies, more carefully selecting which animal model to use, and focusing on evidence-based translation to only do clinical studies on therapies which have a demonstrated preclinical efficacy (de Vries et al. 2014). Some researchers have even developed frameworks to guide the analysis of animal study systematic reviews, with the aim of reducing research waste and enhancing translational efficacy (Hooijmans et al. 2018).

To more clearly demonstrate the impact of preclinical systematic reviews, Menon et al. (2021) conducted a mixed method case study where researchers who conducted preclinical systematic reviews or who attended relevant workshops were
recruited and asked about their experience. The findings revealed that the act of conducting these reviews led to notable improvements in the researchers’ approach. The study participants began planning future studies differently, more rigorously implementing guidelines and power calculations for statistical validity. Transparency in reporting methods and information also improved, with some participants specifically mentioning how systematic reviews helped them identify their passion for open science. Participants also gained new skills that were both research-related (meta-analysis, academic writing) and professionally-broad (collaboration, interdisciplinary work). Participants reported that conducting a systematic review changed their mindset, causing improvements in planning, conducting, and reporting research. This experience also helped participants identify problems with poorly designed animal or in vitro studies and issues related to reproducibility. It also assisted researchers with uncovering gaps within their fields. This information led Menon et al. (2021) to conclude that conducting systematic reviews would improve the training and education of trainees and early career researchers.

Preclinical evidence syntheses have a demonstrated value within the field both for the information they present and for the effects that conducting them have on researchers. They offer a formal introduction to the importance of transparency in research, laying the foundation for open science practices within the scientific community.

IV. The relationship between open science and evidence synthesis
Evidence synthesis, by the methodology accepted from those within the field, inherently aligns with open science principles. As previously discussed, when publishing a systematic review or any type of evidence synthesis, authors are often encouraged, or even required by some journals, to adhere to the PRISMA checklist. This checklist includes identification of a protocol or registration, transparent description of how articles were chosen and data collected, and a clear description of the results of the review or meta-analysis (Moher et al. 2009). The PRISMA checklist was developed in order to increase the quality of reporting within systematic evidence synthesis and, in accordance with open science principles, has been made freely accessible on the Annals of Internal Medicine website as well as the PRISMA website (Moher et al. 2009).

The PRISMA checklist asks authors to identify a protocol or registration. Many systematic evidence synthesis reviews are pre-registered, serving as announcements of ongoing reviews and transparent reporting of methodology. Various registries cater to this need. The Open Science Framework (OSF), developed by the Center for Open Science, is a discipline-independent tool that enables researchers to create and manage projects (Foster and Deardorff 2017). This allows researchers to archive the study design, data, or analysis in a way that is publicly available. So while OSF is not specifically for systematic evidence synthesis reviews, they do have a template available for the registration of these reviews that adheres to open science principles (Call 2023). The PROSPERO (International Prospective Register of Systematic Reviews) registry is tailored to systematic, rapid, and umbrella reviews, encompassing both clinical and preclinical studies. PROSPERO explicitly requires researchers to confirm the novelty of their topics in order to avoid duplication (National Institute for Health and Care Research, n.d.). By pre-registering their evidence synthesis review, researchers can ensure transparency and mitigate research waste by making sure their topic is unique (Pieper and Rombey 2022).

After registration, the process of conducting an evidence synthesis review continually entwines with open science. Many evidence syntheses employ software to aid in screening and data extraction. For example, Sysrev, a web platform designed with FAIR (Findability, Accessibility, Interoperability, and Reuse of digital assets) principles, enhances accessibility of data extracted from studies for future researchers. It fosters transparency by enabling public tracking and investigation of projects related to specific reviews (Bozada et al. 2021). Since users can be easily added to a project through their email, it would be easy to use Sysrev as a way to incorporate citizen scientists within the project.
Due to the substantial time commitment often associated with evidence synthesis, a variety of methods to expedite the process have emerged. Machine learning has been one suggestion, with software tools being developed to automate specific processes within evidence synthesis. This includes using active learning to highlight relevant studies during citation screening with the aim of reducing the amount of manual screening that must be done (van de Schoot et al. 2021).

Researchers have also begun utilizing crowdsourcing as a way of facilitating evidence synthesis. This involves drawing on a large collection of people who make small individual contributions to a project, adding up to a huge amount of labor; these small contributions are sometimes called “micro tasks.” While crowdsourcing in systematic evidence synthesis is relatively new, most analyses have focused on public involvement in citation screening (i.e., determining whether articles meet inclusion criteria) and data extraction (Strang and Simmons 2018). A pilot study on crowdsourcing systematic reviews, which looked at a review of pediatric clinical trials of high-dose vitamin D, found that using crowdsourcing was extremely effective (Nama et al. 2017).

Nonetheless, crowdsourcing poses challenges, including concerns about the quality of data generated by citizen scientists (Jialu Chen 2022). For example, it can be difficult to find qualified citizen scientists to perform data extraction, which generally requires more specialized knowledge. In one study, researchers found that only six of the twenty participants could pass the qualification test to see if they would be able to extract data from the abstracts of clinical trials (Lucy Strang and Rebecca Simmons 2018). Another problem is participation, with rates being uneven. In one study where crowdsourcing was used for citation screening, it was found that only twenty of the 100 people who were interested in the review actually completed any screening.

Even in cases where evidence syntheses do not directly involve citizen scientists, open science principles are still essential. Researchers conducting systematic evidence synthesis reviews are expected to report the entire PRISMA checklist (including the eligibility criteria, what data was extracted from studies, and any bias assessment conducted) as well as details on their methodology, like the search string used in each database search. This level of detail is expected within the field and is unusual relative to many other forms of research. This helps increase the potential reproducibility of these reviews. While initial stages of systematic evidence synthesis reviews, such as database searches and initial screening of titles and abstracts, may not require full-text access, the second screening stage (full-text assessment) demands access to entire articles (Figure 3). Although researchers may have access to some articles through university journal...
subscriptions, access to all required articles is unlikely. This necessitates retrieval through interlibrary loans or, in the worst case, payment of an additional fee to the publisher. This can quickly wrack up cost, especially in the case of a large systematic evidence synthesis review. This reliance on access to journal articles means that systematic reviews would be extremely challenging or expensive for citizen scientists without a research institution login. This would hamper the ability of citizen scientists to participate in the stages of systematic evidence synthesis that require access to the full text of a paper. This is why open access (OA), a central tenet of open science, is so important for evidence synthesis. The more journals and publications that are pushed OA, the less complicated, expensive, and time-consuming evidence synthesis becomes. Furthermore, being able to extract data from these papers is an essential part of the evidence synthesis process, which makes the public availability of datasets very important. Many evidence synthesis reviews will support having datasets public by publishing their own retrieved datasets within data repositories, their supplemental files, or data in brief articles.

V. Policy considerations

i. Change the scientific publication model

Research publications in high impact journals play a huge role in how success is validated for researchers in academia. “Publish or perish” is a moniker often quoted around academic institutions to explain the need to produce peer-reviewed articles. Many universities require at least one research journal article published or accepted in order for PhD students to graduate (Moradi 2019). Likewise, publication in esteemed journals significantly influences researchers’ career trajectories (Näre 2022; Adimoelja and Athreya 2022). The scientific research lifecycle is highly dependent on academic publishers. The peer review process is carried out through these journals, with publications in “high-impact” journals lauded as the ultimate goal for many researchers. While the peer-review process is important to ensure high quality work, the traditional scientific publication process has a plethora of problems, particularly in regards to the publication of evidence synthesis. Because of this, open access publication platforms with low authorship fees or a federally run open access publication should be supported to mitigate these problems.

Peer-review, the central value that traditional scientific publication brings, has sometimes failed to uphold a high standard of results. An egregious example of this is within the Alzheimer research field, where multiple high-profile researchers have published manipulated data (Piller 2022; Blaff 2023). The traditional publication process failed to find this, and it was only independent investigations that eventually uncovered this malpractice. Furthermore, there is a huge amount of time required for peer review at traditional publishers (Elliott et al. 2017). Review for articles can be delayed weeks or months, with the results not providing enough constructive commentary to actually improve the work (Emile 2021). In fact, Gropp et al. (2017) described the entire peer review process as “a system under stress” (Gropp et al. 2017).

The flaws of the traditional publication system are apparent when discussing evidence synthesis. Evidence synthesis methods aim to inform various decisions, especially in health, based on “the best available evidence” (Elliott et al. 2017). However, as they are generally static, or only updated intermittently, evidence synthesis can become easily out of date, especially when the current fast rate of research is considered. When conducting an evidence synthesis review, the time between the last database search and publication is often over a year due to the work required to screen citations, extract data, and write the publication (Elliott et al. 2014). This means that by the time of publication, the review is missing a year of newly published studies. By continuously updating a review, the reviews remain accurate. This is especially important as it has been demonstrated that by two years after publication, 23% of clinical systematic reviews will not have evidence that would change the conclusions about the studied therapies (Shojania et al. 2007).

The solution is living systematic reviews, where the reviews are continuously updated, incorporating new evidence as it is published (Elliott et al. 2017). This means that the publication platform must allow for the publication to be frequently updated, with best practices having version updates. Similarly, authorship will change as the review is updated over time and must be easily changed on the platform.

www.sciencepolicyjournal.org
(Elliott et al. 2017). Lastly, the peer review process of these updates would need to be tailored for rapid new review, which is at odds with the current state of peer review. Furthermore, some journals will not publish evidence synthesis. Nature Reviews specifically mentions that they do not take evidence synthesis reviews and that their articles should have “minimal re-analyses of published data” (“Preparing Your Submission” n.d.). When taken together, it becomes clear that the publication model would need to be updated for living systematic reviews to be easily disseminated. Currently, many living systematic reviews are not traditionally published, and instead are published on project websites where the continual updates can be more easily shared (Lesser 2023). As an example, openMetaAnalysis on GitHub provides a platform that helps collaboratively maintain living reviews and other evidence syntheses (OpenMetaAnalysis Contributors n.d.).

Some journals are attempting to redesign this process to promote transparency, ease of update, and open access. The eLife journal, an independent nonprofit publication, changed the typical publication process in hopes of promoting “open and trusted results for the benefit of all.” Their publication process starts by putting up preprints and using public peer review, calling this model “publish, review, curate”. The eLife journal is also OA, and lists openness as a central tenet of their strategic vision (“eLife Latest: A New Vision for Transforming Research Communication” 2022). Similarly, the F1000Research platform also deviates from the traditional model. Researchers submit their articles to the platform, where their editorial staff ensure that their policies and ethical guidelines are followed. Less than a week later the article is published and the process of open peer review and user commenting begins, with expert reviewers invited and their comments publicly available alongside the article. Authors then can publish their revised version of the article, with each version linked and independently citable (“How It Works” n.d.).

Both of these platforms, with their rapid publication models, would be viable for living systematic reviews. F1000Research in particular, with the ability to publish linked revisions, would be ideal. These types of private solutions to the problems of the scientific publication system should be supported and encouraged. As discussed in Section II, the White House OSTP recently released policy changes that recommended federal agencies require their researchers and fundees to make their publications OA by the end of 2025 (Nelson 2022). This has raised concerns about how researchers will afford the costs associated with making articles and data OA, given the substantial OA fees charged by publishers and potential fees for data repositories. The NIH has policies mandating that recipients of their funding make their publications publicly available on PubMed Central within twelve months of acceptance and have data management and sharing plans (“Revised Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research” 2008; Office of The Director 2020). A potential solution could involve establishing a federally funded and operated publisher.

Federal agencies already have a network of public repositories, like PubMed, where agency-funded research is publicly available (Office of Science and Technology Policy 2023) (Table 1). It has been estimated that the federal government spent over $378,000,000 on publication fees associated with federally-funded research. This would suggest that the budget for a federally funded and operated publisher exists. Therefore, existing federal repositories could be transitioned into peer-reviewed journals. These journals would have a few central tenants: open access, free to publish, and required peer review. They would cover a huge variety of federally funded research topics. While there would be no monetary publication fee for authors to publish, properly qualified authors would be required to peer review another paper for the journal. This would help peer review occur more expeditiously, as less time would need to be spent searching for reviewers. One potential concern with such a model would be government censorship of research, with a federal agency choosing what can be published in their associated journal. These federally-funded publishers, however, would be a suggestion, not a requirement, so researchers whose manuscripts are rejected could instead publish in a traditional journal. Furthermore, the reasons that a manuscript is rejected or accepted could be publicly posted while still allowing preprint access to the research. This option would follow the eLife model of publication and could help to ensure transparency.
Table 1: Federal Repositories. Adapted from Office of Science and Technology Policy 2023.

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ii. Increase funding for preclinical systematic evidence synthesis

The topics and methodologies pursued in research are profoundly influenced by available funding opportunities and the lack of funding for preclinical evidence syntheses restricts the potential for these reviews to be produced. As of September 2023, the NIH Guide for Grants and Contracts lists ten active funding opportunities and notices related to meta-analysis and systematic reviews (Table 2). Four of these opportunities explicitly seek evidence synthesis of clinical data, while an additional four emphasize a "patient-focused" approach, although they do not specify secondary analysis of clinical data. These "patient-focused" grants refer to comparative effectiveness research (CER), which is a form of evidence synthesis that compares treatment or intervention benefits and risks among patient subgroups. Even when the funding calls do not explicitly mention clinical data, the use of CER methodology implies a need for such data.

Only one of these grants explicitly mentions considering preclinical evidence synthesis. A search for "systematic review" in the National Science Foundation's active funding opportunities (as of September 26, 2023) yielded no funding opportunities for any type of systematic review or meta-analysis. As mentioned in the previous section, some journals specifically state that they will not publish systematic evidence synthesis reviews. It is likely that the lack of value journals are placing on evidence syntheses will affect the availability of funding for them.
Despite the relative scarcity of funding opportunities dedicated to systematic evidence syntheses, the NIH frequently requests their inclusion in research proposals. Some grants seek applications to reference previous evidence synthesis reviews that support the need for proposed research. The NIH even solicits systematic reviews, though without funding for conducting the evidence synthesis, probably due to the assumption that a review article does not need funding or is relatively cheap (NOT-HL-14-203, RFA-ES-12-006). The costs associated with conducting evidence synthesis, including software, access to non-OA articles, and the significant time investment, make proper funding imperative. While certain software tools like Sysrev, mentioned in Section III, offer free versions, conducting an evidence synthesis review is often financially burdensome. A 2019 study estimated that each clinical systematic review or meta-analysis costs approximately $141,194 to conduct (Michelson and Reuter 2019). Another study analyzed preregistered systematic reviews from the PROSPERO registry and found that, on average, systematic reviews took 67.3 weeks, over a year, to complete, with around five authors reported per review (Borah et al. 2017). The amount of time and resources required to complete evidence synthesis reviews make doing so without proper funding restrictive.

Funding for systematic reviews is not without precedent. Several organizations promote preclinical systematic reviews, offering free resources and funding to support researchers in conducting them. One example is the UK’s NC3Rs, though this is only for researchers whose primary investigator is in the UK (“Introduction to Systematic Reviews” n.d.; “SyRF: The CAMARADES/NC3Rs in Vivo Systematic Review and Meta-Analysis Facility” 2018). Another example, Germany’s Federal Ministry of Education and Research, has released funding specifically for preclinical systematic reviews for German Research institutions (“Notice: Guideline for the Funding of Preclinical Confirmatory Studies and Systematic Reviews” 2022). Encouraging preclinical systematic evidence synthesis through funding incentives can help reduce research waste and facilitate a comprehensive analysis of previously published preclinical research.

VI. Conclusion
Evidence synthesis reviews represent an indisputably crucial component of evidence-based medicine, with preclinical systematic reviews offering a multitude of advantages. These reviews help curtail research waste (particularly concerning animal studies), elevate research quality, and enable meticulous scrutiny of research methodologies. Furthermore, they open the door to the involvement of citizen scientists through crowdsourced screening and data extraction processes.

Citizen science is an important part of open science, which is the principle that science should be transparent and publicly available. This is currently being codified in the U.S. through policy advances by the Biden-Harris Administration. This includes making the findings of research funded by federal agencies immediately available upon publication, as well as the data included within the study.

This assessment has identified two pivotal policy areas that require attention to advance open science and evidence synthesis. First, the traditional publication model, due to its reliance on a costly subscription-based framework, inherently opposes the principles of open science. As a potential remedy, this assessment recommends endorsing and supporting journals that endeavor to reshape the traditional publication model, such as eLife and F1000Research. Minimal authorship fees, transparent peer review, open access, and the ability to easily update manuscripts are a few ways these publication platforms are improving the traditional publication model, which facilitates both open science policy and evidence synthesis reviews. Alternatively, consideration should be given to establishing a federal publisher with open access journals and minimal or no publishing costs to researchers.

The second significant challenge is the insufficient funding allocated for systematic evidence synthesis, despite its evident benefits. It is essential for federal agencies to recognize the value that these reviews bring and to allocate funding to facilitate their creation. This investment not only enhances research quality, but also contributes to the overarching goal of promoting open science and ensuring that valuable research reaches a broad audience.
By examining open science policy through an evidence synthesis lens, the publication and funding challenges become clear. However, this assessment has proposed policy suggestions, like a federally run publisher, to mitigate these challenges. The goals of both open science and evidence synthesis is to promote collaboration and coalition of scientific knowledge to solve problems for society and advance the field, which is why policy should be adjusted to facilitate them.
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<tr>
<td>NEI Research Grant for Vision-Related Secondary Data Analysis (R21 Clinical Trial Not Allowed)</td>
<td>3/16/2022</td>
<td>PAR-22-141</td>
<td>National Eye Institute</td>
<td>Funding for secondary data analysis of vision-related clinical data.</td>
<td>Clinical</td>
<td>$275,000</td>
<td></td>
</tr>
<tr>
<td>AHRQ Mentored Career Enhancement Awards for Established Investigators in Patient-Centered Outcome Research (K18)</td>
<td>12/8/2021</td>
<td>PA-22-051</td>
<td>Agency for Healthcare Research and Quality</td>
<td>Funding for mid or senior investigators who wish to develop new skills in CER methodology and applying these methods to patient research.</td>
<td>Unspecified (but patient focused)</td>
<td>$275,000 annually, cannot be for more than 2 years.</td>
<td></td>
</tr>
<tr>
<td>AHRQ Patient-Centered Outcomes Research (PCOR) Mentored Clinical Scientist Career Development Award (K08)</td>
<td>12/8/2021</td>
<td>PA-22-050</td>
<td>Agency for Healthcare Research and Quality</td>
<td>Funding to support individuals with clinical doctoral degrees to learn CER methodology.</td>
<td>Unspecified (but patient focused)</td>
<td>$115,000 annually for up to 5 years.</td>
<td></td>
</tr>
<tr>
<td>AHRQ Patient-Centered Outcomes Research (PCOR) Mentored Research Scientist Career Development Award (K01)</td>
<td>12/8/2021</td>
<td>PA-22-049</td>
<td>Agency for Healthcare Research and Quality</td>
<td>Funding to support research scientists to learn CER methodology.</td>
<td>Unspecified (but patient focused)</td>
<td>$115,000 annually for up to 5 years.</td>
<td></td>
</tr>
<tr>
<td>Research Resource for Systematic Reviews of Complementary and Integrative Health (R24 Clinical Trial)</td>
<td>7/13/2023</td>
<td>RFA-AT-24-005</td>
<td>National Center for Complementary and Alternative Medicine</td>
<td>Initiative to support the building and maintenance of a database of clinical trials with complementary or</td>
<td>Clinical</td>
<td>$400,000</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2: NIH funding notices for systematic reviews and meta-analysis.

<table>
<thead>
<tr>
<th>Title</th>
<th>Date</th>
<th>Notice</th>
<th>Purpose</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH Announces the Availability of Recovery Act Funds for Administrative Supplements for Comparative Effectiveness Research Workforce Development</td>
<td>1/4/2010</td>
<td>NOT-OD-10-037</td>
<td>An administrative supplement for investigators or institutions that have NIH Grants to learn CER methodology.</td>
<td>Unspecified (but patient focused)</td>
</tr>
</tbody>
</table>

These were retrieved by searching “Systematic Review” in the NIH Guide for Grants and Contracts (September 19th, 2023) and hand-screening the results.
References


Colette S.M. Bilynsky is a Ph.D. Candidate at Carnegie Mellon University in the Biomedical Engineering department. Colette studies macrophage polarization in colorectal cancer, and her projects have focused on developing a method to track this polarization as well as a comprehensive scoping review and meta-analysis of the nanomedicine in this field. She is passionate about open science principles and science communication, and is involved in Carnegie Mellon University’s graduate student assembly’s external affairs committee, helping to organize voter registration drives and meetings with congressmen to discuss graduate student issues. Colette plans on pursuing a career in science policy or communication upon the completion of her PhD.

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