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**Reproducibility and replicability of systematic reviews**

Shokraneh F. Reproducibility and replicability of systematic reviews

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**Abstract**

Irreproducibility of research causes a major concern in academia. This concern affects all study designs regardless of scientific fields. Without testing the reproducibility and replicability it is almost impossible to repeat the research and to gain the same or similar results. In addition, irreproducibility limits the translation of research findings into practice where the same results are expected. To find the solutions, the Interacademy Partnership for Health gathered academics from established networks of science, medicine and engineering around a table to introduce seven strategies that can enhance the reproducibility: pre-registration, open methods, open data, collaboration, automation, reporting guidelines, and post-publication reviews. The current editorial discusses the generalisability and practicality of these strategies to systematic reviews and claims that systematic reviews have even a greater potential than other research designs to lead the movement toward the reproducibility of research. Moreover, I discuss the potential of reproducibility, on the other hand, to upgrade the systematic review from review to research. Furthermore, there are references to the successful and ongoing practices from collaborative efforts around the worlds to encourage the systematic reviewers, the journal editors and publisher, the organizations linked to evidence synthesis, and the funders and policy makers to facilitate this movement to gain the public trust in research.

**Key words:** Systematic review; Meta-analysis; Reproducibility of results; Automation; Data science; Data anonymization; Datasets; Guideline adherence; Guideline; Peer-review

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**Core tip**: Reproducibility increases the practicality of the research findings and gains the public trust in research. The ongoing developments in automation of systematic reviews, availability of pre-registration platform, dealing more with secondary data or anonymized primary data, the collaboration culture among the organizations who produce systematic reviews, and finally having an update step that mandates replicability are all reasons that systematic reviews have the potential to lead the movement toward the reproducibility among the other research designs. Meanwhile, reproducibility can help the systematic reviews to be considered as research design rather than literature review.

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**INTRODUCTION**

Systematic reviews are at high levels of evidence hierarchy in clinical practice[1]. People who are involved in healthcare systems usually use systematic reviews in research, policy, and practice[3] trusting the reproducibility of the results when implemented[2]. As the same time, some criticize that the systematic reviews are literature reviews not research[4,5]. To utilize the systematic reviews in practice and to call them research studies, we need reproducibility testing; and to ensure that a systematic review is reproducible it is important to prioritize and fund, to design, to record and to report systematic reviews in a transparent and reproducible way[6]. Some suggest that a team independent from the original team can repeat the systematic reviews to ensure the reproducibility[7]. Since conducting systematic reviews is already time-consuming[8] and resource-rating[9], it is arguable how adding more steps such as reproducibility test that requires more time and resources could reduce waste and increase value.

In context of this paper, reproducibility is re-conducting the same study, using the same methods and data by a different researcher or team and the replicability is re-doing the same study to gather new data or recollect the data[10].

To provide solutions for irreproducibility, the Interacademy Partnership for Health introduced seven strategy to enhance the reproducibility practice in science[11]. This editorial discusses the progress with using these strategies in systematic reviewing process and calls for collaboration in all levels of system to enhance the reproducibility of systematic reviews.

**STRATEGY 1: PRE-REGISTRATION**

Currently, prospective registration of systematic review protocols in PROSPERO, a register of systematic review protocols, is recommended[12]. Compared to clinical trials with at least 17 registries[13] there is only one register for systematic reviews; however, unlike clinical trials, it is not yet a mandatory to register systematic reviews prospectively[14]. Today, PROSPERO covers only 30000 records of conducted, ongoing, awaiting, and abandoned review family (less than a third of 100000 systematic reviews in MEDLINE)[15], it does not support the quality control mechanism[16], and it lacks a rigor follow-up procedure for abandoned systematic reviews[17]. To look at the bright side, there is an association between registration of the published reviews and the quality of these reviews[18]. Allocating more resources to this register, training and encouraging the systematic reviews to register their reviews, and making the pre-registration a standard for bias control will push the reproducibility theory toward practice.

**STRATEGY 2: OPEN METHODS**

Researchers should share search strategies for all databases[19] and analytical codes for meta-analysis[20] as part of the methods of systematic reviews. Following to the prospective registration of the protocol and publication of the protocol, the researchers and the research audiences could assess the reproducibility and detect if any variation from the protocol could have important implementation messages for research, policy and practice[12]. This practice is not just to test the reproducibility but also to replicate another analysis or a new update for the systematic review. None of these are possible without access to all search strategies and statistical codes for meta-analysis.

**STRATEGY 3: OPEN DATA**

Search results (excluding copyrighted abstract and database-specific meta-data) in Research Information Systems format[21] and extracted data and meta-data from the studies are the main resulting dataset during the systematic reviewing[22-24]. Access to open data from systematic reviews makes it possible to re-screen the search results, to de-duplicate the update searches, to re-run the meta-analyses, and to test the reproducibility of searching, screening, and data analysis steps. Besides, these data will have more value if they have been shared beside their associated meta-data following FAIR guidelines (findable, accessible, inter-operable, and reusable)[25]. There have already been calls for sharing the data from systematic reviews but there is no policy or action in place[22-24]. Sharing the data from all systematic reviews can lead into data-driven innovations with potential for knowledge discovery and saving the waste of resources and lives.

**STRATEGY 4: COLLABORATION**

Collaboration among research teams in small or large scale increases the chance for more expertise input and enhances the error detection and fixation practice[26,27]. Sharing the data among collaborators or interested research groups could bring together the data and resources for re-analyzing the same data[20] or innovations[23] that are impossible without such collaboration. It is not good practice to hold the data for years hoping to receive funding or innovating while sharing could result in faster innovation, receiving credits or collaboration in grant applications[26,27]. It also raises the morality and mortality question that is it ethical to hold the data when sharing it could lead to decisions that can save public resources and lives, and reduce the waste. The data extracted from other primary research for systematic reviews cannot be owned by the systematic reviewers or organizations that produce the systematic reviews.

**STRATEGY 5: AUTOMATION**

International Collaboration for the Automation of Systematic Reviews produces annual report of progress for automation of systematic reviews[28-30]. This collaboration seems to understand well that the automation is a key for reproducibility and follows Vienna Principles that also emphasize on the replicability of automation activities and sharing the program codes for wider use by the community[28]. The value of the automation becomes more obvious looking at reports of human errors in systematic reviews in searching[31] and data extraction steps[32]. The service provided by machine can speed the process and reduce the waste caused by human errors through standardization of practices such as statistical analysis or systematic review write-up steps[30,33]. Despite all technological development, systematic reviewers have underused the automation tools[34]. Currently, Systematic Review Data Repository[35], EPPI-Reviewer[36], Study-Based Registers[37], and Evidence Pipeline as semi-automated systems have the potential to evolve into automated systems for systematic reviews.

**STRATEGY 6: REPORTING GUIDELINES**

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[38] now celebrates a decade of being used in reporting step of systematic reviews and major journals enforce the systematic reviewers to follow the PRISMA family guidelines in reporting. Such reporting guidelines are helping researchers to report certain items for publications and it is not their primary purpose to advocate the reproducibility[6]. There is an update of PRISMA 2019 in progress that will include more items and some these items can maximize the reproducibility practice[6].

**STRATEGY 7: POST-PUBLICATION REVIEW**

Pre-publication peer-reviews are limited to a few people while post-publication reviews give chance for wider audience to publicly share, comment, appraise and criticize some aspect of the research. Post-publication activities take many forms including letter to editor, commentary, blogs, and other social media posts[26]. These reviews are separate and independent from the original research and the only connection is through a link or citation. As a result, it is hardly impossible to find all these reviews integrated in one place. This problem expands when there are retractions to the original systematic reviews or the findings are publication in salami of papers. Such post-publication reviews, however, are encouraged specifically for systematic reviews because they can be taken into account in the next updates of the current systematic review. Having an update step in development of systematic reviews, unlike other published literature, is a unique advantage of systematic reviews allowing the reviewers to correct their mistakes and errors or to consider addition of new data or aspect to the review.

**OPEN PROCESS: EMBEDDED REPRODUCIBILITY IN AGREEMENT CHECKS**

As an addition to these strategies, it is also important not to overlook the process of the systematic reviewing and its connection to reproducibility. The routine practice in systematic reviews is to involve at least two researchers in screening and data extraction steps to reduce human errors[32,39] through double-checking of the decision and to reach an agreement. Such agreement sometimes requires a discussion between two or inviting the comments from another usually senior researcher. It means the decision on eligibility of studies or accuracy of data extraction is being replicated twice or three times. Since this process itself is replicating part of the review and has value for improving the reproducibility, some of the automation and semi-automation systems allow the researchers to document the process of double- and triple-checking within the system but for transparency purposes, this needs to be shared as well. In over words, the process should be documented and publicly shared.

**SYSTEMATIC REVIEWS AS ROLE MODEL FOR OTHER RESEARCH DESIGNS**

Systematic reviews have the great potential to lead the reproducibility practice in the rest of study designs in scientific fields: A: Having an update step allows the systematic reviews to be corrected and helps in advancing what is called ‘living systematic reviews’; B: Making a unique progress in automation of systematic reviews helps researchers to save time and resources on every step of systematic reviewing; C: Provision of protocol and methods facilitates the replication of systematic review in update step. To make such role model, the organizations whose main activity includes producing systematic reviews should come together and collaborate on developing policies on reproducibility and sharing the data and methods from within the systematic reviews. On the other hand, these organizations have their own journal platforms and the journal publishers themselves need to engage in this policy development as well. To avoid a meta-waste, Cochrane Database of Systematic Reviews, *Systematic Reviews* journal, *World Journal of Meta-Analysis*, *JBI Database of Systematic Reviews and Implementation Reports*, and *Environmental Evidence* now have a great opportunity to come together and set the bars on reproducibility of systematic reviews.

**REFERENCES**

1 **Centre for Evidence-based Medicine**. Oxford Centre for Evidence-based Medicine – Levels of Evidence, 2009. Available from: URL: https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

2 **Ahmad N**, Boutron I, Dechartres A, Durieux P, Ravaud P. Applicability and generalisability of the results of systematic reviews to public health practice and policy: a systematic review. *Trials* 2010; **11**: 20 [PMID: 20187938 DOI: 10.1186/1745-6215-11-20]

3 **Chalmers I**, Fox DM. Increasing the Incidence and Influence of Systematic Reviews on Health Policy and Practice. *Am J Public Health* 2016; **106**: 11-13 [PMID: 26562111 DOI: 10.2105/AJPH.2015.302915]

4 **Campbell A**. A Quick Guide to Research Methods. *ANZJFT* 2004; **25**: 165-167 [DOI: 10.1002/j.1467-8438.2004.tb00610.x]

5 **Petticrew M**. Systematic reviews from astronomy to zoology: myths and misconceptions. *BMJ* 2001; **322**: 98-101 [PMID: 11154628 DOI: 10.1136/bmj.322.7278.98]

6 **Page MJ**, Altman DG, Shamseer L, McKenzie JE, Ahmadzai N, Wolfe D, Yazdi F, Catalá-López F, Tricco AC, Moher D. Reproducible research practices are underused in systematic reviews of biomedical interventions. *J Clin Epidemiol* 2018; **94**: 8-18 [PMID: 29113936 DOI: 10.1016/j.jclinepi.2017.10.017]

7 **Faggion CM Jr**. Should a systematic review be tested for reproducibility before its publication? *J Clin Epidemiol* 2019 [PMID: 30772455 DOI: 10.1016/j.jclinepi.2019.02.008]

8 **Sampson M**, Shojania KG, Garritty C, Horsley T, Ocampo M, Moher D. Systematic reviews can be produced and published faster. *J Clin Epidemiol* 2008; **61**: 531-536 [PMID: 18471656 DOI: 10.1016/j.jclinepi.2008.02.004]

9 **Borah R**, Brown AW, Capers PL, Kaiser KA. Analysis of the time and workers needed to conduct systematic reviews of medical interventions using data from the PROSPERO registry. *BMJ Open* 2017; **7**: e012545 [PMID: 28242767 DOI: 10.1136/bmjopen-2016-012545]

10 **Patil P,** Peng RD, Leek JT. A statistical definition for reproducibility and replicability. *bioRxiv* 2016: 066803 [DOI: 10.1101/066803]

11 **The Interacademy Partnership for Health.** A call for action to improve the reproducibility of biomedical research. Available from: URL: https://research-integrity.uq.edu.au/files/4502/IAPforHealth-statement-Sep2016.pdf

12 **Stewart L**, Moher D, Shekelle P. Why prospective registration of systematic reviews makes sense. *Syst Rev* 2012; **1**: 7 [PMID: 22588008 DOI: 10.1186/2046-4053-1-7]

13 **World Health Organization.** International Clinical Trial Registry Platform: Data Providers, 2019. Available from: URL: https://www.who.int/ictrp/search/data\_providers/en/

14 **Booth A**, Stewart L. Trusting researchers to use open trial registers such as PROSPERO responsibly. *BMJ* 2013; **347**: f5870 [PMID: 24088555 DOI: 10.1136/bmj.f5870]

15 **Page MJ**, Shamseer L, Tricco AC. Registration of systematic reviews in PROSPERO: 30,000 records and counting. *Syst Rev* 2018; **7**: 32 [PMID: 29463298 DOI: 10.1186/s13643-018-0699-4]

16 **Booth A**, Clarke M, Dooley G, Ghersi D, Moher D, Petticrew M, Stewart L. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. *Syst Rev* 2012; **1**: 2 [PMID: 22587842 DOI: 10.1186/2046-4053-1-2]

17 **Andrade R**, Pereira R, Weir A, Ardern CL, Espregueira-Mendes J. Zombie reviews taking over the PROSPERO systematic review registry. It's time to fight back! *Br J Sports Med* 2017 [PMID: 29021246 DOI: 10.1136/bjsports-2017-098252]

18 **Sideri S**, Papageorgiou SN, Eliades T. Registration in the international prospective register of systematic reviews (PROSPERO) of systematic review protocols was associated with increased review quality. *J Clin Epidemiol* 2018; **100**: 103-110 [PMID: 29339215 DOI: 10.1016/j.jclinepi.2018.01.003]

19 **Koffel JB**, Rethlefsen ML. Reproducibility of Search Strategies Is Poor in Systematic Reviews Published in High-Impact Pediatrics, Cardiology and Surgery Journals: A Cross-Sectional Study. *PLoS One* 2016; **11**: e0163309 [PMID: 27669416 DOI: 10.1371/journal.pone.0163309]

20 **Goldacre B**. All BMJ research papers should share their analytic code. *BMJ* 2016; **352**: i886 [PMID: 26892475 DOI: 10.1136/bmj.i886]

21 **Shokraneh F.** Reproducible and Replicable Search for Research Methods in Systematic Reviews. Search Solutions 2018; 2018 Nov 26; London, UK

22 **Haddaway NR.** Open Synthesis: on the need for evidence synthesis to embrace Open Science. *Environmental Evidence* 2018; **7**: 26 [DOI: 10.1186/s13750-018-0140-4]

23 **Shokraneh F**, Adams CE, Clarke M, Amato L, Bastian H, Beller E, Brassey J, Buchbinder R, Davoli M, Del Mar C, Glasziou P, Gluud C, Heneghan C, Hoffmann T, Ioannidis JP, Jayaram M, Kwong J, Moher D, Ota E, Sheriff RS, Vale L, Goldacre B. Why Cochrane should prioritise sharing data. *BMJ* 2018; **362**: k3229 [PMID: 30061322 DOI: 10.1136/bmj.k3229]

24 **Wolfenden L**, Grimshaw J, Williams CM, Yoong SL. Time to consider sharing data extracted from trials included in systematic reviews. *Syst Rev* 2016; **5**: 185 [PMID: 27809924 DOI: 10.1186/s13643-016-0361-y]

25 **Wilkinson MD**, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, Blomberg N, Boiten JW, da Silva Santos LB, Bourne PE, Bouwman J, Brookes AJ, Clark T, Crosas M, Dillo I, Dumon O, Edmunds S, Evelo CT, Finkers R, Gonzalez-Beltran A, Gray AJ, Groth P, Goble C, Grethe JS, Heringa J, 't Hoen PA, Hooft R, Kuhn T, Kok R, Kok J, Lusher SJ, Martone ME, Mons A, Packer AL, Persson B, Rocca-Serra P, Roos M, van Schaik R, Sansone SA, Schultes E, Sengstag T, Slater T, Strawn G, Swertz MA, Thompson M, van der Lei J, van Mulligen E, Velterop J, Waagmeester A, Wittenburg P, Wolstencroft K, Zhao J, Mons B. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* 2016; **3**: 160018 [PMID: 26978244 DOI: 10.1038/sdata.2016.18]

26 **Academy of Medical Sciences**. Reproducibility and reliability of biomedical research: improving research practice, 2015. Available from: URL: https://acmedsci.ac.uk/policy/policy-projects/reproducibility-and-reliability-of-biomedical-research

27 **Academy of Medical Sciences**. Improving research reproducibility and reliability: progress update from symposium sponsors, 2016. Available from: URL: https://mrc.ukri.org/documents/pdf/reproducibility-update-from-sponsors/

28 **Beller E**, Clark J, Tsafnat G, Adams C, Diehl H, Lund H, Ouzzani M, Thayer K, Thomas J, Turner T, Xia J, Robinson K, Glasziou P; founding members of the ICASR group. Making progress with the automation of systematic reviews: principles of the International Collaboration for the Automation of Systematic Reviews (ICASR). *Syst Rev* 2018; **7**: 77 [PMID: 29778096 DOI: 10.1186/s13643-018-0740-7]

29 **O'Connor AM**, Tsafnat G, Gilbert SB, Thayer KA, Wolfe MS. Moving toward the automation of the systematic review process: a summary of discussions at the second meeting of International Collaboration for the Automation of Systematic Reviews (ICASR). *Syst Rev* 2018; **7**: 3 [PMID: 29316980 DOI: 10.1186/s13643-017-0667-4]

30 **O'Connor AM**, Tsafnat G, Gilbert SB, Thayer KA, Shemilt I, Thomas J, Glasziou P, Wolfe MS. Still moving toward automation of the systematic review process: a summary of discussions at the third meeting of the International Collaboration for Automation of Systematic Reviews (ICASR). *Syst Rev* 2019; **8**: 57 [PMID: 30786933 DOI: 10.1186/s13643-019-0975-y]

31 **Sampson M**, McGowan J. Errors in search strategies were identified by type and frequency. *J Clin Epidemiol* 2006; **59**: 1057-1063 [PMID: 16980145 DOI: 10.1016/j.jclinepi.2006.01.007]

32 **Buscemi N**, Hartling L, Vandermeer B, Tjosvold L, Klassen TP. Single data extraction generated more errors than double data extraction in systematic reviews. *J Clin Epidemiol* 2006; **59**: 697-703 [PMID: 16765272 DOI: 10.1016/j.jclinepi.2005.11.010]

33 **Tsafnat G**, Glasziou P, Choong MK, Dunn A, Galgani F, Coiera E. Systematic review automation technologies. *Syst Rev* 2014; **3**: 74 [PMID: 25005128 DOI: 10.1186/2046-4053-3-74]

34 **van Altena AJ**, Spijker R, Olabarriaga SD. Usage of automation tools in systematic reviews. *Res Synth Methods* 2019; **10**: 72-82 [PMID: 30561081 DOI: 10.1002/jrsm.1335]

35 **Li T**, Vedula SS, Hadar N, Parkin C, Lau J, Dickersin K. Innovations in data collection, management, and archiving for systematic reviews. *Ann Intern Med* 2015; **162**: 287-294 [PMID: 25686168 DOI: 10.7326/M14-1603]

36 **Park SE**, Thomas J. Evidence synthesis software. *BMJ Evid Based Med* 2018; **23**: 140-141 [PMID: 29880698 DOI: 10.1136/bmjebm-2018-110962]

37 **Shokraneh F**, Adams CE. Study-based registers of randomized controlled trials: Starting a systematic review with data extraction or meta-analysis. *Bioimpacts* 2017; **7**: 209-217 [PMID: 29435428 DOI: 10.15171/bi.2017.25]

38 **Moher D**, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009; **6**: e1000097 [PMID: 19621072 DOI: 10.1371/journal.pmed.1000097]

39 **Carroll C**, Scope A, Kaltenthaler E. A case study of binary outcome data extraction across three systematic reviews of hip arthroplasty: errors and differences of selection. *BMC Res Notes* 2013; **6**: 539 [PMID: 24344873 DOI: 10.1186/1756-0500-6-539]

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