

## **Open Medicine endorses PROSPERO**

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"'Tis as impossible that he's undrowned  
as he that sleeps here swims."

- William Shakespeare, *The Tempest*, 2.1

Systematic reviews, which synthesize the data from individual studies, are considered the highest level of evidence for evaluating the effectiveness of health care interventions. They inform clinical practice guidelines and are used by health-policy makers to guide key decision-making. They can point to gaps in knowledge where new research is needed and provide knowledge about the saturation of evidence about effectiveness and where new research is not needed and indeed might be unethical (1). On February 22, 2011, the Centre for Reviews and Dissemination, University of York launched PROSPERO, an international prospective register of systematic review protocols. The registry was developed to address excessive duplication of systematic reviews, improve transparency and minimize reporting biases. *Open Medicine* endorses systematic review protocol registration at PROSPERO and encourages prospective authors to register their review protocols on health care interventions at <http://www.metaxis.com/PROSPERO/>.

One recent study estimated that 11 new systematic reviews are published daily (2). There is currently substantive duplication of specific review topics, each of which might have slightly varied methods and quality (3), resulting in an unnecessary waste of academic resources without necessarily bringing us closer to the 'truth'. This duplication is also an ineffective use of taxpayer dollars, particularly when such reviews are funded by public agencies. If adopted widely, PROSPERO will allow review authors to quickly familiarize themselves with ongoing reviews in order to avoid duplication. Practitioners will be able to use the

protocols database to search for reviews, either published or impending, to learn best practices for patient care. Policy makers will be better able to identify those questions regarding health care effectiveness requiring urgent investigation versus those already underway. Funders can also use the register to help identify instances of excessive duplication. PROSPERO may serve to increase the visibility of a particular review and potentially foster collaboration between various groups. Such collaboration could also expand a review group's ability to assess non-English language evidence.

This plethora of reviews is known to be of variable quality (4). In their 2009 call to improve the transparency of reporting systematic reviews, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement called for the registration of systematic review protocols to reduce the probability of biased post hoc decisions and selective outcome reporting (5). Synthesis methods such as systematic reviews and meta-analysis were originally developed to *reduce* bias and error when assessing the treatment effect of a particular health care intervention. These approaches work on the condition that acceptable methods of searching and appraising the evidence are undertaken.

However, a number of studies have found that publication bias and selective reporting biases may threaten the validity of some systematic reviews (6-9). Selective outcome reporting bias occurs when changes are made after seeing the results for the included studies – can potentially lead to misleading interpretation if the outcome reported is changed on the basis of the reviews' findings (6). Kirkham *et al* compared the published Cochrane systematic review to the protocol and found that 22% (64/288) had a discrepancy in at least one outcome measure and 75% of these discrepancies were due to changes in the primary

outcome. The changes were sometimes made after the results of the individual trials were known (7). In fact, new research indicates that the selective outcome reporting bias in systematic reviews may be underestimated. Kirkham *et al* found that outcome reporting bias was suspected in at least one randomized control trial in over one-third (N=96) of the 283 Cochrane systematic reviews they examined in detail. Among the 81 reviews that included a single meta-analysis of a primary outcome, the sensitivity analysis revealed that the selective outcome reporting bias overestimated the treatment effect estimates by 20% in about 23% of the meta-analyses (8). This compounding of bias means that authors of systematic reviews must be scrupulously careful and transparent.

Despite the knowledge that completed reviews frequently deviate from their protocols, to date most systematic reviews do not have publicly accessible protocols. The PROSPERO registry allows editors, peer reviewers and other stakeholders to better assess the methods reported in the systematic review and to examine whether the review deviated from the original protocol and why. One can also review the methods used to minimize these biases given that the information would be far more transparent.

From the journal editor's perspective the data elements for the systematic review protocol registration provide enhanced transparency and increase the probability of publishing credible evidence. A competing interest statement would help the editors, peer reviewers and readers consider if conflict of interest might have affected the methods and interpretation of results. A publicly accessible systematic review protocol registry would also improve reproducibility in that any protocol changes would be documented and a rationale provided.

In our current environment of proprietary ownership of health care knowledge, PROSPERO can only be a first, albeit crucial step in improving the quality of synthesis research. PROSPERO will act as an open repository of data provided by those authors who chose to register, important for all of the reasons described above. One substantial limitation to PROSPERO's ability to ensure transparency between the protocol and the final review is the fact that even if the protocol is

accessible, the final review, will not be unless it is published, optimally, in an open access journal, such as *Open Medicine*, or made free access in the more traditional closer access journals. *Open Medicine* will continue to engage the scientific community in committing to the ongoing improvement of transparency in health care research (see text box below). Second, PROSPERO currently supports protocol registration for formal systematic reviews of health care interventions, whereas we know that other knowledge syntheses such as scoping and rapid reviews are also populating the published and grey literature and may equally require attention to methodological clarity and transparency (10, 11). Finally, PROSPERO cannot act as a watchdog in the systematic review community, and we recognize that well conducted systematic reviews are incredibly time-consuming endeavours. Given the importance of systematic reviews in clinical and health policy decision-making, protocol registration should be mandated by funding bodies and in the future, by scholarly journals to enhance the transparent reporting of systematic reviews.

**Text box: Building on PROSPERO**

- Encourage authors to concomitantly submit a PRISMA checklist and flow diagram
- Encourage authors to share their study inclusion and risk of bias (quality) assessment tools with the ultimate aim of streamlining the way reviews are performed
- Encourage that systematic reviews be made freely available, so that they can be read and compared by stakeholders to protocols on PROSPERO, or made open access such that their contents can be shared, copied and used to make derivative works, including other systematic reviews
- Consider novel ways of publishing systematic reviews, such as wiki platforms, in order to experiment with ways of keeping reviews current and open to scrutiny (12)

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Competing interests: All authors are members of the Open Medicine editorial team and David Moher contributed to the creation of PROSPERO – will need a clearer role to be specified.