Published in *KT Update* (Vol. 5, No. 3 – March 2017) [http://ktdrr.org/products/update/v5n3]
An e-newsletter from the Center on Knowledge Translation for Disability and Rehabilitation Research

PROSPERO and PRISMA-P

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KT Update *presents another in a series of brief articles by Dr. Marcel Dijkers. This article describes the origin of PROSPERO (an international database of prospectively registered systematic reviews in health and social care) and PRISMA-P (a listing of preferred reporting items for a protocol for a systematic review or meta-analysis).*

It must have been two decades ago that, during the discussion period for a paper that I was presenting at a conference, a colleague remarked something like, "Dr. Dijkers tortures the data until it confesses." He meant that as a compliment, and that's how I took it. In hindsight, I would say that he approved that I habitually engaged in data dredging, selective reporting, and various other unsavory tactics to make it possible to report at least one significant *p*-value—the holy grail of simplistic research. We (or at least I) have since learned about the deleterious effects of publication bias, switching the primary outcome of studies for a secondary one and vice versa, selective reporting of outcomes, (unplanned) subgroup analyses, and so on.

Registering Trials

Already back in the 1970s a proposal was made to register trials as a (partial) antidote to these shady tactics, which aim to make investigators, their studies, and (sometimes) their sponsors look their best. The reasoning went as follows: If researchers register their study protocols before they enroll the first subject, that permanent record makes it possible to determine what studies have not been published, or which ones in their reporting make unjustified changes to a protocol or statistical analysis plan. Pressure from biomedical journal editors, researchers themselves (especially those engaged in creating systematic reviews [SRs]), and governmental and nongovernmental sponsors of research, as well as the Food and Drug Administration and other regulatory agencies, resulted in the creation of registries such as ClinicalTrials.gov, which began operation in 2000.

These trial registries work in a very simple fashion. A researcher about to start a study creates (voluntarily or forced by her sponsor or the journal in which he wants to publish) an entry for the study, completing a number of fields with administrative and design information. This minimal protocol can be changed if realities on the ground make that necessary, but the registry keeps all versions on display; as a result, for anyone curious to know how the published data relate to the original research plan, there is a paper trail to follow back. ClinicalTrials.gov and other national and international registries have largely lived up to expectations and now there is an ongoing discussion whether researchers should also be required to submit to the website all or at least summary data from their studies. This would satisfy a second purpose of registries: the public availability of information on research sponsored with public or private funds and involving the volunteer time and effort of hundreds—if not thousands—of subjects.

PROSPERO

Clinical trials and other primary studies are not the only research that may undergo selective reporting. There is now a modest body of research demonstrating that SRs also may be reported selectively, for instance, Kirkham, Altman, & Williamson, 2010; Silagy, Middleton, & Hopewell, 2002; and Siontis, Hernandez-Boussard, & Ioannidis, 2013. Because SRs increasingly are considered the most comprehensive and least biased evidence for use in Evidence Based Practice and Evidence Based Medicine (EBP & EBM) (at the apex of the "evidence pyramid"), that is of no small concern. And a parallel solution has been suggested: the prospective registration of SRs. Although there are multiple registries for primary research, for SRs there is only one: PROSPERO—International prospective register of systematic reviews. While the name suggests "PROSPEctive Register," I have found no mention of the origin of the appellation; maybe it was borrowed from Shakespeare, whose Prospero (in *The Tempest*) was a sorcerer. PROSPERO is financed by the United Kingdom's National Institute for Health Research (NIHR) and run by the University of York Centre for Reviews and Dissemination.

After an international Delphi project to determine what elements should be contained in the registry (Booth et al., 2011), PROSPERO opened for business in 2011 and quickly

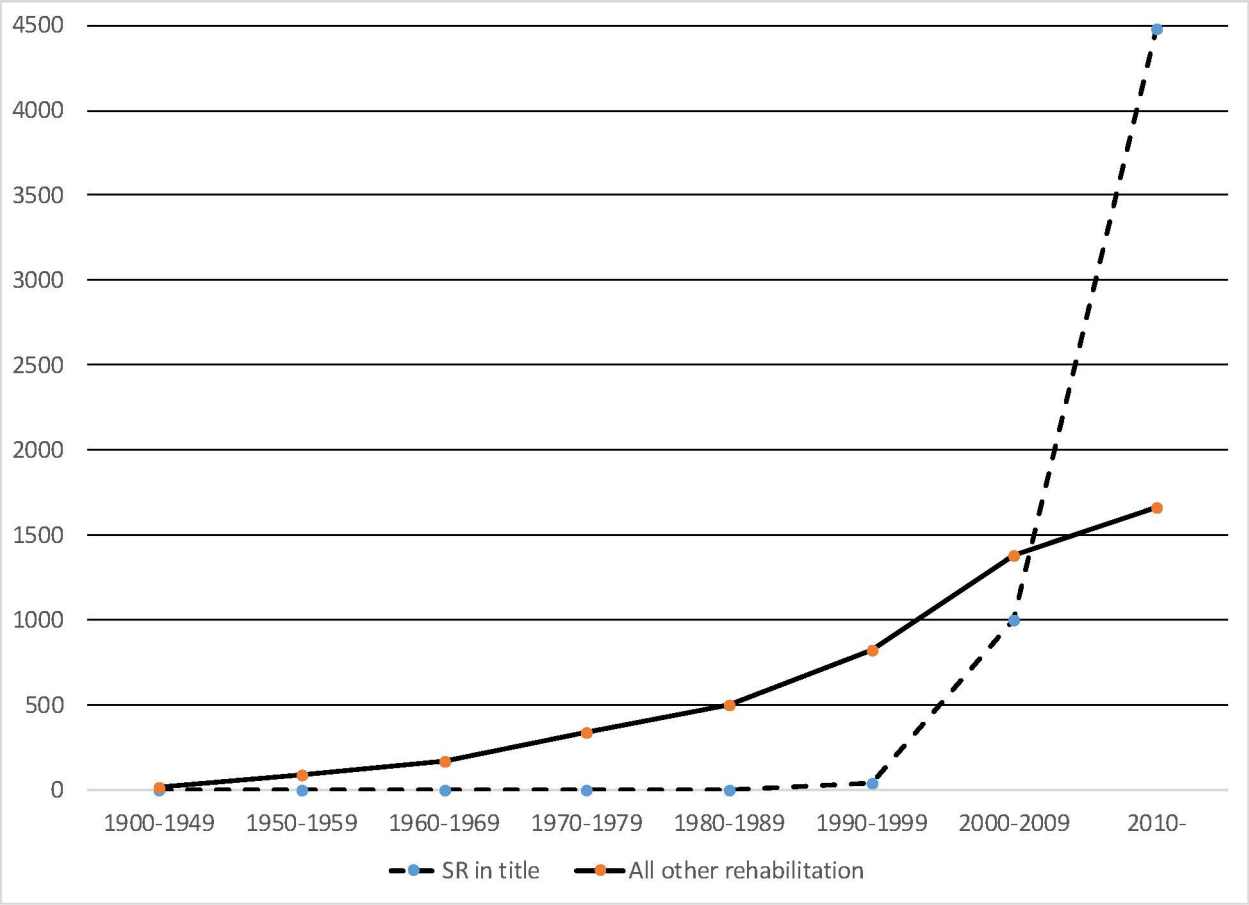
started cataloguing more than 90 SRs per month (Booth et al., 2013; Booth, 2013); now (February 2017) it contains more than 20,000 records, of which more than 1,300 concern rehabilitation and disability. The concept of registering SRs, or the PROSPERO site specifically, has been endorsed by a number of entities, including the Canadian Institutes of Health Research, which has gone as far as requiring applicants seeking grant funding for a trial to conduct an SR to demonstrate the need for the trial (Graham, 2012). Others include Guidelines International Network (Van der Wees et al., 2012); NIHR (Davies, 2012); and the *Public Library of Science* journals (Booth et al., 2012), as well as journals such as *Open Medicine* (Palepu, Kendall, & Moher, 2011), *British Journal of Obstetrics and Gynaecology* (Chien, Khan, & Siassakos, 2012), and *Systematic Reviews* (Booth et al., 2012). Also on board are organizations such as the International Network of Agencies for Health Technology Assessment and the international Campbell and Cochrane Collaborations (Booth et al., 2012).

The PROSPERO registry has a number of major purposes:

- Function as an archive of SR proposals, which journal editors, peer reviewers, readers, and others can use to determine the discrepancies between the protocol and the published report that authors do not declare and justify in their journal report.
- Serve transparency by making publicly available information on which SRs are being done, using what methods, and by whom (Davies, 2012).
- Improve the quality of SRs by inviting researchers to create a protocol before searching the literature (planless SRs apparently are still a common occurrence, per Moher, Tetzlaff, Tricco, Sampson, & Altman, 2007) to reduce confusion and "ensure that all investigators are working from the same work plan" as Chang and Slutsky (2012, p. 2) formulate it.
- Fill in gaps in knowledge by offering an opportunity to see which areas still lack a systematic review or meta-analysis (Graham, 2012).
- Offer an opportunity for researchers to avoid unplanned duplication of SRs, and to find ongoing work by scientists with similar interests whose efforts they might join.

Duplication is not an imaginary problem. The number of SRs being published each year is mushrooming (even in the area of rehabilitation; see Figure 1), and overlapping SRs are not an uncommon phenomenon. Replication is something to be desired, but, as Moher (2013) pointedly asks, how much replication is too much?

Figure 1. Number of PubMed entries of "rehabilitation" articles with "systematic review" in the title, and number of all other "rehabilitation" articles, by time period*



*Numbers for "other rehabilitation" articles have been divided by 100 to make trends clear.

Source: Author's compilation of data obtained from PubMed search.

PROSPERO works in a way similar to the clinical trial registries: A researcher who wants to register an SR submits administrative and scientific information to the website. These SRs may focus on "health and social care, welfare, public health, education, crime, justice, and international development, as long as there is a health related outcome" (PROSPERO, 2016, p. 3), but scoping reviews and literature reviews are not eligible. The information submitted gets a quick administrative review (Right type of study? Sufficiently clear and informative entries in all required and optional fields?), and when approved (typically, in a few business days) becomes publicly available. Registering an SR is free, as is searching the registry for information. Registration should happen before the systematic reviewers start extracting information from the primary studies, but there is some flexibility. Cochrane protocols are automatically added to PROSPERO (Moher, 2013). Table 1 contains an overview of the items on initial registration; there are 22 required and 18 optional fields, and it is estimated that registration takes about 60 minutes—even less for researchers who already have a written protocol (Booth et al., 2012).

Table 1. Required and optional fields for a PROSPERO registration

1. Review title*
2. Original language title
3. Anticipated or actual start date*
4. Anticipated completion date*
5. Stage of the review at the time of submission*
6. Name of contact person*
7. Email address of contact person*
8. Address of contact person
9. Telephone number of contact person*
10. Organization with which the review is affiliated*
11. Members of the review team and the organization(s) with which they are affiliated
12. Funding sources/sponsors*
13. Conflicts of interest*
14. Collaborators
15. Review question(s)*
16. Literature searches (bibliographic databases; language or publication date restrictions)*
17. URL for search strategy
18. Condition or domain being studied*
19. Population(s) being studied*
20. Interventions or exposures*
21. Comparators or controls*
22. Types of study designs to be included initially*
23. Context for the SR; background for inclusion/exclusion criteria*
24. Primary outcome(s)*
25. Secondary outcomes*
26. Data extraction (selection and coding)
27. Risk of bias (quality) assessment*
28. Strategy for data synthesis*
29. Analysis of subgroups or subsets*
30. Type (method) of review (menu)
    - Diagnostic
    - Epidemiologic
    - Intervention
    - Prevention
    - Prognostic
    - Service delivery
    - Etc.

    Area of review (menu)
    - Alcohol/substance misuse/abuse
    - Crime and justice
    - Education
    - Health inequalities
    - Mental health and behavioral conditions
    - Nursing
    - Physical therapy
    - Public health
    - Rehabilitation
    - Social care
    - Etc.
31. Language(s) of SR (menu)
32. Country (menu)
33. Other registration details
34. Reference and/or URL for published protocol
35. Dissemination plans
36. Keywords
37. Details of any existing reviews on the same topic by the same authors
38. Review status (menu)
    - Ongoing
    - Completed but not yet published
    - Completed and published
    - Completed, published, and being updated
    - Abandoned
39. Additional information
40. Link to publication of the final report

*indicates a required field

NOTE: Adapted from PROSPERO, 2016, pp. 7–21. Slightly modified from the document *Guidance notes for registering a systematic review protocol with PROSPERO* from the website PROSPERO – International prospective register of systematic reviews.
https://www.crd.york.ac.uk/prospero/aboutreg.php

Any changes in the protocol (SRs often undergo changes because of information found or not found in the literature) are to be submitted, and the paper trail is kept for public inspection. PROSPERO sends investigators e-mails to remind them to update their registration as stages in the review are completed (Booth & Stewart, 2013). It also encourages users to submit their published paper or other report to the website once the study is complete.

PRISMA and PRISMA-P

Which brings us to PRISMA-P. PRISMA stands for "Preferred Reporting Items for Systematic Reviews and Meta-Analyses," and it was first published in 2009 to offer authors guidance on how to report their systematic reviews (Liberati et al., 2009; Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009). Under Methods, PRISMA suggests reporting an SR's "Protocol and registration: item 5: Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number" (Moher et al., 2009, p. 339). The authors of PRISMA suggested that this information be provided because they recognized how important it was for reviewers and readers of an SR to have the opportunity to compare the plan with the actuality, and to be able to determine changes in review methodology as well as selective reporting. They have now gone a step further and have published specific guidance for the contents of such a protocol: the final P of PRISMA-P stands for *protocol* (Moher et al., 2015; Shamseer et al., 2015). As do all the other members of the PRISMA family, PRISMA-P comes in the form of a checklist, which authors can use to determine whether they have included all relevant items in their protocol (see Table 2). It consists of 17 items—26 if subitems are counted as separate entities (see Table 2). Completing a protocol is expected to benefit SR authors, funders of secondary research, clinical practice guidelines developers, policymakers, journal editors, and peer reviewers, as well as educators and students (Moher et al., 2015; Palepu et al., 2011; Stewart, Moher, & Shekelle, 2012).

Table 2. PRISMA-P: preferred items for reporting the protocols for systematic reviews and meta-analyses

Section/topic	Item #	Checklist item
ADMINISTRATIVE INFORMATION		
Title		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number
Authors		
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review

Section/topic	Item #	Checklist item
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., *I* 2, Kendall's tau)
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned

Section/topic	Item #	Checklist item
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)

Source: Moher et al., 2015.
http://prisma-statement.org/documents/PRISMA-P Statement - Moher Sys Rev Jan 2015.pdf

With manuscript page numbers entered, authors can submit the PRISMA-P checklist along with their protocol manuscript to a journal such as *Systematic Reviews* to make review of their manuscript easier for the editors and peer reviewers. Such publication of protocols is increasingly common; in January 2017, more than 150 were published (as shown in a PubMed search), of which 189 concerned rehabilitation and disability topics. The PRISMA-P authors structured the checklist in such a way that a protocol can easily be turned into a report on the results of the SR or meta-analysis: the items are harmonized with the PRISMA items (Moher et al., 2015). PRISMA-P is intended primarily for the preparation of protocols for reviews of aggregate data reported in the literature. It is not optimal for meta-analysis of individual patient/participant data, the topic of a previous *KT Update* article (Dijkers, 2016), but it would not be surprising if PRISMA-IPDMA were to follow in the near future.

If the objective is to go on public record to declare the aim and methods of an SR, registration on PROSPERO *and* a published manuscript following the guidance of PRISMA-P seem duplicative but cannot hurt. If sunshine (the opportunity for or threat of public scrutiny) helps to keep researchers, including SR authors, on the straight and narrow, then more sunshine should be welcome. In the end, it is better for all patients, participants, clients, and subjects for whom we write our SRs.

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The contents of this article were developed under grant number 90DP0027 from the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR). NIDILRR is a Center within the Administration for Community Living (ACL), Department of Health and Human Services (HHS). The contents of this article do not necessarily represent the policy of NIDILRR, ACL, HHS, and you should not assume endorsement by the Federal Government.