PROSPERO
International prospective register of systematic reviews

NHS
National Institute for Health Research

Registration of experimental studies and systematic reviews

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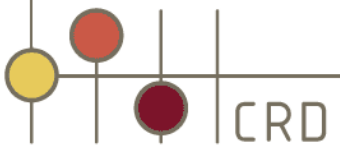
Overview of presentation

- Principles and practice of registration
- Barriers and facilitators to registration
- Development and evaluation of utility of PROSPERO
- The future

Principles of registration

- Availability of evidence to inform health care decisions
- Avoidance of publication bias and selective reporting bias
- Requirement of The Declaration of Helsinki
- Avoid unnecessary duplication
- Identify gaps in research
- Facilitate recruitment
- Promoting collaboration
- Early identification of potential problems

WHO ICTRP: www.who.int/ictrp/en/



Practice of registration

- Accessible to the public at no charge
- Accept registrations from anyone (unduplicated, eligible and complete)
- Managed by a not-for-profit organisation
- Validate entries (within scope and complete)
- Electronically searchable
- Provide a unique identification number for each record
- Require provision of a minimum data set
- Permanent entries

ICMJE criteria for clinical trial registers: www.icmje.org/update_june07.html

Publication bias and selective reporting of outcomes

- In animal studies
  - Sena ES, van der Worp HB, Bath PM, et al: **Publication bias in reports of animal stroke studies leads to major overstatement of efficacy.** PLoS Biol. 2010 Mar 30;8(3):e1000344.
  - Kilkenny C, Parsons N, Kadyszewski E, et al. (2009) **Survey of the Quality of Experimental Design, Statistical Analysis and Reporting of Research Using Animals.** PLoS ONE 4(11): e7824.
- In clinical trials
  - Song F, Parekh S, Hooper L, et al: **Dissemination and publication of research findings: an updated review of related biases.** Health Technol Assess 2010, **14:**1-193.
  - Smyth RM, Kirkham JJ, Jacoby A, et al. **Frequency and reasons for outcome reporting bias in clinical trials: interviews with trialists.** BMJ. 2011 Jan 6;342:c7153.
- In systematic reviews
  - Tricco AC, Pham B, Brehaut J, et al. **An international survey indicated that unpublished systematic reviews exist.** Journal of clinical epidemiology 2009: 62(6):617-623.e5.
  - Kirkham JJ, Altman DG, Williamson PR (2010) **Bias Due to Changes in Specified Outcomes during the Systematic Review Process**. PLoS ONE 5(3): e9810.

How registration can help

- Records key planned features of the research
  - randomisation/inclusion criteria
  - primary and secondary outcomes and measures
- Allows comparison of published results with what was planned in the corresponding registration record
  - readers can judge whether any discrepancies are likely to have introduced bias
- Registration should allow amendments and maintain audit trail (not unreasonable to make changes, but need to know why)

Avoiding unintended duplication

- Research can be invasive/time consuming and costly
- Often duplicate or very similar studies are undertaken
- Unintended duplication is economically wasteful

- Registration should allow those planning research to check whether there are any studies already in the ‘pipeline’ that address their topic of interest

- They can then decide whether or not to proceed

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Practical barriers to registration

- Availability of a registry

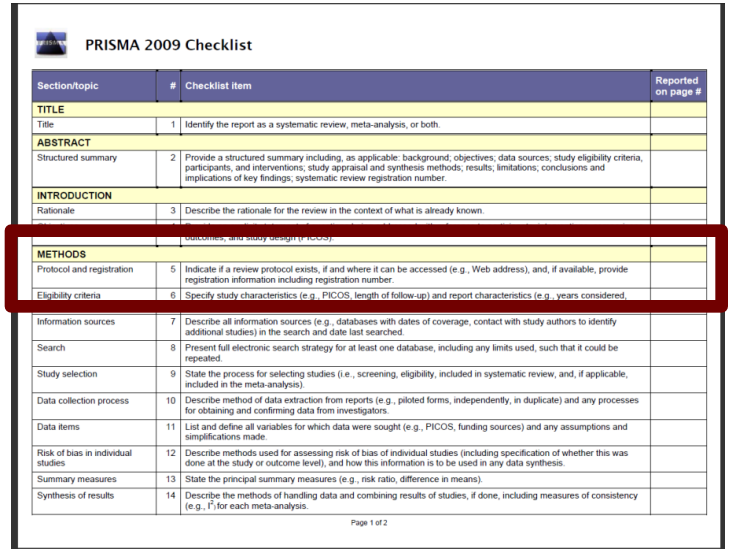
- Process for process sake
  - no legal or ethical imperative: ? value to registrant
- Safeguarding privacy
  - focus/topic of investigation
  - researchers carrying out the investigation
- Timing
  - too soon – lots of amendments
  - too late – fails to fulfil purpose of registration
- Costs
  - time, effort and money

Benefits of registration

- Researchers
- Commissioners and funders
- Guideline developers
- Journal editors and peer reviewers
- Methodologists
- The public

Prospective registration of systematic review protocols

- Importance increasingly recognised
- PRISMA 2009 advocated registration
- No open access facility to formally register systematic review protocols
  - Cochrane and Campbell Collaboration protocol registration limited to their own organisations



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
		outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	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.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered,	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

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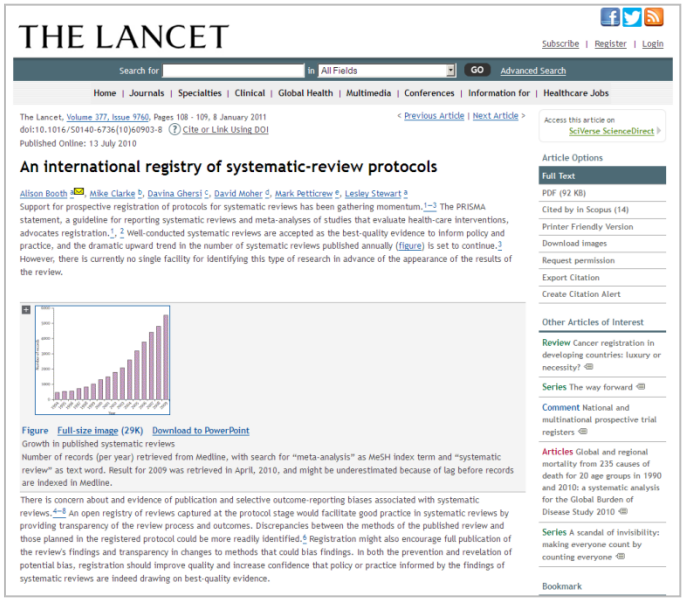
Development of PROSPERO

- CRD initiated development of PROSPERO in 2010
- International Advisory Group
- Minimum dataset agreed by international consultation
  - 22 required fields
  - 18 optional fields



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An international registry of systematic-review protocols

Alison Booth, Mike Clarke, Davina Ghersi, David Moher, Mark Petticrew, Lesley Stewart

Support for prospective registration of protocols for systematic reviews has been gathering momentum.[1–3] The PRISMA statement, a guideline for reporting systematic reviews and meta-analyses of studies that evaluate health-care interventions, advocates registration.[1, 2] Well-conducted systematic reviews are accepted as the best-quality evidence to inform policy and practice, and the dramatic upward trend in the number of systematic reviews published annually (figure) is set to continue.[3] However, there is currently no single facility for identifying this type of research in advance of the appearance of the results of the review.

Figure Full-size image (29K) Download to PowerPoint

Growth in published systematic reviews

Number of records (per year) retrieved from Medline, with search for "meta-analysis" as MeSH index term and "systematic review" as text word. Result for 2009 was retrieved in April, 2010, and might be underestimated because of lag before records are indexed in Medline.

There is concern about and evidence of publication and selective outcome-reporting biases associated with systematic reviews.[4–8] An open registry of reviews captured at the protocol stage would facilitate good practice in systematic reviews by providing transparency of the review process and outcomes. Discrepancies between the methods of the published review and those planned in the registered protocol could be more readily identified.[6] Registration might also encourage full publication of the review's findings and transparency in changes to methods that could bias findings. In both the prevention and revelation of potential bias, registration should improve quality and increase confidence that policy or practice informed by the findings of systematic reviews are indeed drawing on best-quality evidence.

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Lancet 2011;377(9760):108-109

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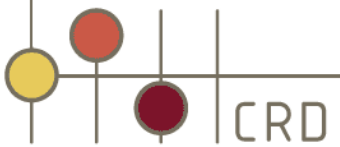
Inclusion/exclusion and timing

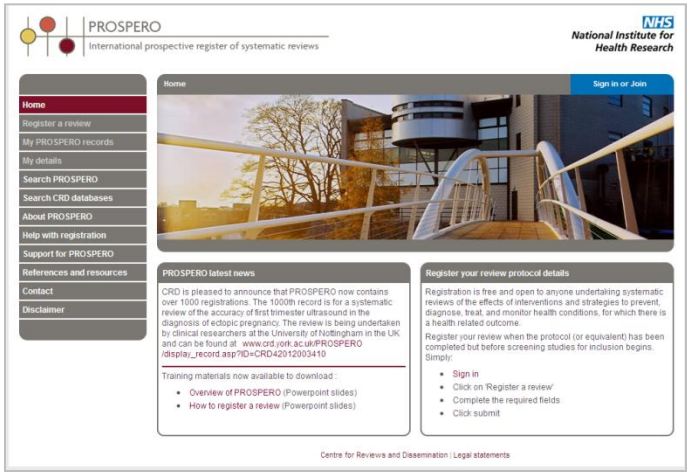
- Ongoing systematic reviews that have a health related outcome in the broadest sense
  - Systematic reviews of reviews
  - Reviews of methodological issues with an outcome that can be used in health care practice

  - Scoping reviews – excluded as are not systematic reviews
  - Reviews of animal studies – excluded as outcomes not of direct relevance in health care practice

- Registered before screening against eligibility criteria commences (currently accepted as long as they have not progressed beyond the completion of data extraction)



PROSPERO launched February 2011



- Web based
- Free to register, free to search
- Users create and **update** their own records
- Record content is responsibility of review author
- Administrators check for “sense” **not** peer review
- An audit trail of amendments is maintained
- Registration record indexed by the PROSPERO team
- As many administration tasks as possible are automated
- Minimum data set

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One year evaluation of utility

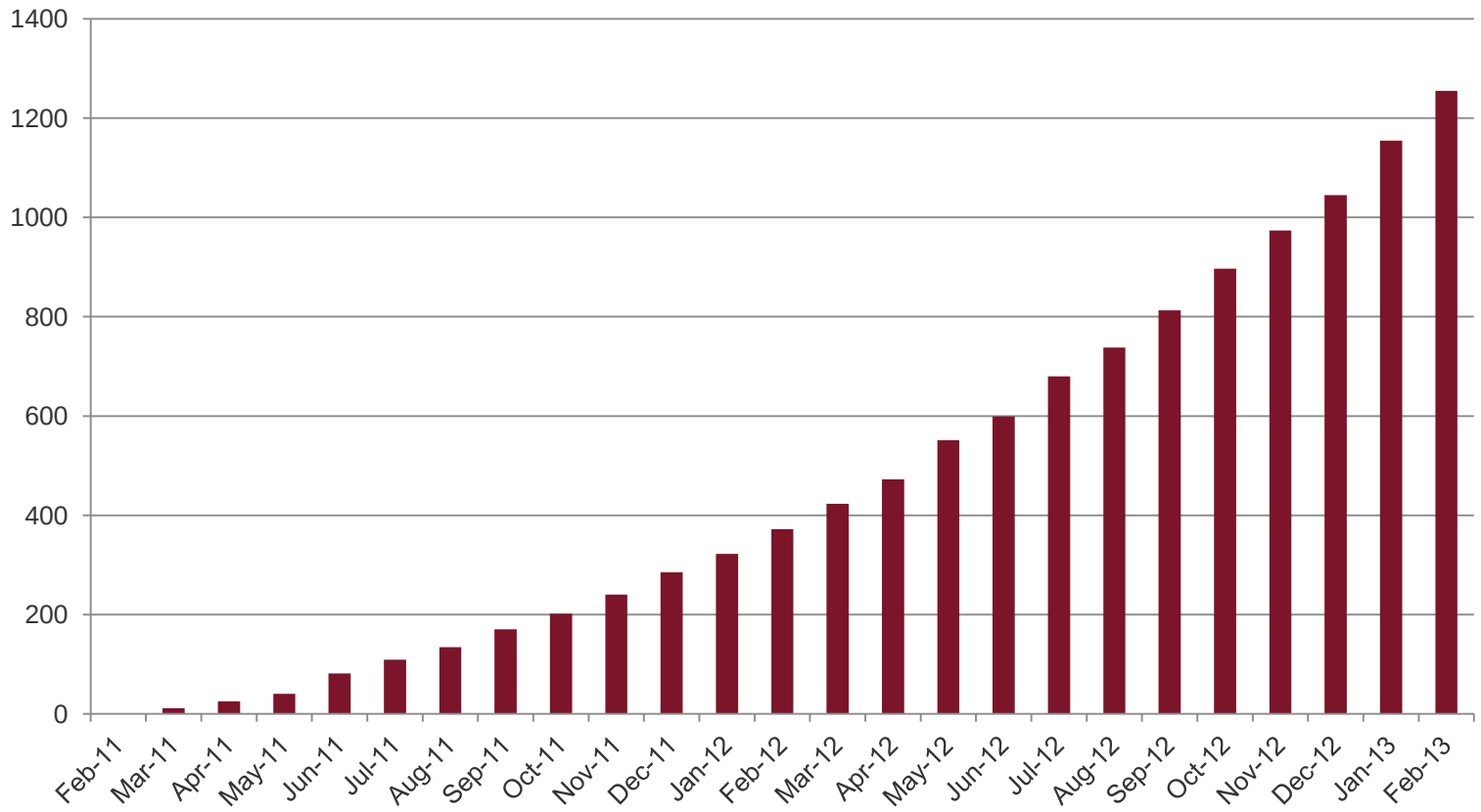
- Based on 232 responses from users (response rate 22%)
  - 80% found registration fields relevant to their review
  - 99% found joining and navigation was easy/very easy
  - 96% found turn round time was good/excellent
  - 80% found supporting materials helpful/very helpful
- 99% rated their overall experience of registering with PROSPERO as good or excellent
- 79% completed the registration form in 60 minutes or less
- Conclusion: registration of systematic review protocols is feasible and not overly burdensome for those registering their reviews

Booth et al.Systematic Reviews 2013;2:4

Criticisms of the dataset

- *'Form bias towards reviews that involve statistical data analysis rather than narrative or qualitative reviews'*
- *'Some leaders assert that systematic reviews are exploratory in nature and should not have pre-determined primary outcomes'*
- *Legitimate reasons why data extraction, risk of bias (quality) assessment and data analysis all started but not completed*

Cumulative totals for new registrations



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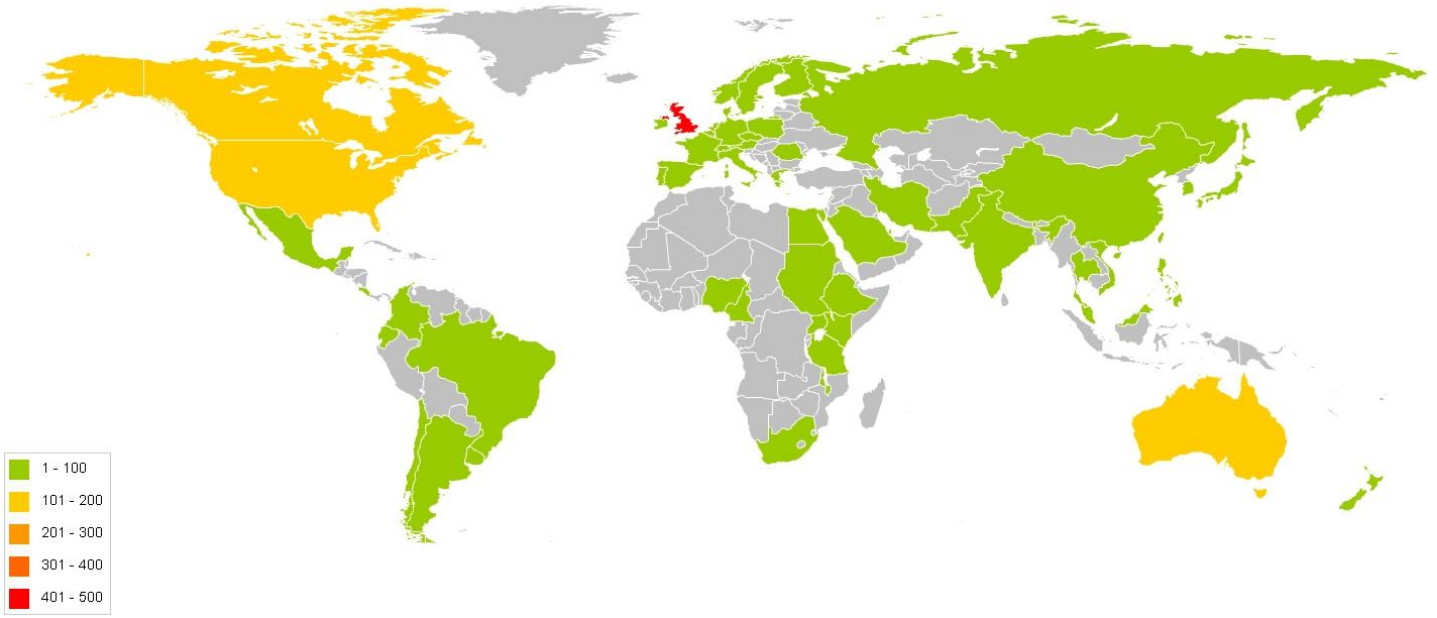
Countries where registered reviews are being conducted



March 2013: PROSPERO contains details of 1260 reviews being carried out in 57 different countries.

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The future

- Improve functionality of form and search interface
- Expand the scope to include all systematic reviews for which there is a health related outcome in the broadest sense
- Continue to encourage registration and use of the database
- Work on a programme of methodological research

- Potentially help support development of satellites *(X-3 or Miranda?)*

- With the right support and flexible pragmatic approach - setting up a register is possible

Thank you

The development and ongoing management of PROSPERO is supported by CRD's core work programme which is funded by the National Institute for Health Research, England; the Department of Health, Public Health Agency, Northern Ireland and the National Institute for Social Care and Health Research, Welsh Government.

www.crd.york.ac.uk/PROSPERO

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