



Ottawa Hospital  
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# Registration and Publication of Preclinical Systematic Review Protocols

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# What is a pre-specified protocol?

- Protocols explicitly state hypotheses, and methods *prior* to knowledge of the data
- Systematic reviews, like primary research studies, are prone to bias (systematic variation)
  - e.g. data ‘dredging’ and ‘post-diction’
- Protocols are a fundamental strategy to minimize bias

Sena et al. 2014 JCBFM doi:10.1038/jcbfm.2014.28

Silagy et al. 2002 JAMA doi:10.1001/jama.287.21.2831



# Where do Protocols Fit in the Systematic Review Process?





# Why Develop a Protocol?

- **A *priori* consideration of methodological and analytical approaches**
  - enables review teams to formalize development
  - provides readers with explicit documentation
  
- **Explicit guide for review conduct**
  - eliminates bias from arbitrary decision-making during review process (e.g. data dredging, ‘post-diction’)



# Protocol Development

- Clearly define the:
  - Research question/objectives
  - Inclusion criteria
  - Search strategy
  - Data collection processes
  - Data analysis plan.
- “A protocol should allow readers to judge whether the final study did indeed follow a pre-specified plan”



# Guides for Protocol Development

- Standardized Protocols for Clinical Systematic Reviews
  - PRISMA-Protocol (Shamseer et al 2014. BMJ; Moher et al 2014 Systematic Reviews)
  - Cochrane Handbook (Higgins & Green 2011)
- **A protocol format for systematic reviews of animal intervention studies**
  - Rob de Vries, 13:00 TODAY!



# Why Register a Protocol

- **Facilitate selective reporting detection**
  - 22% of Cochrane SRs had  $\geq 1$  discrepant outcome from protocol
  - Significant outcomes more likely to be ‘included’ or ‘upgraded’
- **Reduce unintended duplication and facilitate collaboration**
  - 67% of overlapping meta-analyses on the same topic (*Siontis BMJ 2013*)
- **Documentation of changes to the protocol**

Kirkham et al. 2010 PLOS One doi:10.1371/journal.pone.0009810

Siontis et al. 2013 BMJ doi: 10.1136/bmj.f4501



# Protocol Registration

- **CAMARADES**

- <http://www.dcn.ed.ac.uk/camarades/research.html#protocols>

Efficacy and safety of mesenchymal stromal cell therapy in preclinical models of acute lung injury: a systematic review

06/2013, posted 03/2014

Lauralyn McIntyre, Ottawa Hospital Research Institute,  
Canada





# Protocol Registration

- **PROSPERO International prospective register of systematic reviews: An expanding resource**  
Registration of Clinical Systematic Review
  - Alison Booth 9:30am Friday

UNIVERSITY *of York*  
Centre for Reviews and Dissemination

**NHS**  
National Institute for  
Health Research

- Home
- Register a review
- My PROSPERO records
- My details
- Search PROSPERO
- Search CRD databases
- About PROSPERO
- Inclusion criteria
- Help with registration

Home Sign in or Join

**Welcome to PROSPERO**  
International prospective register of systematic reviews



# Why Publish a Protocol

- Peer Review
  - Feedback on drafts
  - Anticipate potential problems
- More detail than in registry
  - Expanded background, methods, analysis plan etc.
  - Facilitates updating of systematic review



# Where to Publish a Protocol

Evidence-based  
Preclinical Medicine  
Open Access



SYSTEMATIC  
REVIEWS

**Protocol** [Open Access](#)

**Efficacy and safety of mesenchymal stromal cells in preclinical models of acute lung injury: a systematic review protocol**

Manoj M Lalu, David Moher, John Marshall, Dean Fergusson, Shirley HJ Mei, Malcolm Macleod, Gilly Griffin, Alexis F Turgeon, Michael Rudnicki, Jason Fishman, Marc T Avey, Becky Skidmore, Jeremy M Grimshaw, Duncan J Stewart, Kavita Singh, Lauralyn McIntyre, the Canadian Critical Care Translational Biology Group

*Systematic Reviews* 2014, **3**:48 (23 May 2014)

[Abstract](#) | [Full text](#) | [PDF](#) | [ePUB](#) | [PubMed](#)



# Best Practice in Systematic Reviews: The Importance of Protocols and Registration

The *PLoS Medicine* Editors\*

- PLoS Journals (e.g. Biology/Medicine/One)
  - “Authors whose systematic review was prospectively registered (e.g. in a registry such as [PROSPERO](#)) should also provide the registry number in their abstract.”
  - “Registry details and protocols will be made available to editors and reviewers, and included alongside the paper for readers if the report is ultimately published.”  
(<http://www.plosmedicine.org/static/policies>)



# The Three Steps of Pre-specified Protocols

Develop  
Protocol

Register  
Protocol

Publish  
Protocol



# Support



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NEUROLOGICAL  
DISORDERS AND STROKE