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Developing a protocol for a systematic review

NRSGH Systematic review and meta-analysis

Thanks to Kjetil G Brurberg and Signe A. Flottorp for sharing their slides

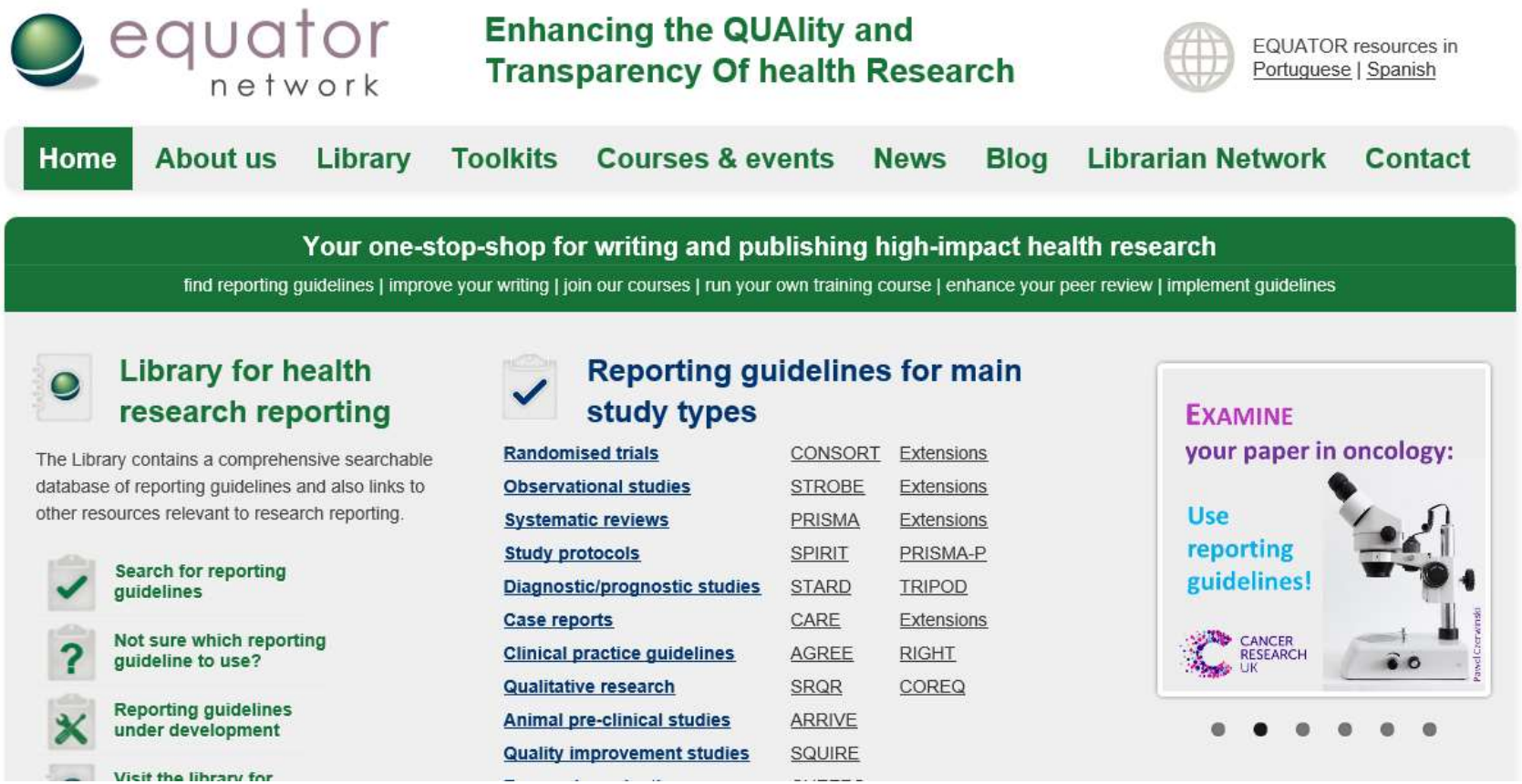
Why protocols?

- Progress
- Validity

Solutions to biased and incomplete SRs

- The quality of reporting of meta-analyses (QUOROM) guideline - 1999
- Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guideline in 2009
- The first international registry for systematic reviews (PROSPERO) - 2011.
- BioMed Central's Systematic Reviews – first journal dedicated to SRs including protocols 2012
- PRISMA guidance for protocols (PRISMA-P) 2015

Equator network



Protocol Guidance

Several resources are available to help authors prepare a protocol for a systematic review:

- PRISMA extension for Protocols
- Cochrane Handbook - Chapter 4
- Institute of Medicine – Standards for systematic reviews (section 2.6)

Moher et al. Systematic Reviews 2015, 4:1
http://www.systematicreviewsjournal.com/content/4/1/1

SYSTEMATIC REVIEWS

RESEARCH Open Access

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement

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Abstract

Systematic reviews should build on a protocol that describes the rationale, hypothesis, and planned methods of the review; few reviews report whether a protocol exists. Detailed, well-described protocols can facilitate the understanding and appraisal of the review methods, as well as the detection of modifications to methods and selective reporting in completed reviews. We describe the development of a reporting guideline, the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015). PRISMA-P consists of a 17-item checklist intended to facilitate the preparation and reporting of a robust protocol for the systematic review. Funders and those commissioning reviews might consider mandating the use of the checklist to facilitate the submission of relevant protocol information in funding applications. Similarly, peer reviewers and editors can use the guidance to gauge the completeness and transparency of a systematic review protocol submitted for publication in a journal or other medium.

Background

Systematic reviews are the reference standard for synthesizing evidence in health care because of their methodological rigor. They are used to support the development of clinical practice guidelines and inform clinical decision-making. They are becoming increasingly common; in 2010, 11 new reviews were estimated to be published daily [1]. Ideally, systematic reviews are based on pre-defined eligibility criteria and conducted and using data from primary research, since planning provides an opportunity for the review team to anticipate potential problems. When clearly reported protocols are made available, they enable readers to identify deviations from planned methods in completed reviews and whether they bias the interpretation of a review results and conclusions. Bias related to the selective reporting of outcomes has been characterized as a serious problem in clinical research, including systematic

Protocol (Prisma P terminology)

- In the context of systematic reviews and meta-analyses, a protocol is a document that presents an explicit plan for a systematic review. The protocol details the rationale and *a priori* methodological and analytical approach of the review

Reason I

Plans and time schedules = progress

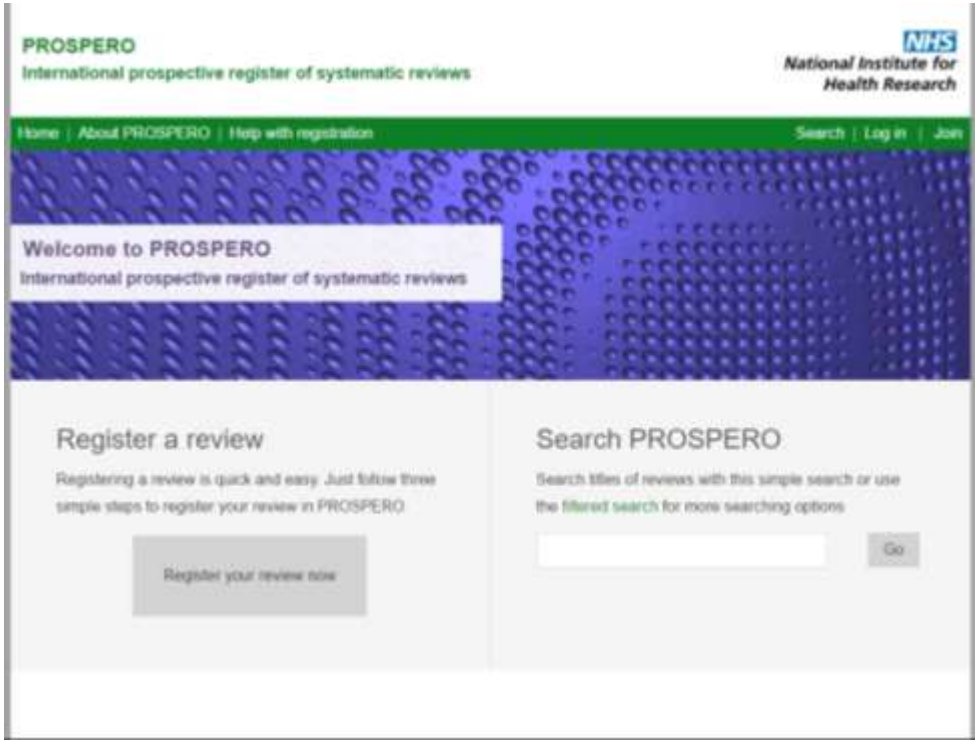
- Who will do what, and when?
- If appropriately registered, we may avoid duplication

Background: the need for registration

- Systematic reviews usually provide the evidence base upon which health and social care decisions are made so they should be robust and free from bias
- To reduce risk of publication and selective outcome reporting biases
- Unplanned duplication of reviews is a waste of resource

PROSPERO: International prospective register of systematic reviews

- Web based
- Free to register
- Free to search
- Users create and update their own records
- Minimum data set required
- Record content is the responsibility of review lead
- Administrators check for “sense” **not** peer review
- A public audit trail of amendments is maintained



PROSPERO: International prospective register of systematic reviews

- Protocol details for systematic reviews relevant to health and social care, welfare, public health, education, crime, justice, and international development, where there is a health related outcome.
- Systematic review protocols on PROSPERO can include any type of any study design.
- Reviews of reviews and reviews of methodological issues that contain at least one outcome of direct patient or clinical relevance are also accepted.

PROSPERO cont.

- Completed reviews are not accepted
- Registration should take place once the systematic review protocol is finalised, but ideally before screening studies for inclusion begins
- Working on automatic upload of Cochrane protocols, so they should not be registered individually

Reason II
A priori decissions increase the validity

- Helps to define perspective and context and choose an appropriate methodologic strategy (e.g. laymen versus professionals
- A priori decissions protect against biased conclusion
- Ad hoc reasoning may lead to exclusion of unwanted trials or inappropriate (sexy) subgroup analysis

Protocols should answer questions like

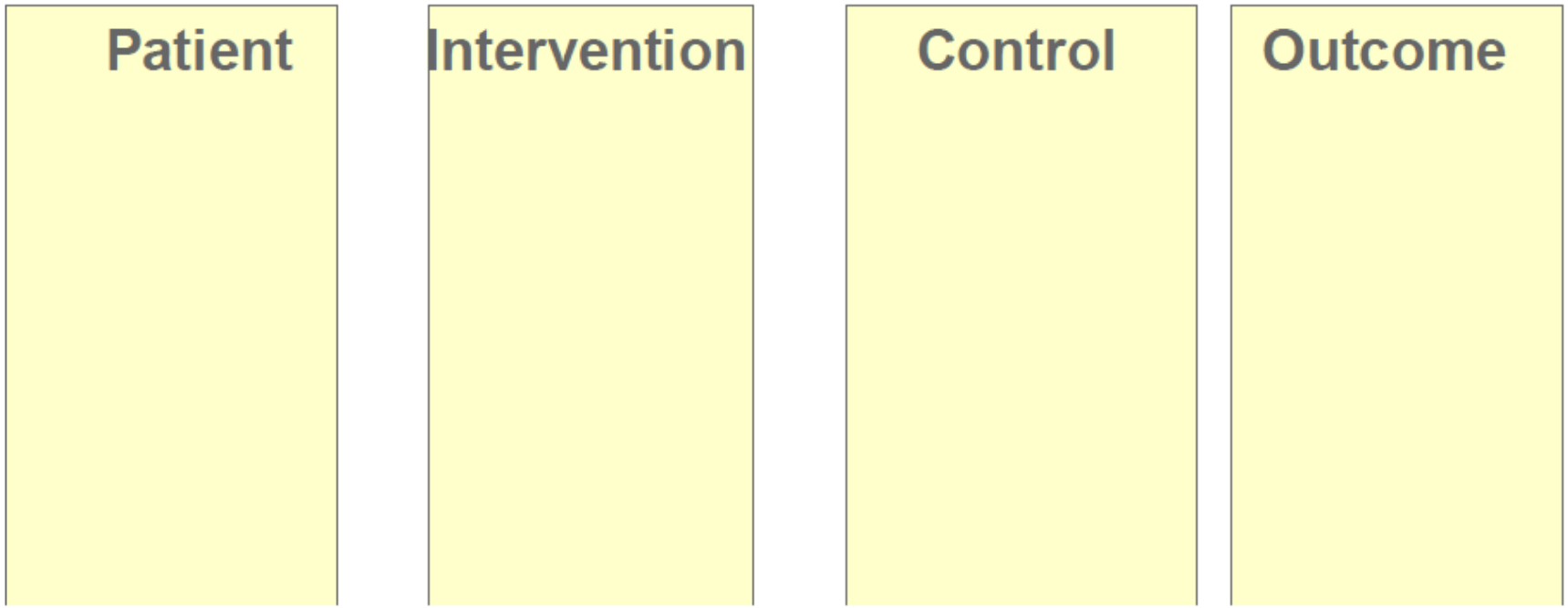
- What do you want to achieve?
- Which question(s) do you want to answer?
- How do you plan to retrieve relevant studies?
- How du you plan to select the relevant ones?
- How do you plan to assess the quality of the studies?
- How do you intend to extract and analyse your data?
- Which outcomes do you consider to be most important?
- Do you intend to do subgroups analysis, which and why?
- Who will be involved, and what are they intended to do?
- PRISMA

Core questions

Core question	Knowledge about
How many people are affected (e.g. have a health related problem, diagnosis)	Prevalence or incidence
Why are some affected, and others not?	Etiology
How can we decide whether a person has the problem?	Diagnosis
What can we do to prevent, treat, rehabilitate?	Effect of interventions
What will happen to those who are affected?	Prognosis
What are the experiences of people living with the condition? What are the likely determinants of effective interventions?	Experiences, attitudes

Name	Tentative research question
Flora	What is the impact of electronic health records on time efficiency of nurses in Primary Healthcare settings
Nazar	
Melf	What do we know about the cost effectiveness of SMS reminders to increase adherence to preventive therapies in sub-Saharan Africa?
Soheir	The Prevalence of Non-communicable Disease Risk Factors in East Africa Adults
Tekle Airgecho	Antimicrobial peptides are emerging topics of interest to fight against antimicrobial drug resistance. The bacterial toxin anti-toxin (TA) system, is less studied yet its promising results attracted attention of experts in the area. ''So, what is the TA system in bacteria: its biology, mechanism of action, possibilities and implication in public health intervention'' will be my topic during the systematic review course
Bezawit	
Binyam	Does behavior change communication applied in developing text message intervention in maternal and child health?
Josien	What are essential clinical decision making skills for Caesarean section in Low and Middle income countries
Berit	Is Postpartum depression a determinant when evaluating models of maternal care in developing countries?
Erik Oftedahl	metaanalyse eller review om assosiasjonen mellom sivilstatus og selvmord
Israel Paul	What is the prevalence of hearing loss among noise-exposed workers in Africa?
Thandile	Iron supplementation in children with severe acute malnutrition
Olive	Severe illness among infants, a systematic reveiw
Mari	o what degree do patients adhere to anticoagulation treatment in secondary prevention after cardioembolic stroke? Which factors may affect the level of adherence?
Ingrid Kristine	To assess the effect of the Prosigna Breast Cancer Prognostic Gene Signature Assay (Prosigna test) for predicting disease recurrence in breast cancer patients.
Martina Reiten	Which instruments are used for measuring pain after stroke in the literature?

Formulating precise clinical questions (PICOs)



Population – what to consider?

- Type of disease
- Diagnostic criteria
- Who diagnoses the patient
- Population specific characteristics
- Demographic factors (e.g. age and sex)
- What is the setting (e.g. in-/out-hospital)
- Exclusion criteria (e.g. co-intervention/comorbidity)
- How will you handle studies including only subgroups of ’your’ population?

Intervention – what to consider?

- Characteristics of the intervention you want to study
- Do you expect variation in dose, intensity, administration, personnel etc., and what do you consider relevant?
- Exclusion criteria, need for thresholding?
- How to handle studies looking at parts of an intervention?
- How to handle studies in which you intervention is one part of a more complex intervention?
- Imprecise description of interventions hinder implementation

Comparison/control – what to consider?

- What can serve as a control (no/placebo/active treatment)?
- Is best practise included as a possible comparison?
- Do you expect variation in e.g. dose, intensity, administration, personnel, can some be used as a control?
- Plan to handle trials with multiple arms

Outcome – what to consider?

- Primary outcomes are critical to decision making - often patient centred
- Primary outcomes can include positive as well as negative outcomes (benefit and harm)
- Other important outcomes are included as secondary outcomes
- Potential adverse effects should included
- Consider to include outcomes that reflect different perspectives; patient, doctor, politician, community and economy
- For each outcome - what is an appropriate follow-up

Design – what to consider?

- Which design is best suited to answer my question?
- Is it appropriate to include other design?
- Wrong choices may lead to erroneous conclusions

How to handle included studies

- A plan for critical appraisal
- A plan for data extraction
- A plan for analysis (e.g. effect size and statistical models)
- A plan for subgroup and sensitivity analysis
- A plan for grading the quality of the total body of evidence (i.e. how certain are the effect estimates, how sure are we about the conclusion?)

A plan for analysis, lumping or splitting

- Lumping: wide questions
  - Antibiotics for bronchitis
  - Hospital at home
  - Prevention of myocardial infarct

- Splitting: specific questions
  - Antibiotic (x) for bronchitis
  - H@H for acute COPD exacerbations
  - Green prescriptions for middle aged men with high BP with respect on MI prevention

Potential challenges with SRs

- Misjudge the PICO
- Answer with little relevance for practice
- Empty reviews
- Less rigorous studies may be useful?

Get started with your own question

EBP Skill Development Tool

Please write the answers in a concise and precise manner
Describe your clinical scenario:

1 Information need

Describe your clinical scenario:

2 Question formulation

Fill in relevant PICO elements:

(P)	Population	
(I)	Intervention	
(C)	Comparison intervention	
(O)	Outcome	

Formulate your PICO question: (e.g. In patients with...does ...?)

What kind of clinical question is this?

Until we meet again

- Home assignment – search in Cochrane
- Presentation of own protocol (5 min) for a group of fellow students on November 20th
- Prepare feedback to at least two protocols from fellow students by November 20th
- Do at least the search modules in Cochrane online learning – possibly even more…
- Lectures and teaching materials will be available on NRSGH website