Systematic Reviews & Meta-Analysis

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Year ↓	Documents ↑
2021	312
2020	42466
2019	36747
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2017	29410
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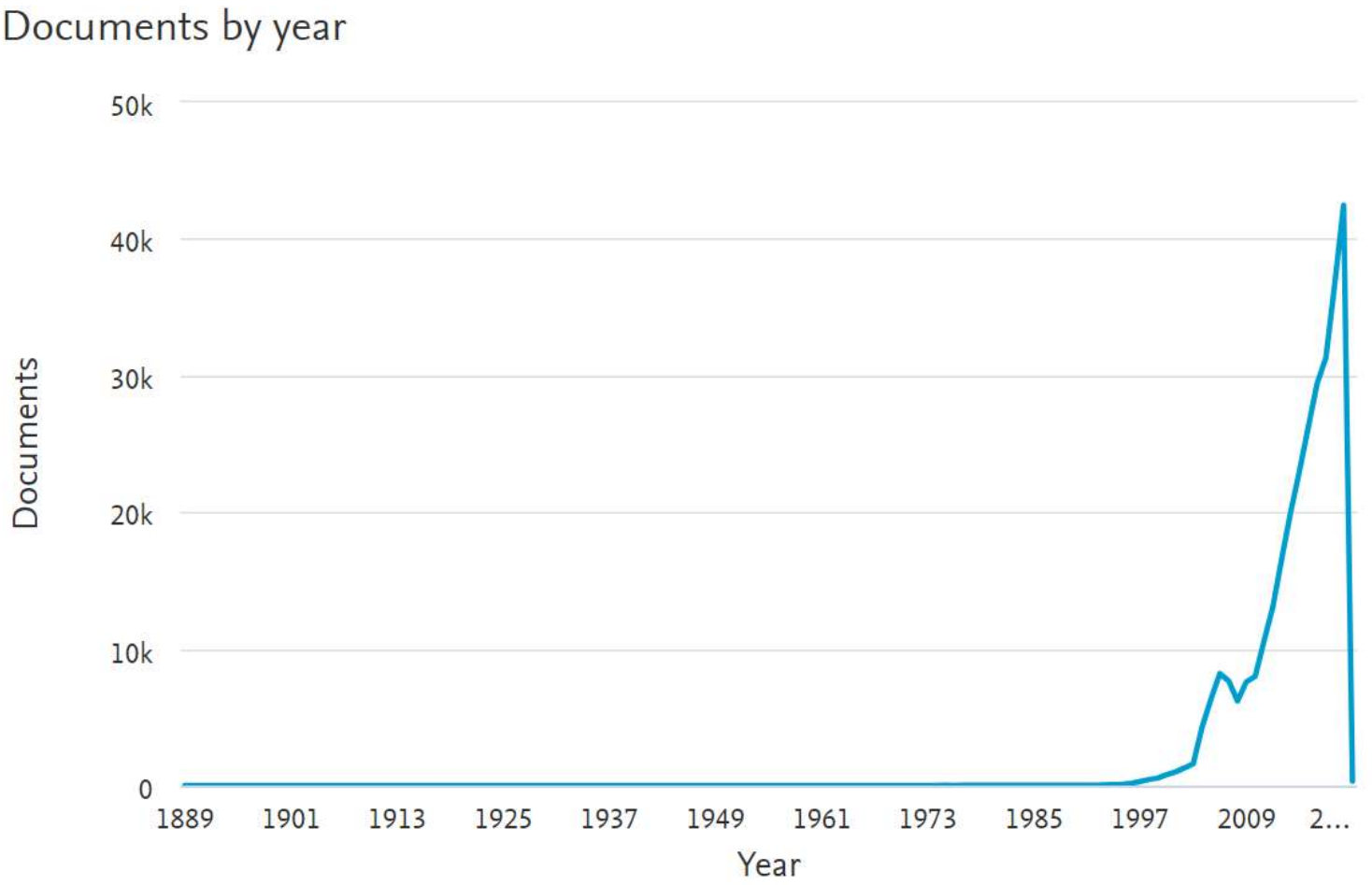

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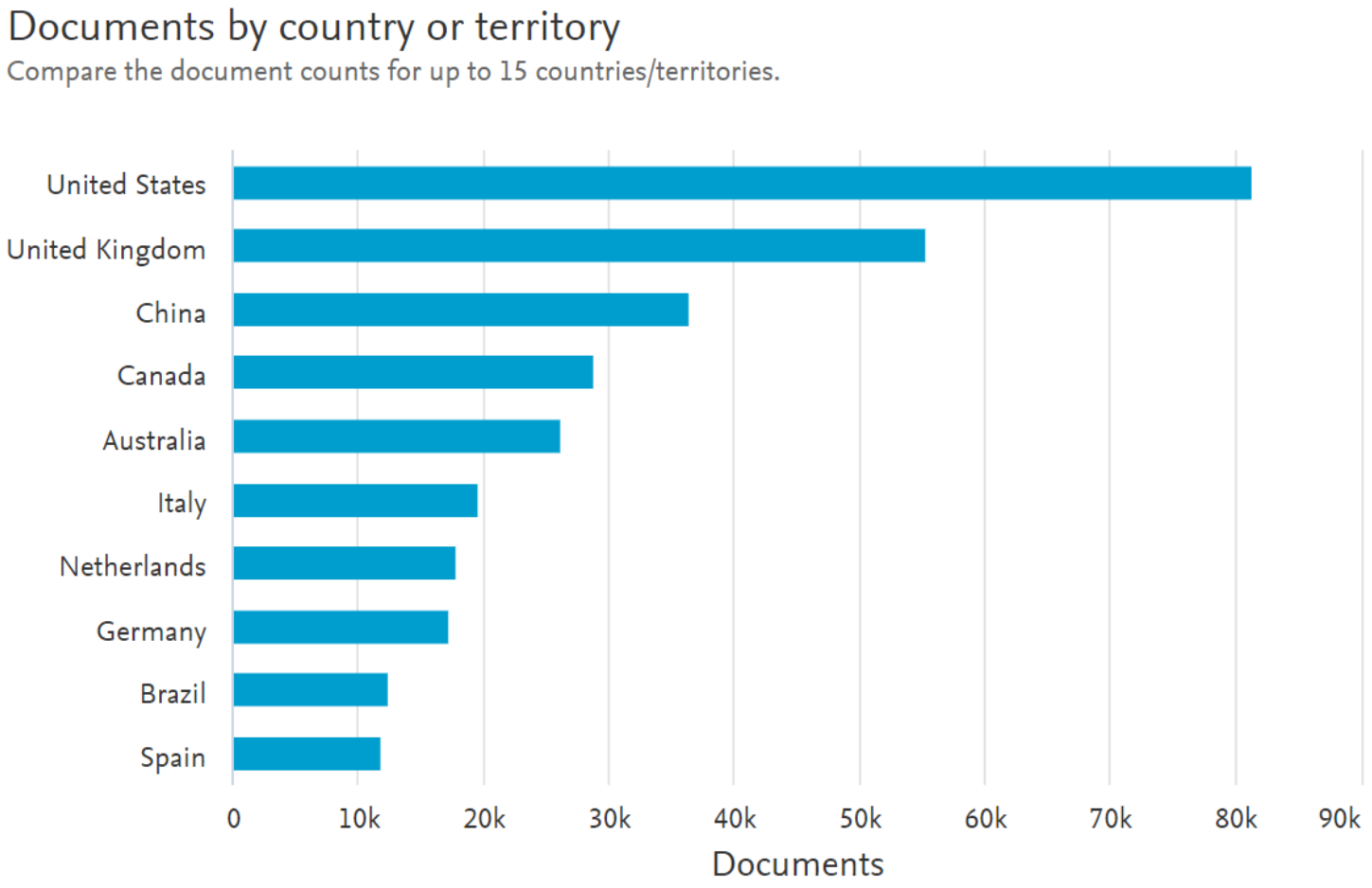

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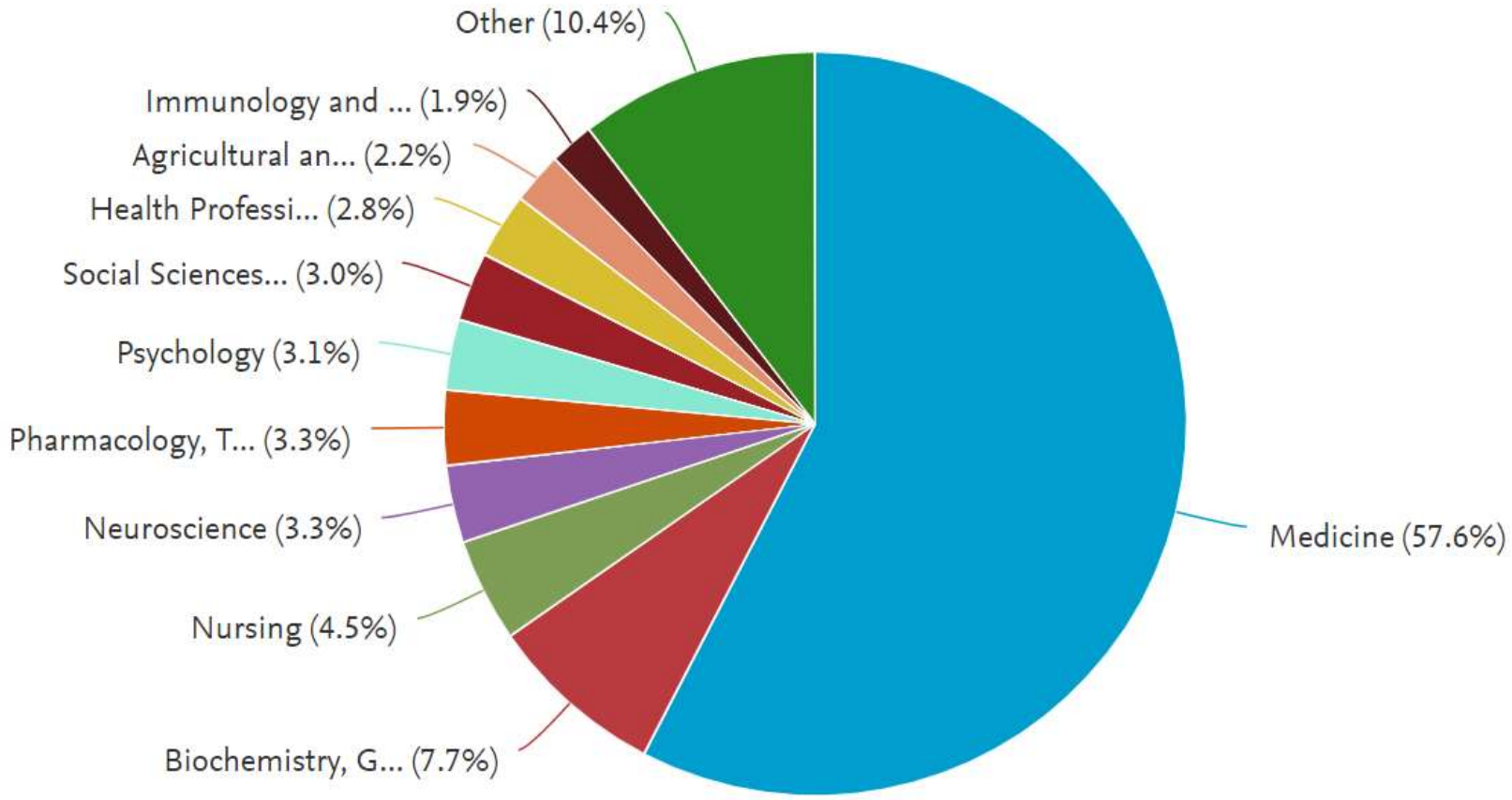

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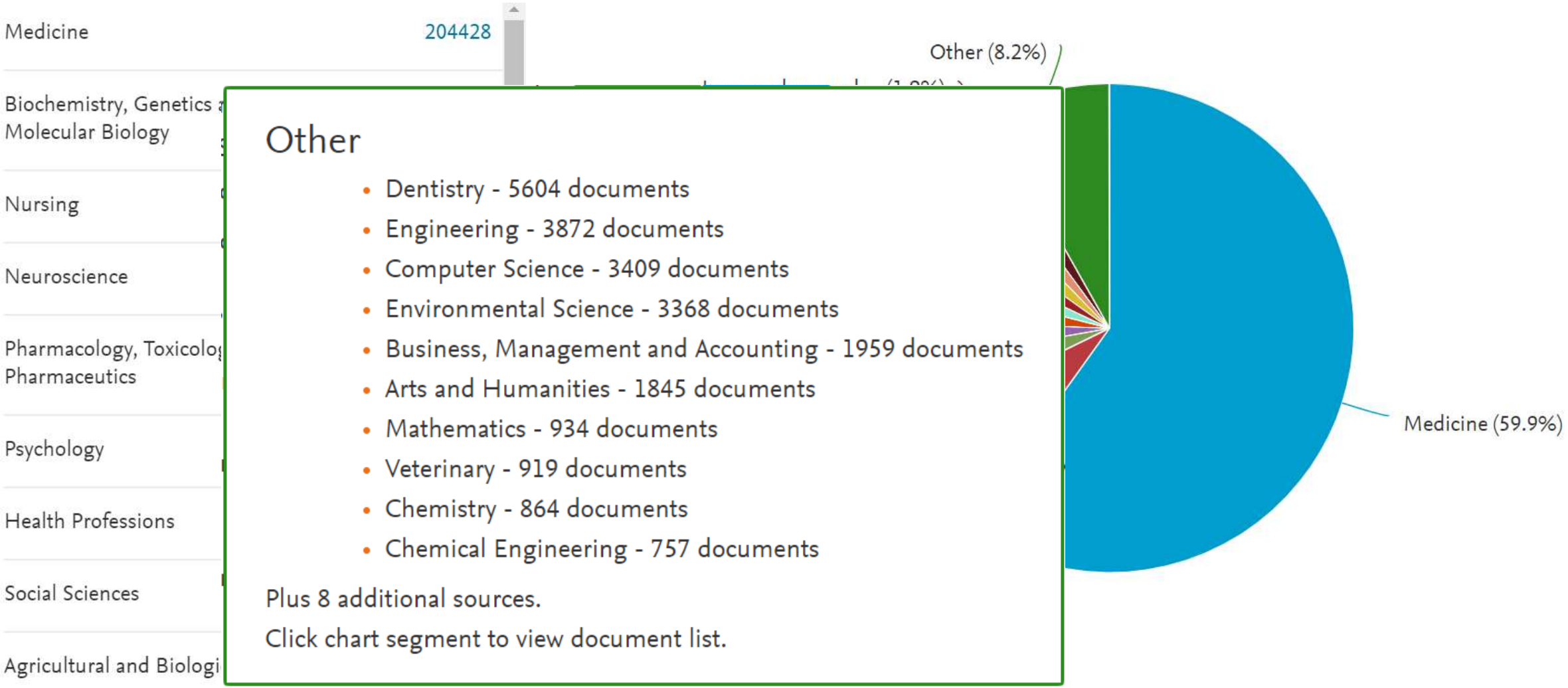
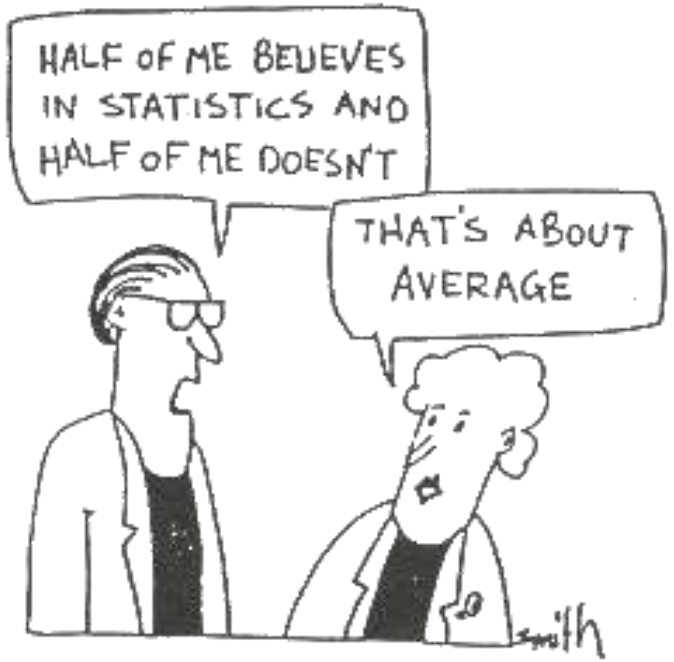


Information overload

Ask somebody to find all studies, select the best, …

What do you do?

- For an acutely ill patient, you do a search
- You find several studies: some find that it works; some do not
- What do you do?



You find this review

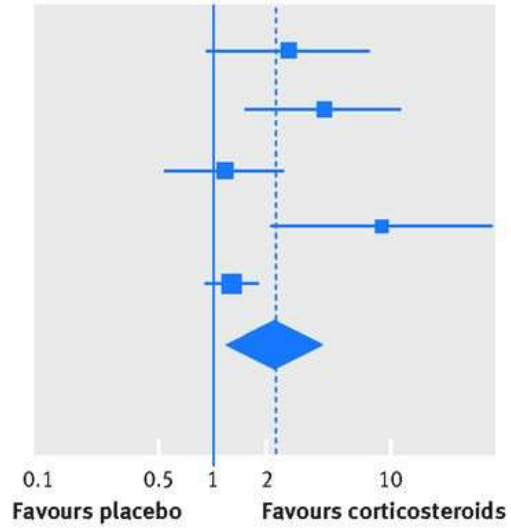
BMJ

RESEARCH

Corticosteroids for pain relief in sore throat: systematic review and meta-analysis

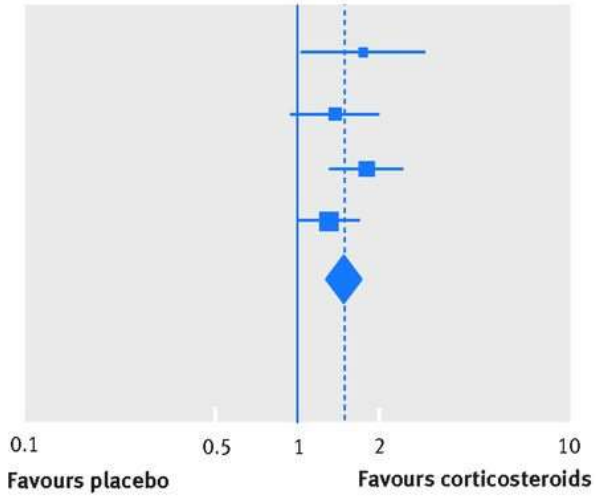
Gail Hayward, academic F2 in general practice,[1] Matthew Thompson, senior clinical scientist,[1] Carl Heneghan, clinical lecturer in general practice,[1] Rafael Perera, medical statistician,[1] Chris Del Mar, dean, faculty of health sciences and medicine,[2] Paul Glasziou, professor of evidence based medicine[1]

Study	Events/total Treatment	Events/total Control	Weight (%)	RR (95% CI)
Wei 2002	12/41	4/36	18	2.63 (0.93 to 7.45)
Kiderman 2005	17/40	4/39	18	4.14 (1.53 to 11.22)
Niland 2006	12/39	8/30	22	1.15 (0.54 to 2.46)
Tasar 2008	13/31	2/42	13	8.81 (2.14 to 36.23)
Hayward 2017	65/288	49/277	30	1.28 (0.92 to 1.78)
Overall (I^2=69%, P=0.012)	119/439	67/424	100	2.24 (1.17 to 4.29)



During the first ۲۴ hours

Study	Events/total Treatment	Events/total Control	Weight (%)	RR (95% CI)
Kiderman 2005	23/40	13/39	10	1.73 (1.03 to 2.89)
Niland 2006	21/27	17/30	19	1.37 (0.95 to 1.99)
Tasar 2008	29/31	22/472	29	1.79 (1.32 to 2.42)
Hayward 2017	102/288	75/277	42	1.31 (1.02 to 1.68)
Overall (I^2=3%, P=0.377)	175/386	127/388	100	1.48 (1.26 to 1.75)



During the first ۴۸ hours

History

- James Lind, ۱۸th century
  - Critically reviewed a number of reports on the prevention and treatment of scurvy

What is a systematic review?

- **SYSTEMATIC**: Done or acting according to a fixed plan or system: methodical

- **REVIEW:** A critical appraisal of a book, play or other work

What is a systematic review?

- “A systematic review is a review in which there is a comprehensive search for relevant studies on a specific topic, and those identified are then appraised and synthesized according to a predetermined and explicit method.” (Klassen ۱۹۹۸)

- A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusions can be drawn and decisions made (Antman ۱۹۹۲, Oxman ۱۹۹۳)

What is a systematic review?

- Use explicit and rigorous methods to:
  - Identify
  - Critically appraise
  - Synthesize
- Look for the whole “truth” (not just a part…a single or few studies)
  - Assemble **all** available evidence (e.g., all controlled studies)

Unique characteristics of a systematic review

- A systematic review must have:
  - *Clear question to answer*
  - *Clear inclusion and exclusion criteria*
  - *Explicit search strategy*
  - *Systematic coding and analysis of included studies*
  - *Meta-analysis (where possible)*

What is Meta Analysis

- Statistical methods may or may not be used to analyze and summarize the results of the included studies.

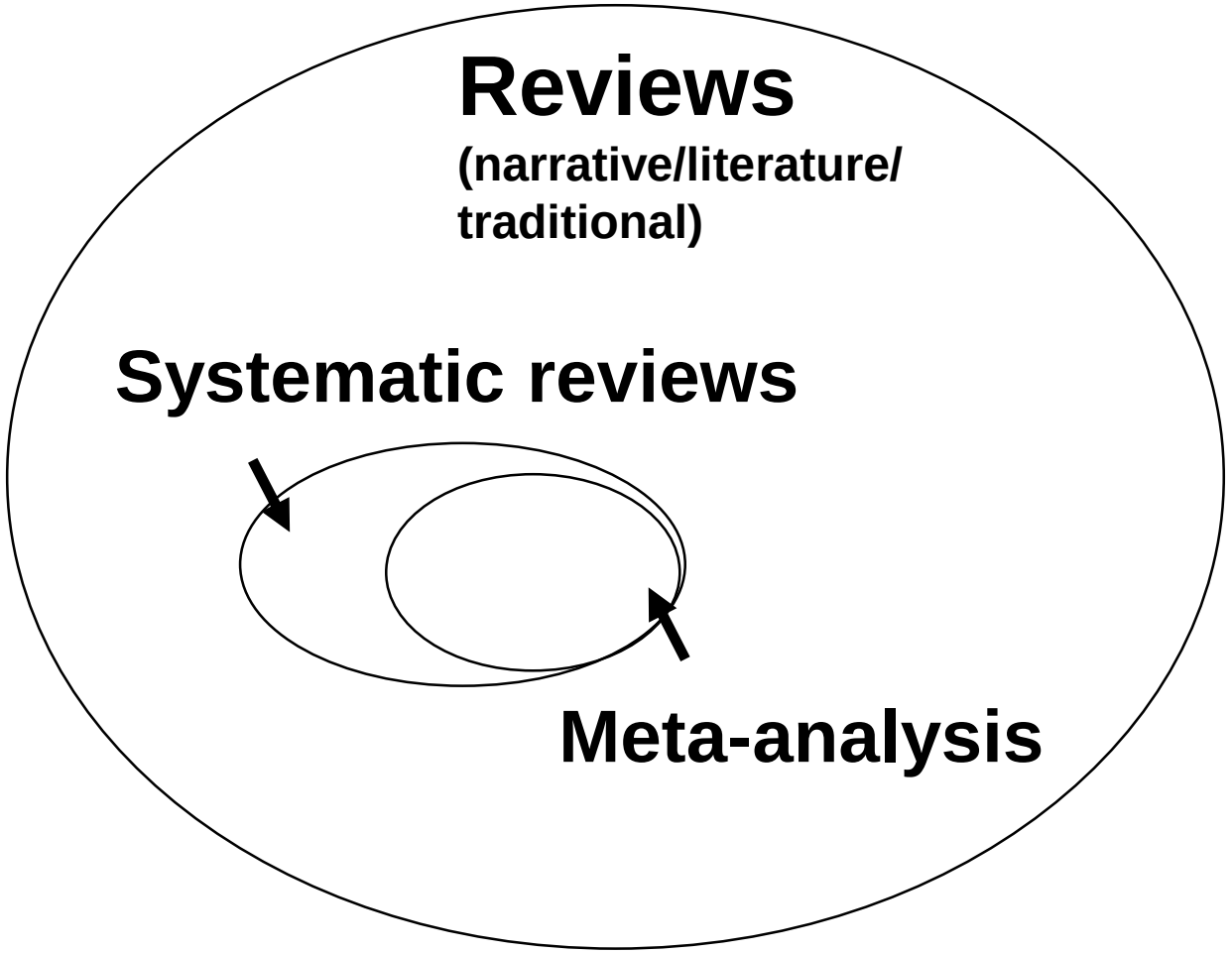
"the use of statistical methods to summarize the results of independent studies "

- i.e. A specific type of systematic review

What is a meta-analysis?

- Optional component of a systematic review
  - *A statistical analysis of results from individual studies*
    - Increase power
    - Improve estimates of the size of the effect

Types of reviews



Narrative/traditional reviews

- Usually written by experts in the field
- Use informal and subjective methods to collect and interpret information
- Usually narrative summaries of the evidence

Read: Klassen et al. Guides for Reading and Interpreting Systematic Reviews. Arch Pediatr Adolesc Med ۱۹۹۸;۱۵۲:۷۰۰-۷۰۴.

Narrative vs systematic review

Narrative

- Many questions
- Unclear how conclusions follow from included studies
  - No search methods
  - No inclusion criteria
  - No combining studies
- Prone to random and systematic error
- May not consider quality of included studies

Systematic

- One question
- Methods transparent and reproducible
  - Explicit search
    - Reproducible
  - Explicit inclusion criteria
  - Combine study results (meta-analysis)
- Standardised critical appraisal across included studies

Why use systematic reviews?

- Minimise the impact of bias/errors
- Can help to end confusion
- Highlight where there is not sufficient evidence
- Combining findings from different studies can highlight new findings
- Can mitigate the need for further trials

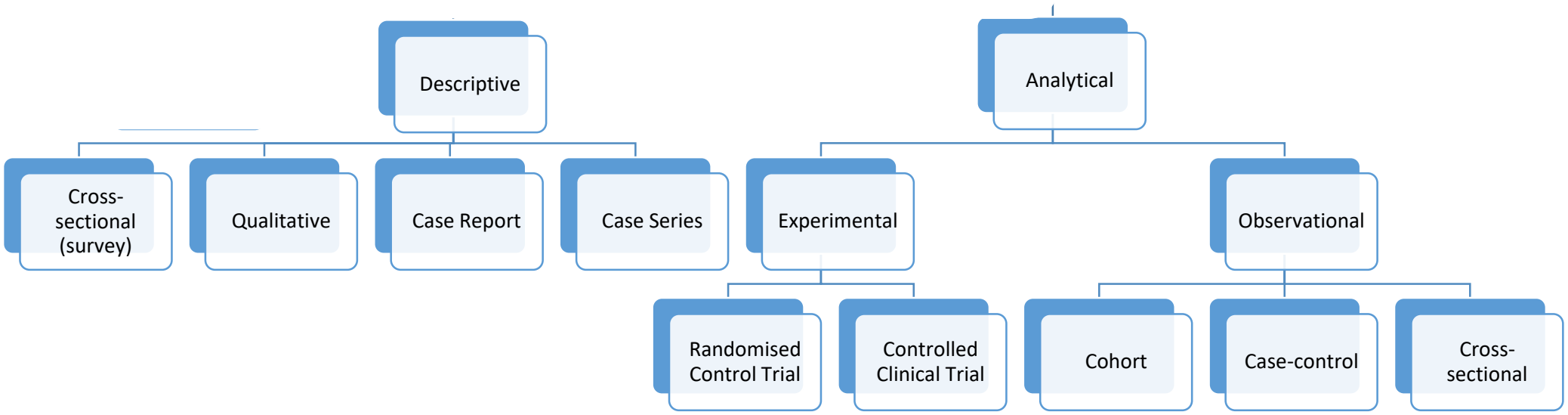
Why use systematic reviews?

- Facilitate rational decision making
- Health care providers, researchers and policy makers are inundated with unmanageable amounts of information
  - Over ۲۰ million citations in PubMed
  - Approx. ۷۵ to ۱۰۰ RCTs published daily
  - Usually impossible to consider all relevant individual primary research studies in a decision making context
- Enable practitioners to keep up to date and practice evidence-based medicine

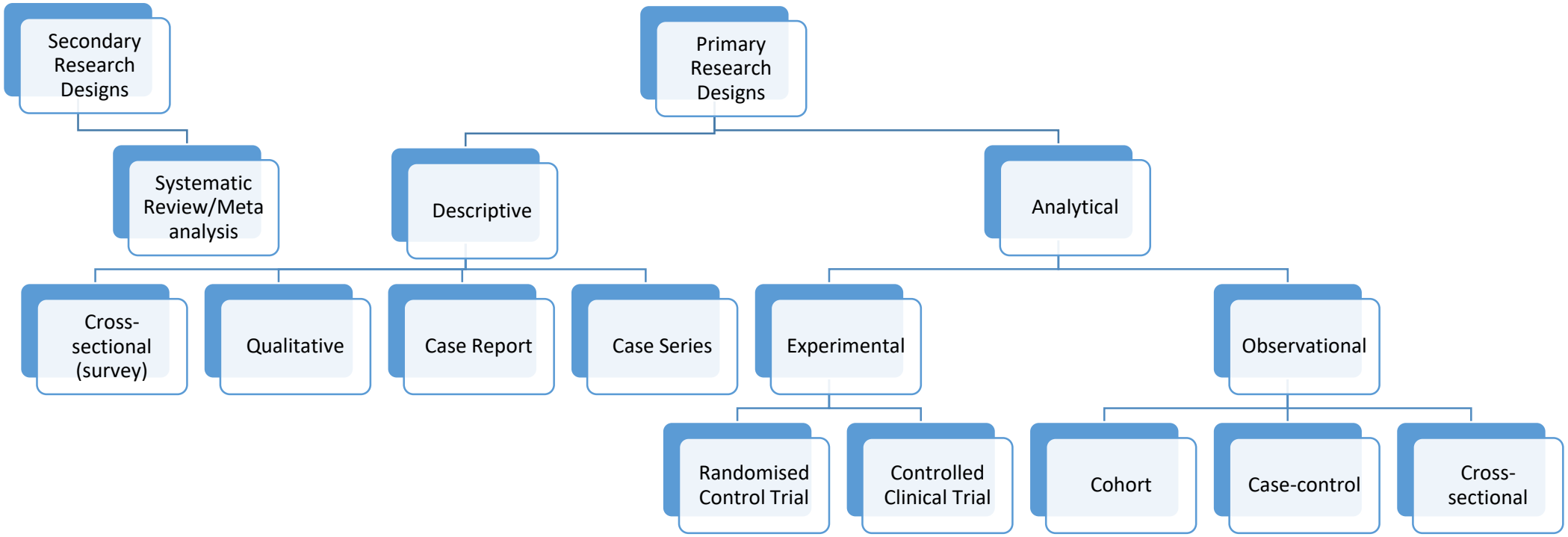
Advantages of systematic reviews

- Reduce bias
- Replicability
- Resolve controversy between conflicting studies
- Identify gaps in current research
- Provide reliable **basis** for decision making

Research designs

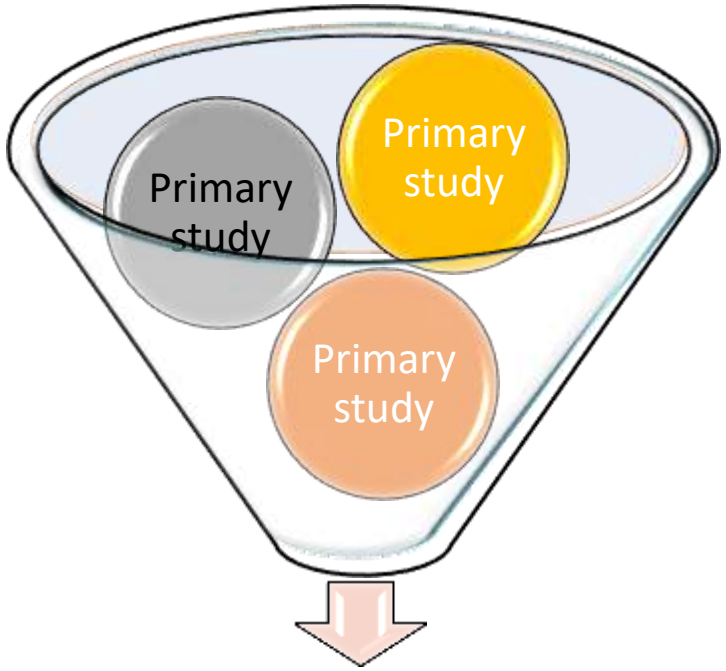


Research designs



Introduction

- Primary studies and Secondary studies



Hierarchy of evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

Levels of Evidence

Level of Evidence	Type of Study
۱a	Systematic reviews of randomized clinical trials (RCTs)
۱b	Individual RCTs
۲a	Systematic reviews of cohort studies
۲b	Individual cohort studies and low-quality RCTs
۳a	Systematic reviews of case-controlled studies
۳b	Individual case-controlled studies
۴	Case series and poor-quality cohort and case-control studies
۵	Expert opinion based on clinical experience

Adapted from: Sackett DL et al. *Evidence-Based Medicine: How to Practice and Teach EBM*. ۲nd ed. Churchill Livingstone; ۲۰۰۰.

Who undertakes systematic reviews?

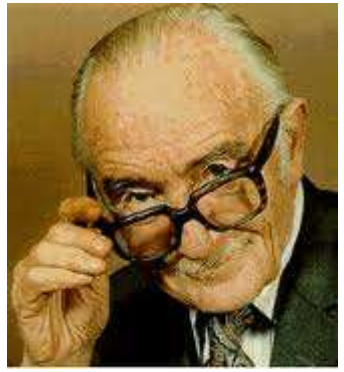
- Cochrane
- Campbell Collaboration
- EPPI-Centre
- PROSPERO
- EQUATOR
- Joana Bridges Institute

Introduction to Cochrane

- Archie Cochrane (۱۹۰۹-۸۸)
  - British epidemiologist
  - Advocated RCTs to inform healthcare practice

- Cochrane collaboration
  - Cochrane Reviews (>۴’۰۰۰) registered
  - Identify, appraise and synthesise research-based evidence and present it in accessible format; regularly updated
  - Focus on interventions
  - Outstanding general resource

History



The School of Medicine, Cardiff University and the Cochrane Archive

- Archie Cochrane, an epidemiologist, published an influential book in ۱۹۷۲ (Effectiveness and Efficiency)
  - criticized our collective ignorance about the effects of health-care.

"It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, updated periodically, of all relevant randomized controlled trials"

History

- In ۱۹۸۷ Cochrane referred to a systematic review of corticosteroid treatment in pre-term births
  - showed that a short-inexpensive course of corticosteroid treatment substantially reduced the risk of premature deaths due to complications
  - evidence showed that had a systematic review been done ۱۰ years earlier we could have prevented many premature deaths

Introduction to Campbell Collaboration

- Systematic reviews of the effects of social interventions
- Prepare, maintain and disseminate systematic reviews in education, crime and justice, and social welfare
- Register relevant reviews
- Links to useful methodology sites
  - Effect sizes
  - Campbell Collaboration Resource Centre

Introduction to EPPI-Centre

- Evidence for Policy and Practice Information and Co-ordinating Centre
- Systematic reviews of public policy
  - Education, health promotion, employment, social care, criminal justice
- Online evidence library
- Methods, tools and databases (quantitative and qualitative)
- EPPI-Centre (March ۲۰۰۷) EPPI-Centre methods for conducting systematic reviews. London: EPPI-Centre, Social Science Research Unit, Institute of Education, University of London.

Introduction to PROSPERO

- Centre for Reviews and Dissemination, York
- Evaluate the effects of health and social care interventions and the delivery and organisation of health care
- Guidance on systematic reviews
- PROSPERO
  - International prospective register of SRs

Introduction to EQUATOR

- Enhancing the QUAlity and Transparency Of health Research
- Started March ۲۰۰۶
- Grew from guideline development groups (including CONSORT)
- Aim to:
  - provide resources and education enabling the improvement of health research reporting
  - monitor progress in the improvement of health research reporting

Introduction to EQUATOR

- Detailed reporting guidelines
  - CONSORT Statement (reporting of randomized controlled trials)
  - STARD (reporting of diagnostic accuracy studies)
  - STROBE (reporting of observational studies in epidemiology)
  - PRISMA (reporting of systematic reviews), which replaced
  - MOOSE (reporting of meta-analyses of observational studies)

- Minimum Information for Biological and Biomedical Investigation (MIBBI) portal
  - e.g. minimum dataset for fMRI studies

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http://www.equator-network.org/resource-centre/library-of-health-research-reporting/

Joanna Bridges Institute

“For over ٢٠ years the Joanna Briggs Institute has supported health professionals to improve health outcomes globally and create ripples of change by providing the best available evidence to inform clinical decision making.”

Key elements of a systematic review

Define research/review question
In consultation/collaboration with the clinical community, commissioners and patient/public representatives

Develop review protocol
Pre-specify the type of studies to be included, the methods of collating, appraising and analysing data

Identify relevant studies
Develop a comprehensive search strategy and undertake systematic searches of the literature

Assess eligibility
Select those studies which meet the pre-defined inclusion criteria

Data extraction /checking
Develop data extraction from into which study information and outcome data can be extracted, checked & verified

Study assessment/appraisal
Assess the quality and validity of the included studies using the pre-defined method.

Synthesis
Narratively and/or statistically summarise/describe the data, exploring similarities and differences between studies.

Dissemination
Publish the result


THANK
YOU !