

An Introduction to Systematic Reviews & Meta-Analysis

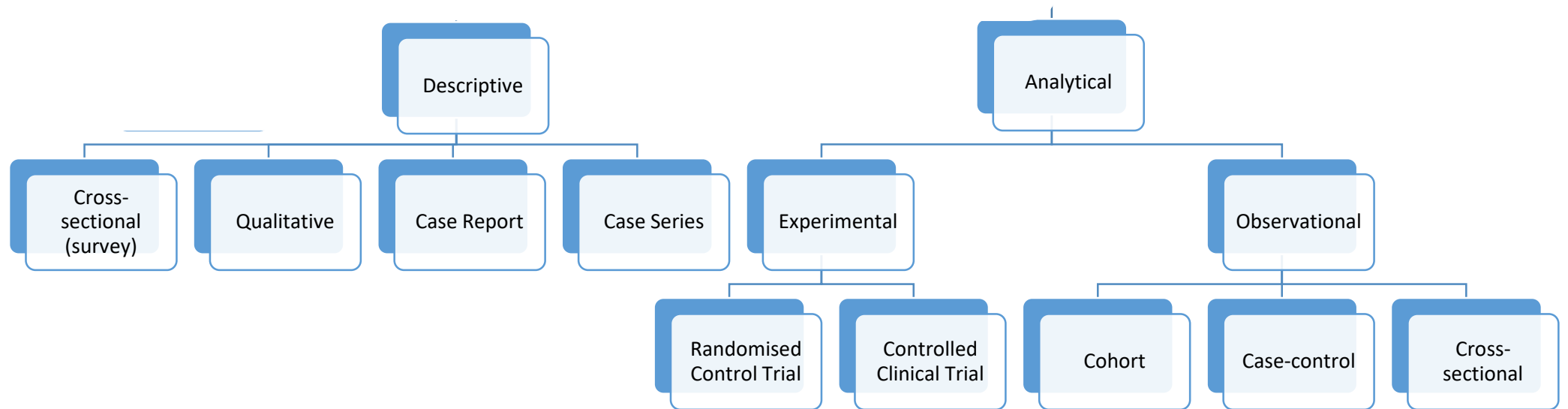
Dr Roya Safari-Faramani

Assistant Professor with the Department of Epidemiology

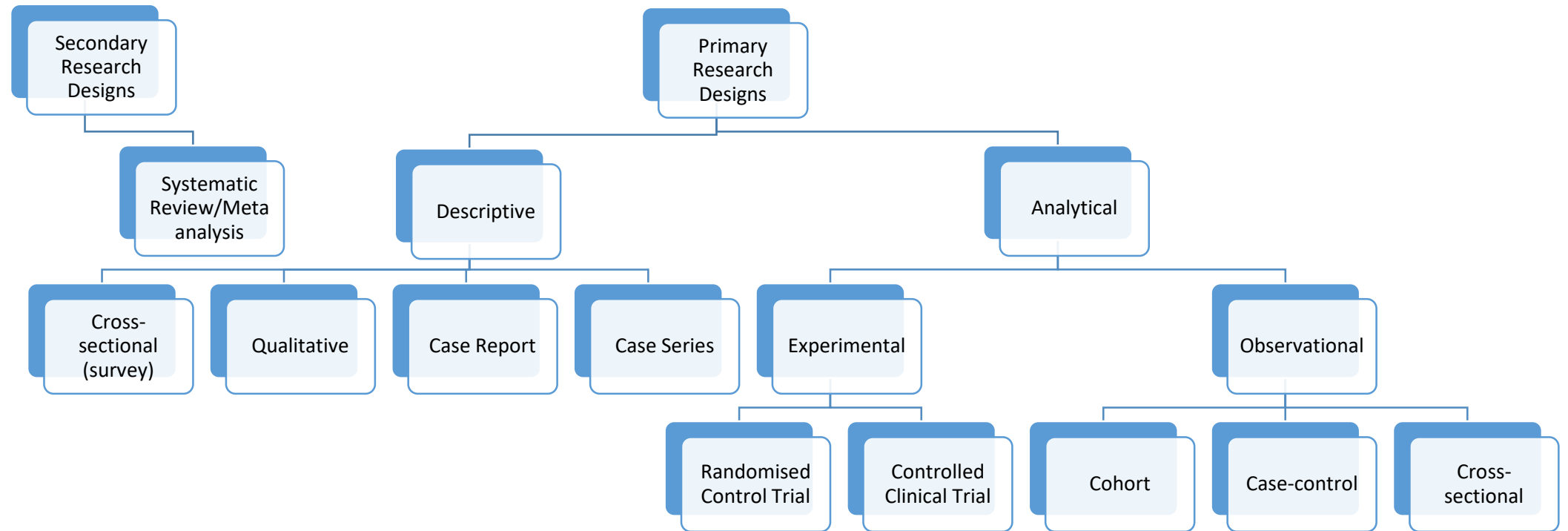
Kermanshah University of Medical Sciences

r.safari84@gmail.com

Research designs



Research designs



Hierarchy of evidence



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Chinese herbal medicine (Rupi Sanjie capsule) for the treatment of breast pain: A systematic review and meta-analysis of randomized clinical trials
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Lai, B.-Y., Jia, L.-Y., Yu, B.-W., (...), Liu, J.-P., Pei, X.-H.

2021

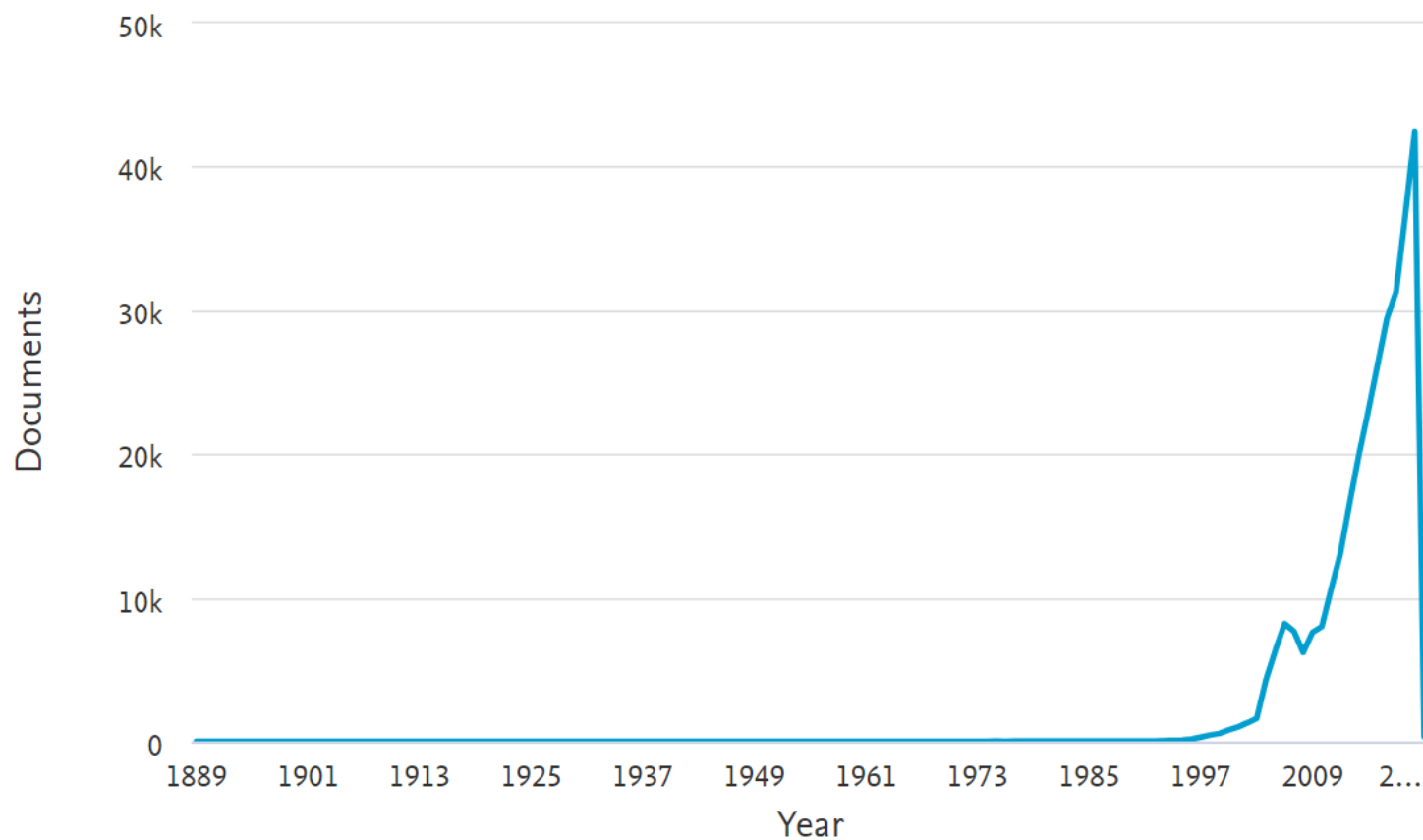
Integrative Medicine Research
10(2),100491

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Documents by year

Year ↓	Documents ↑
2021	312
2020	42466
2019	36747
2018	31315
2017	29410
2016	26211
2015	22994
2014	19965
2013	16587
2012	13068

Documents by year

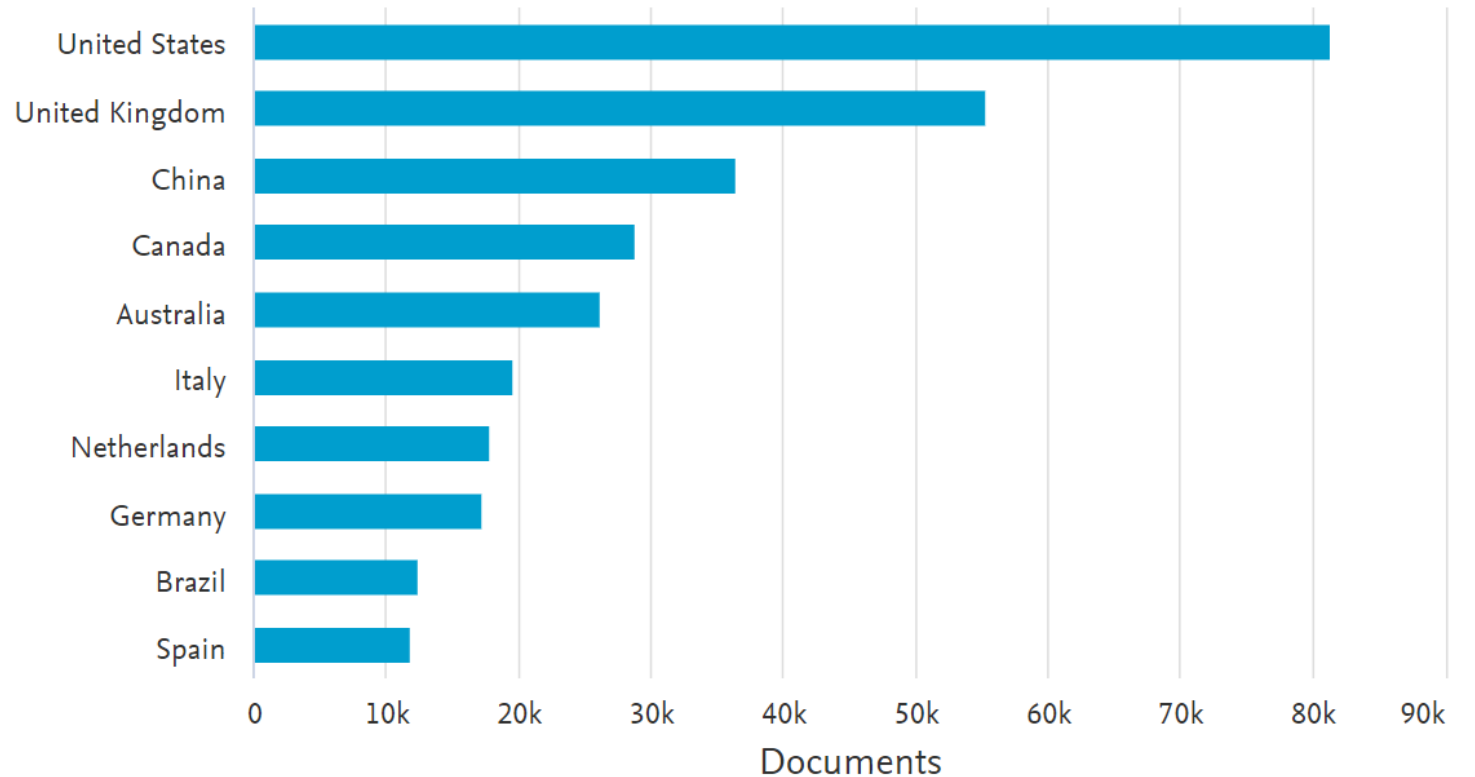


Documents by country

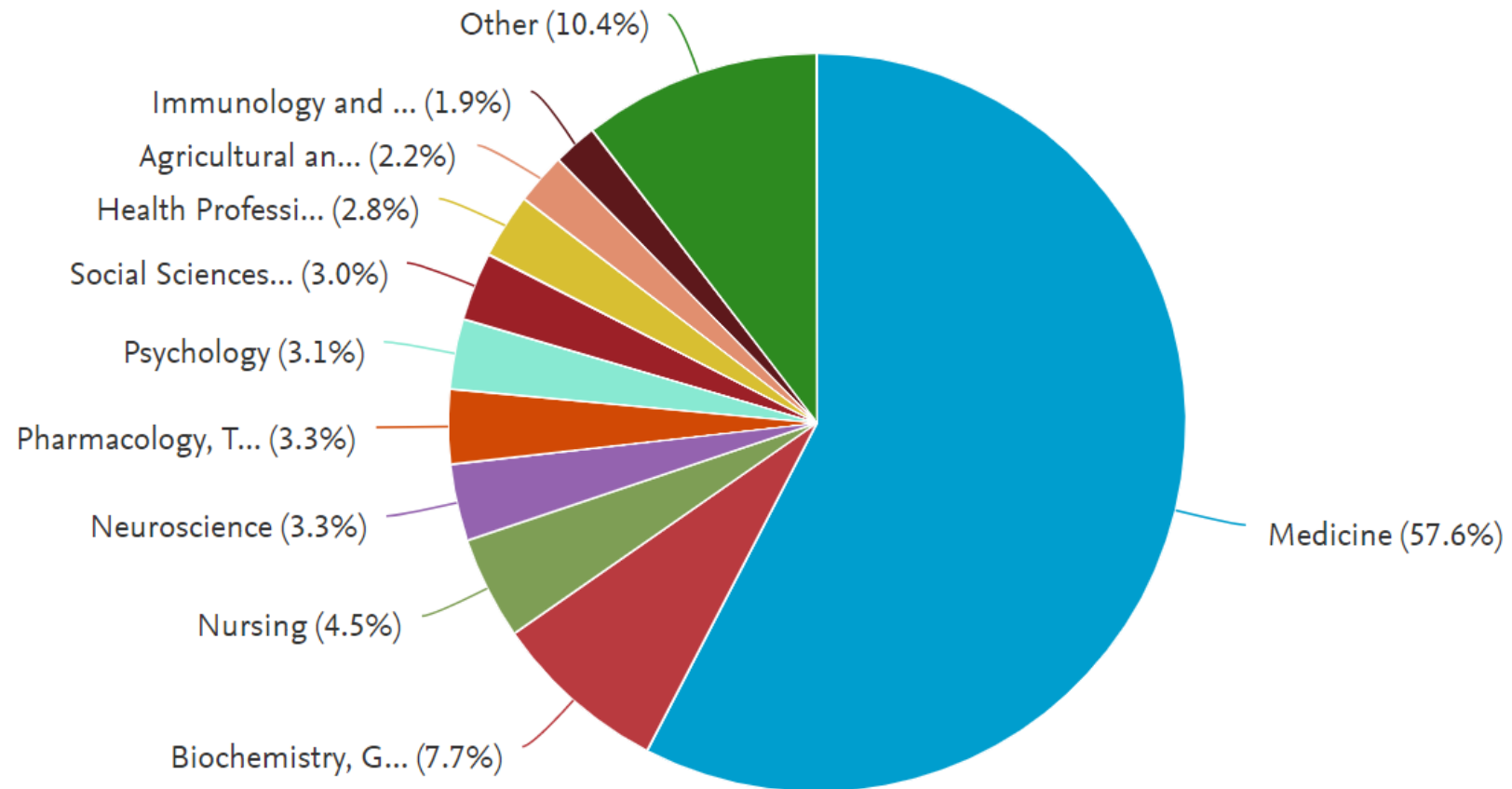
Country/Territory ↑	Documents ↓
<input checked="" type="checkbox"/> Italy	19510
<input checked="" type="checkbox"/> Netherlands	17771
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<input type="checkbox"/> Switzerland	8674
<input type="checkbox"/> Iran	6479
<input type="checkbox"/> Belgium	6051

Documents by country or territory

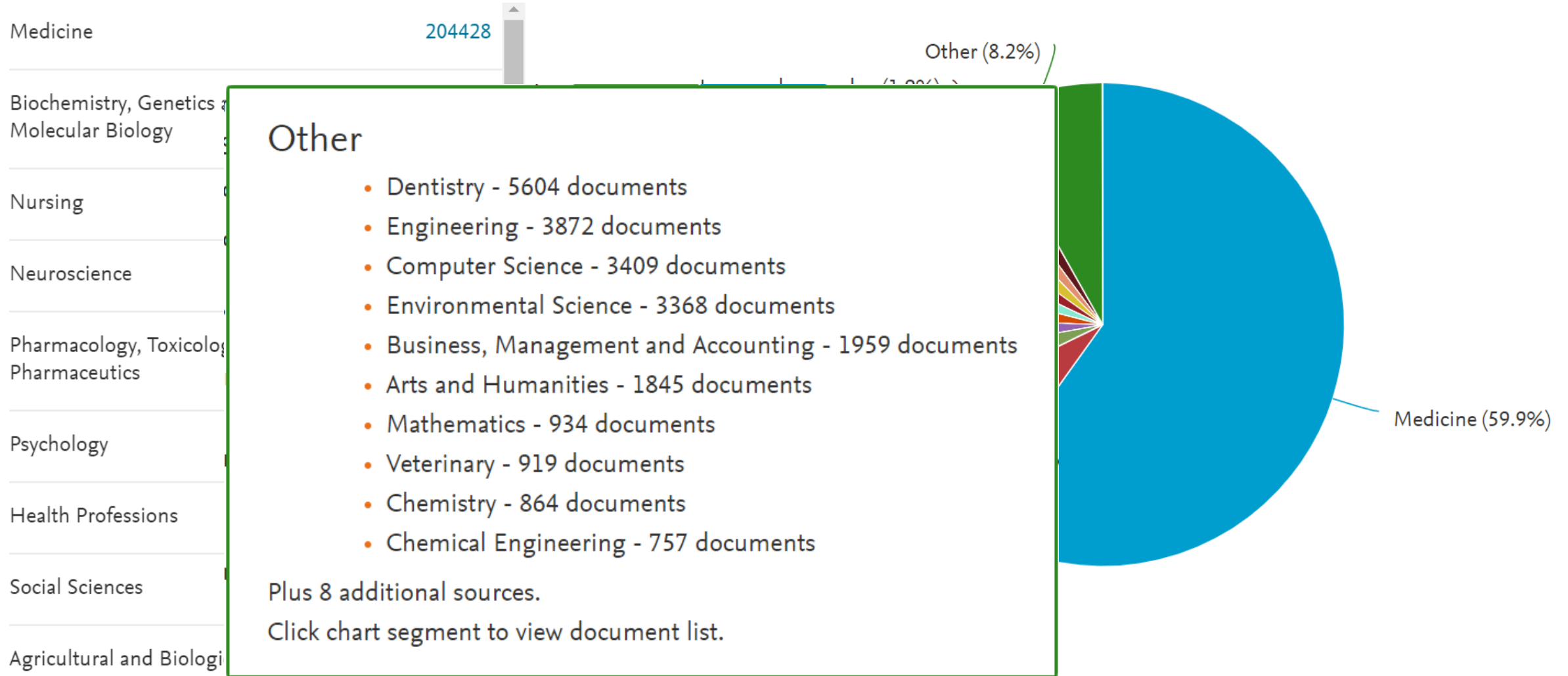
Compare the document counts for up to 15 countries/territories.



Documents by subject area



Documents by subject area

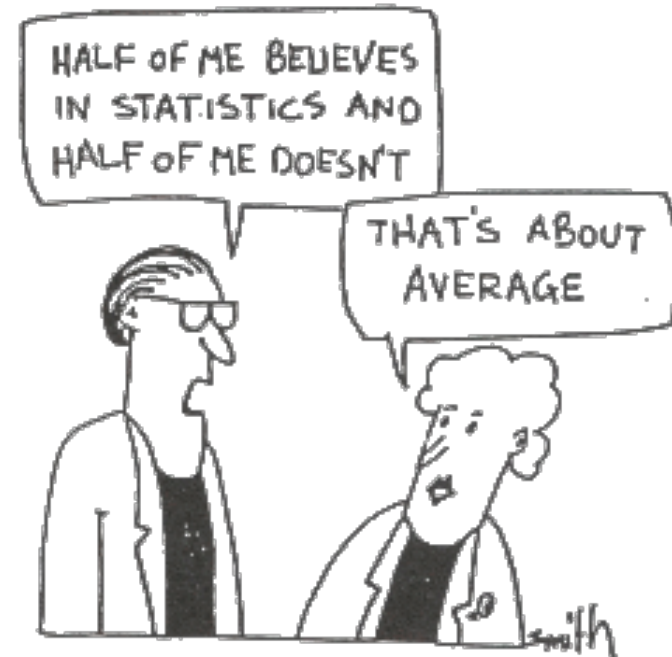


Information overload



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?



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



You find this review

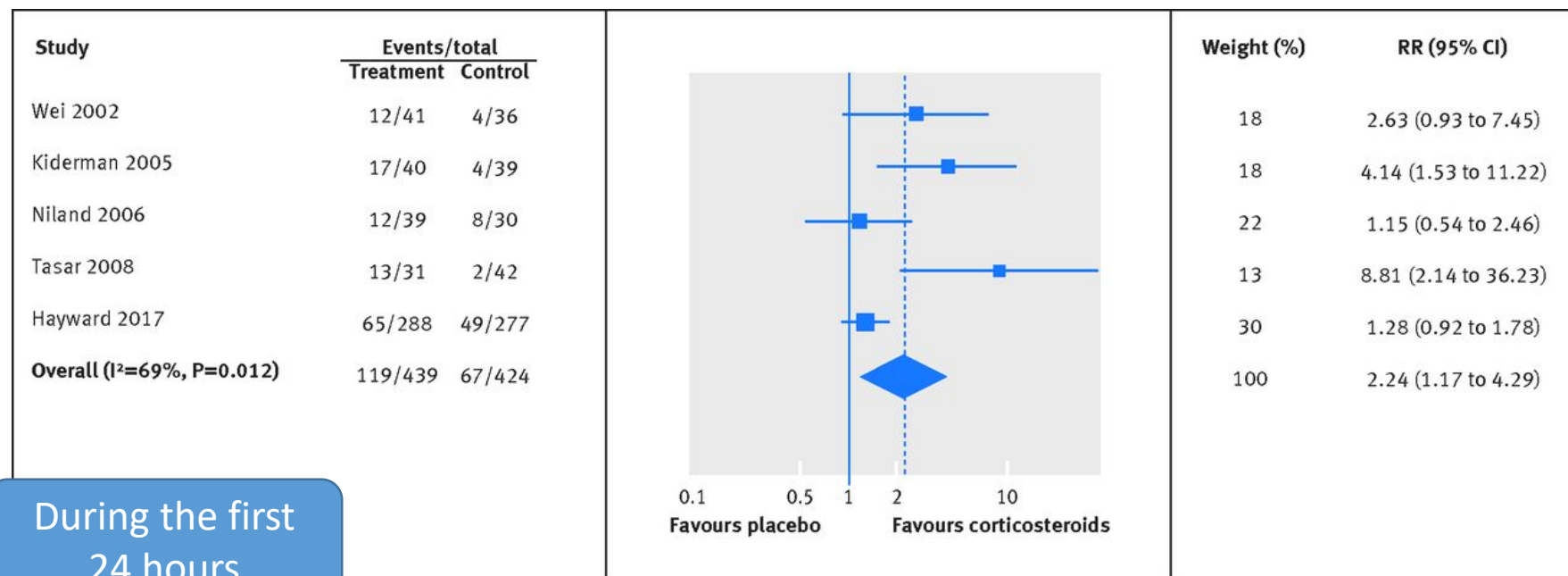


BMJ

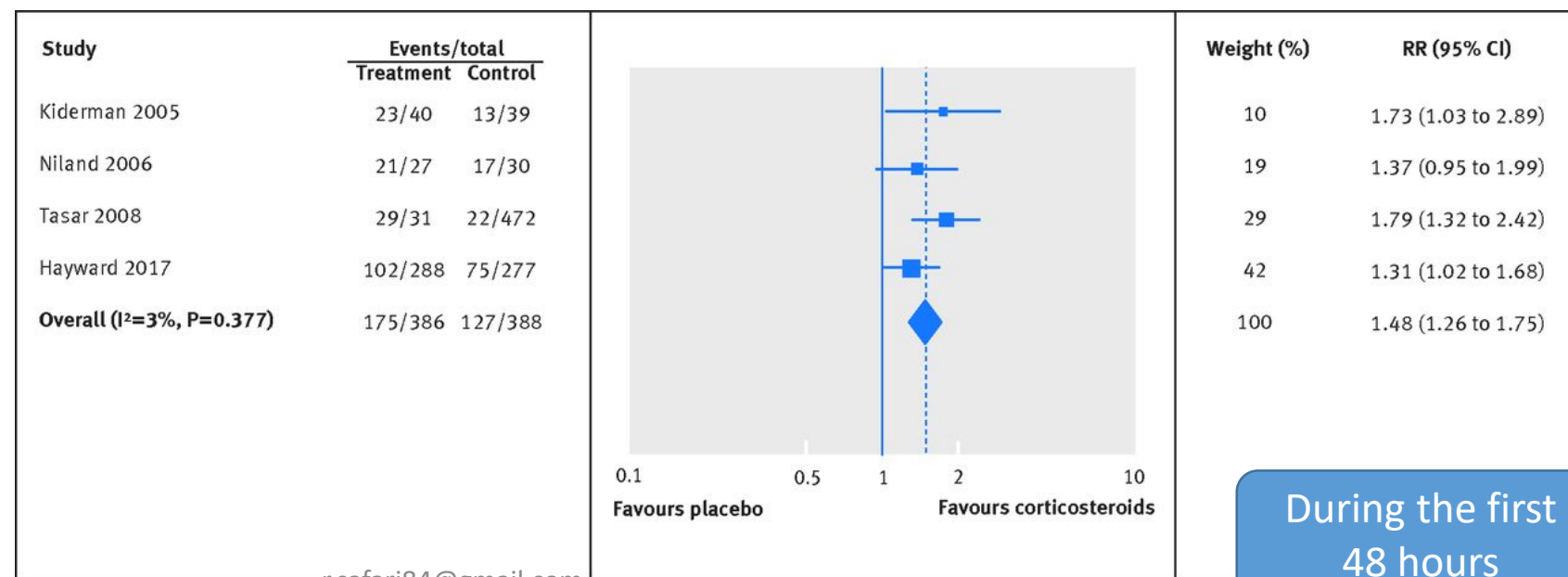
RESEARCH

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 medicine¹



During the first
24 hours



During the first
48 hours

History

- James Lind, 18th 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 1998)
- 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 1992, Oxman 1993)

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.

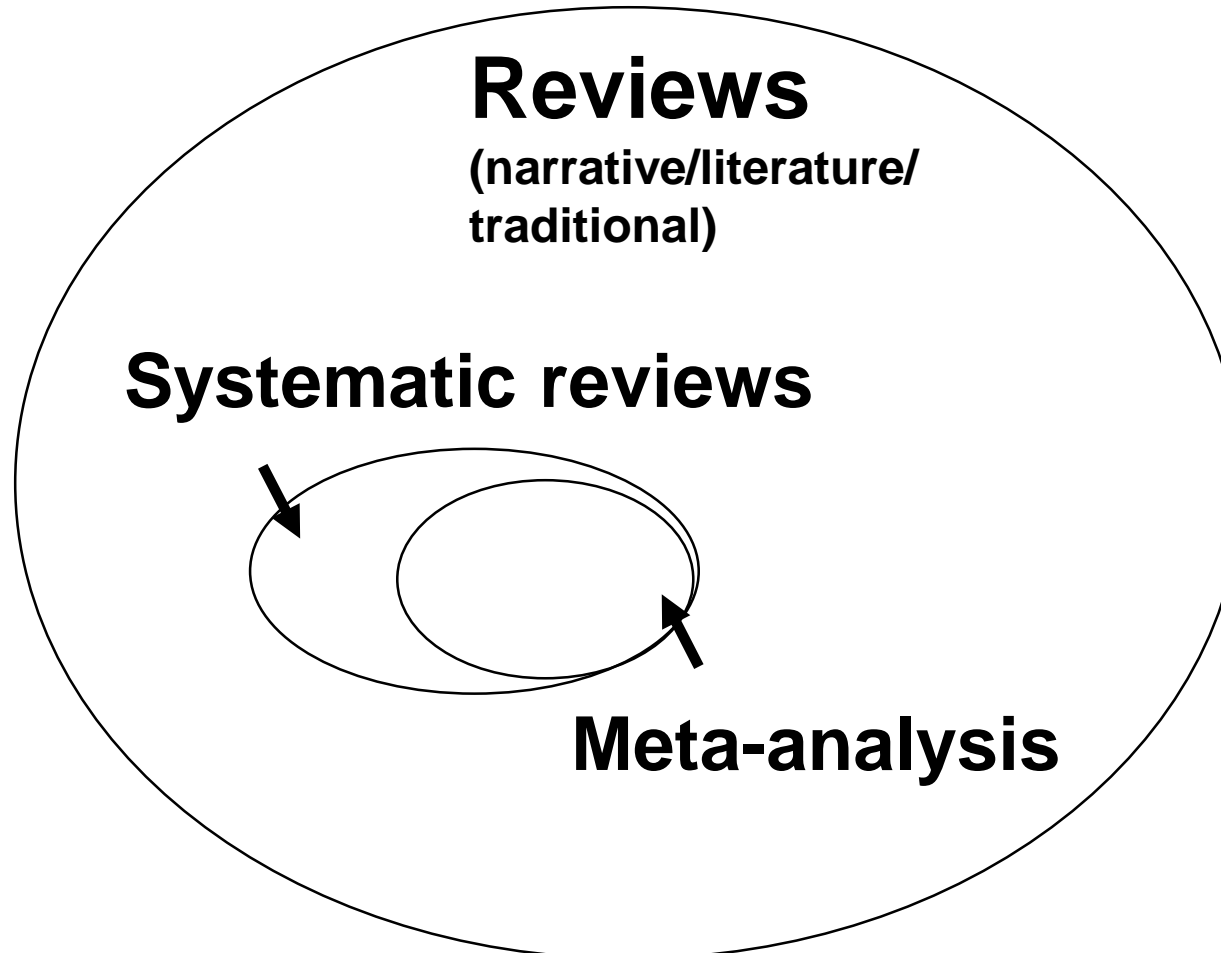
“the use of statistical methods to summarize the results of independent studies ”

- 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 1998;152:700-704.

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 20 million citations in PubMed
 - Approx. 75 to 100 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

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 <i>n</i> -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, <i>n</i> -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 <i>n</i> -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
r.safari84@gmail.com

Levels of Evidence

Level of Evidence	Type of Study
1a	Systematic reviews of randomized clinical trials (RCTs)
1b	Individual RCTs
2a	Systematic reviews of cohort studies
2b	Individual cohort studies and low-quality RCTs
3a	Systematic reviews of case-controlled studies
3b	Individual case-controlled studies
4	Case series and poor-quality cohort and case-control studies
5	Expert opinion based on clinical experience

Who undertakes systematic reviews?

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

Introduction to Cochrane

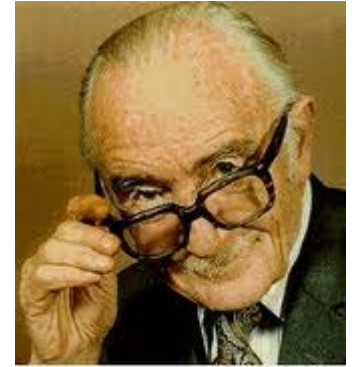
- Archie Cochrane (1909-88)
 - British epidemiologist
 - Advocated RCTs to inform healthcare practice
- Cochrane collaboration
 - Cochrane Reviews (>4,000) registered
 - Identify, appraise and synthesise research-based evidence and present it in accessible format; regularly updated
 - Focus on interventions
 - Outstanding general resource



History

- Archie Cochrane, an epidemiologist, published an influential book in 1972 (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”



The School of Medicine,
Cardiff University and the
Cochrane Archive

History

- In 1987 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 10 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](http://www.campbellcollaboration.org/)



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 \(March 2007\) 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 2006
- 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 QUOROM
 - MOOSE (reporting of meta-analyses of observational studies)
- Minimum Information for Biological and Biomedical Investigation (MIBBI) portal
 - e.g. minimum dataset for fMRI studies



Joanna Bridges Institute



“For over 20 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

