Evidence Synthesis: The Hows and Whys?

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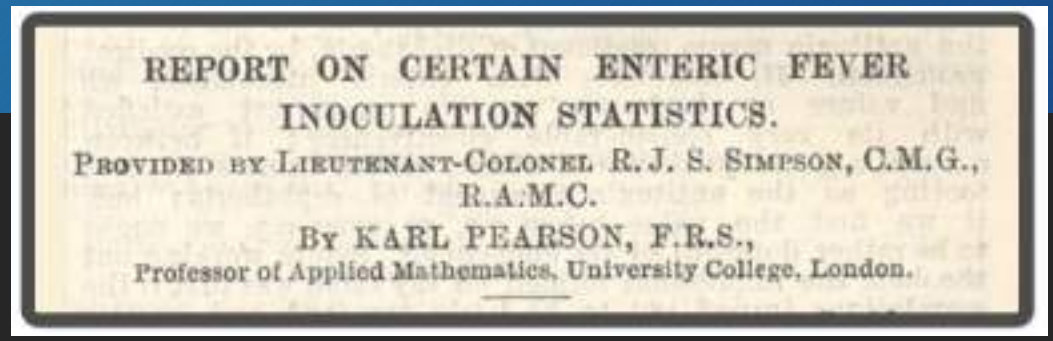
Purpose of Evidence Synthesis

Summarize existing empirical research to:

- Take stock of a body of research
- Identify gaps in knowledge
- Organize knowledge (master the information tsunami)
- Provide directions for further research
- Inform policy and practice

The past

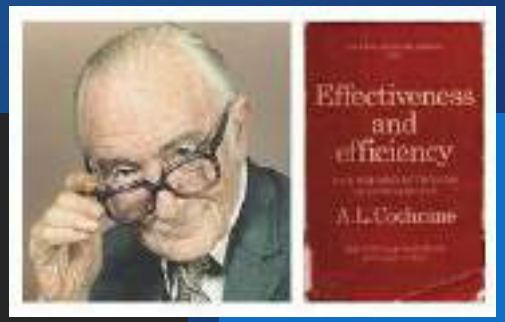


REPORT ON CERTAIN ENTERIC FEVER INOCULATION STATISTICS.

PROVIDED BY LIEUTENANT-COLONEL R. J. S. SIMPSON, C.M.G., R.A.M.C.

BY KARL PEARSON, F.R.S.,

Professor of Applied Mathematics, University College, London.



- First example of a systematic review was conducted in 1753 by James Lind through paper on evidence on scurvy
- Karl Pearson, one of the founders of the British school of statistics, assessed the effects of inoculation on enteric fever (typhoid) in the British army using ‘meta-analysis’ to combine statistics from separate but similar studies
- Archie Cochrane published a book “Effectiveness and efficiency: Random reflections on health service” on importance of RCTs in treatment effectiveness
- Glass & Smith, 1979 (Class size), Smith, Glass & Miller, 1980 (psychotherapy) coined critical appraisal and synthesis of research
- Sackett et. al. (1996) urged practitioners to practice evidence-based medicine

CPHR
Centre for Public Health Research

T...

- Cochrane Collaboration opened its Center in 1992
- Joanna Briggs Institute (JBI): Founded by Professor Alan Pearson established as a research institute in 1996, based at the Royal Adelaide Hospital in South Australia
- The EPPI-Centre is based in the Social Science Research Unit in the Department of Social Science, UCL Institute of Education, University College London. The work of the centre started in 1993, the name ‘EPI-Centre’ was used from 1995 and we then changed to the current name of ‘EPPI-Centre’ from 2001.Campbell Collaboration started in 2000
- Campbell Collaboration started in 2000

Evidence Synthesis International

equator network

The present

SR TOOL BOX

- Beyond effectiveness reviews (typology of systematic reviews)
- GRADE extensions- qualitative (GRADE-CERQual), network meta-analysis (CINEMA)
- EQUATOR-Network : Enhancing quality and transparency of health research
- Newer methods (SWiM, NMA, Scoping Reviews, Evidence and Gap Maps)
- Reporting structures (PRISMA-2020, PRISMA-S)
- Growing need for efficient production and timelines (Cochrane Rapid Reviews)
- Use of systematic review software (Rayyan, Covidence, CADIMA, SR Toolbox)
- Use of machine learning filters (EPPI Reviewer, Distiller SR) and artificial intelligence (Distiller SR) in screening
- Evidence Synthesis International (ESI)

CPHR Centre for Public Health Research

Literature reviews vs Systematic reviews

Stage	Systematic review	Literature review
Search	Comprehensive and exhaustive	Selective, may miss areas of literature especially grey material
Screening / inclusion	Clearly stated, systematically applied inclusion criteria	May be arbitrary, affected by author bias
Data extraction	Uses a clear framework	Done in non-transparent manner
Data synthesis	Meta-analysis where applicable; qualitative synthesis using matrices	Uses arbitrary or incorrect approaches
Presentation	All results are presented	Selective presentation of results
	All the above down by two, with independent arbitration	Usually done by one person with no checks or balances

Characteristics of traditional literature reviews, scoping reviews and systematic reviews

	TLR	Scoping Reviews	Systematic Reviews
A priori review protocol	No	Yes (some)	Yes
PROSPERO registration	No	No	Yes
Search strategy	No	Yes	Yes
Data extraction forms	No	Yes	Yes
RoB assessment	No	No	Yes
Synthesis	No	No	Yes

What are systematic reviews?

‘the most reliable and comprehensive statement about what works’

Systematic reviews involve identifying, synthesising and assessing all available evidence, quantitative and/or qualitative, in order to generate a robust, empirically derived answer to a focused research question.

- van der Knaap, L.M (2008)

How are systematic reviews conducted?

- A systematic review is usually produced by a team rather than an individual, has at least 2 people selecting results to minimise bias, and can take up to 2 years to complete.
- Involves the following steps:

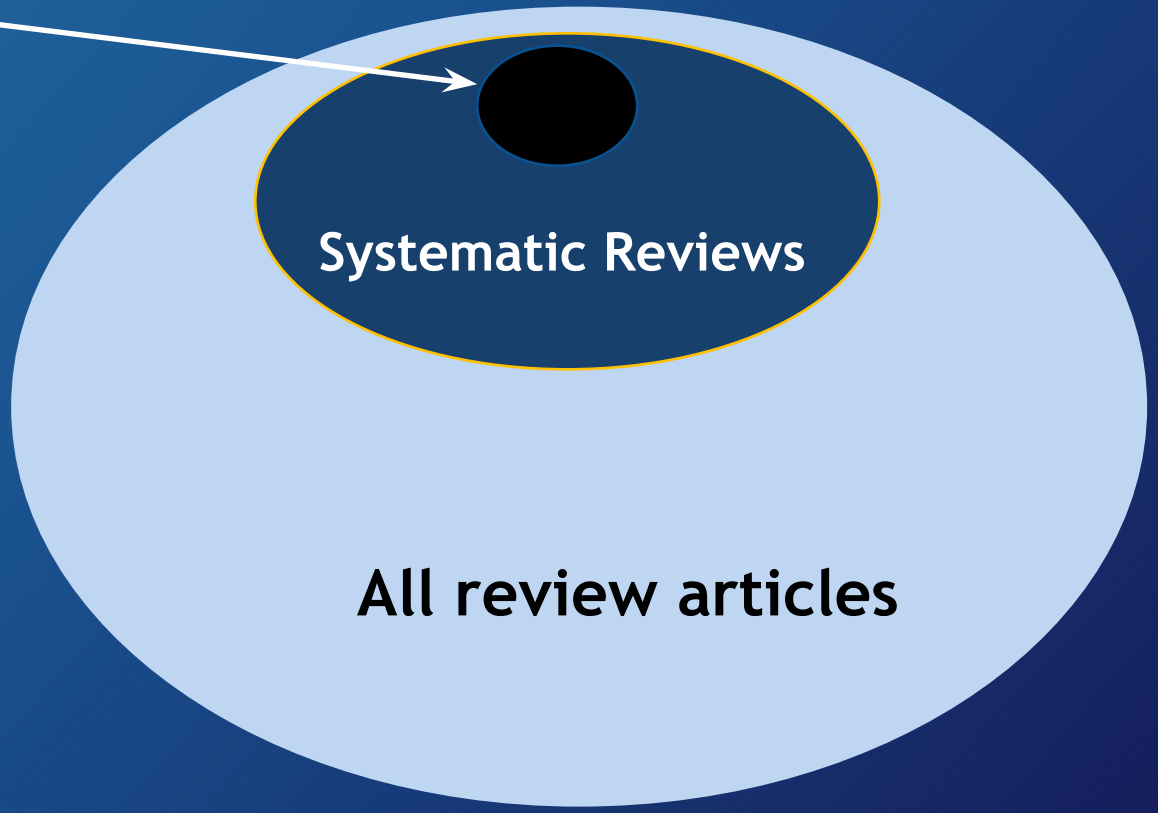
- Research question by considering population(P), intervention (I),outcome (O), and comparator (C)
- Developing protocol that describes definitions, search strings, search strategy, inclusion and exclusion criteria and approach to synthesis
- Systematic search is conducted
- Studies are retrieved and screened (TiAb and full text)
- Appraising the quality of the research included in the review
- Synthesis

What is meta-analysis?

Meta-analysis

A statistical technique for combining effect sizes (impact estimates) into a single average (or sub group) treatment effect

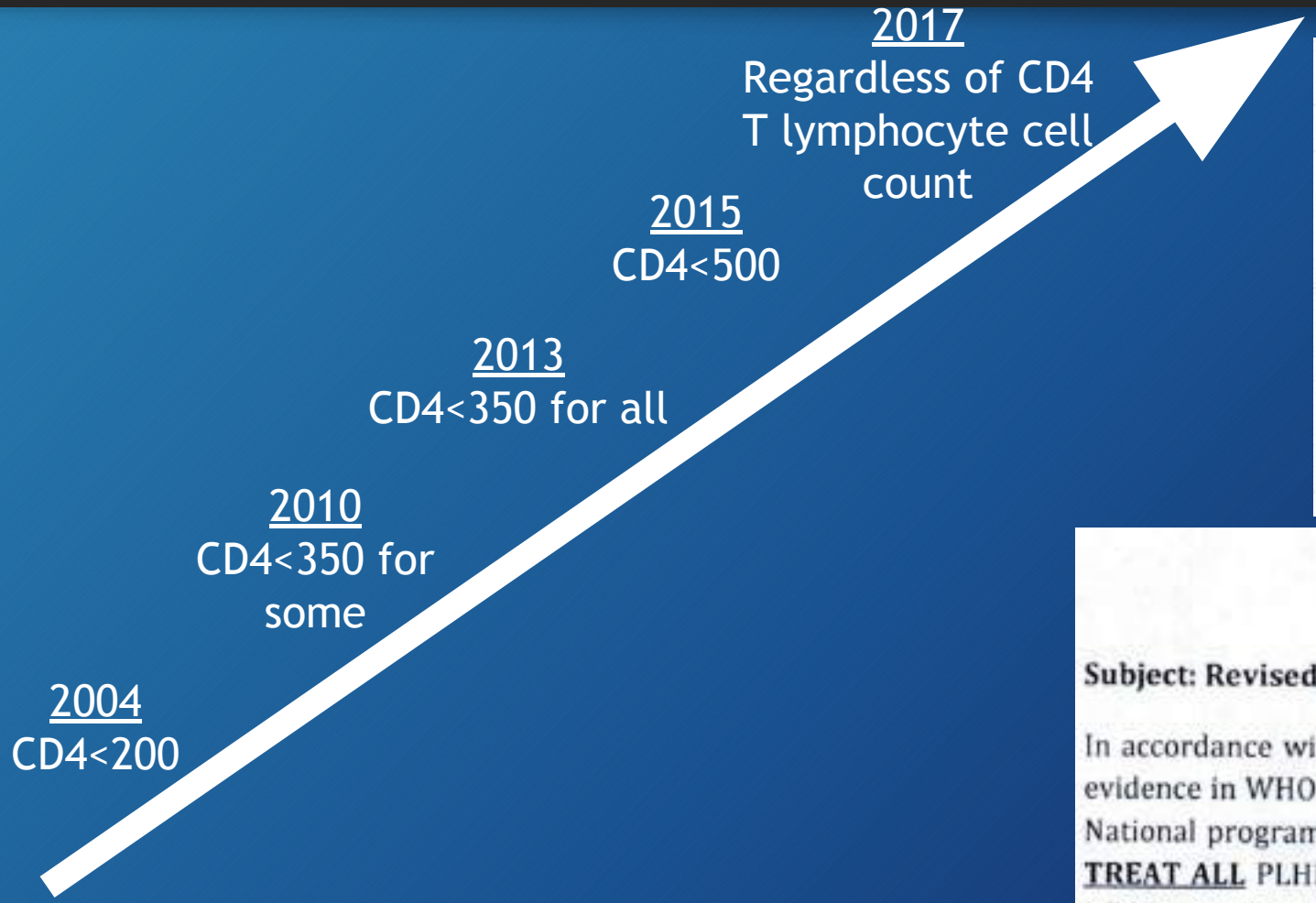
40% of reviews will not have a meta-analysis possible due to heterogeneity



PRENATAL CORTICOSTEROIDS FOR REDUCING MORBIDITY AND MORTALITY AFTER PRETERM BIRTH

In the late 1960s, doctors thought that if you gave a pregnant woman expecting to give birth prematurely a dose of steroids, you could reduce respiratory failure and respiratory illness in the infant. Research involving more than 1,000 pregnant women revealed a clear clinical benefit – if the mother was given steroids, the infant would be less likely to have problems. This could have had a significant positive impact on infant mortality rates, but because the results weren't communicated quickly, it didn't filter into general practice.

Evolution of ART guidelines



The 2013 WHO systematic review found evidence suggesting that early ART initiation (at CD4 count between 350 and 500 cells/mm^3) may reduce the risk of HIV disease progression or death, reduce the risk of being diagnosed with a non-AIDS defining illness and may increase the likelihood of immune recovery. Further, this previous review found that grade 3 or 4 laboratory abnormalities are more often found in people who initiate ART early rather than defer their treatment to CD4 counts <350 cells/ mm^3).

Dated: 05th May, 2017

Office Memorandum

Subject: Revised guidelines on initiation of Antiretroviral Therapy (ART).

In accordance with recommendations of Technical Resource group on ART and review of evidence in WHO 2016 ART Guidelines, the guidelines for initiation of ART in PLHIV under National programme have been revised. As per revised guidelines, it has been decided to **TREAT ALL** PLHIV with Antiretro viral Therapy **regardless of CD4 count, clinical stage, age or population**.

Evidence generation is a continuous process

Cochrane Database Syst Rev.**2000**;(4). Kangaroo mother care to reduce morbidity and mortality in low birthweight infants

3 studies including 1362 infants, No evidence of a difference in infant mortality. KMC appears to reduce severe infant morbidity without any serious deleterious effect reported

Cochrane Database Syst Rev. **2011** Mar 16;(3 Kangaroo mother care to reduce morbidity and mortality in low birthweight infants.

16 studies, including 2518 infants. KMC was associated with a reduction in the risk of mortality. KMC was found to increase some measures of infant growth, breastfeeding, and mother-infant attachment

Cochrane Database Syst Rev. **2014** Apr 22;(4) Kangaroo mother care to reduce morbidity and mortality in low birthweight infants.

18 studies including 2751 infants, fulfill inclusion criteria. KMC was associated with a reduction in the risk of mortality. KMC was found to increase some measures of infant growth, breastfeeding, and mother-infant attachment.

But, Systematic Reviews can also be biased

Review

May 20, 1998

Why Review Articles on the Health Effects of Passive Smoking Reach Different Conclusions

Deborah E. Barnes, MPH; Lisa A. Bero, PhD

≫ Author Affiliations

JAMA. 1998;279(19):1566-1570. doi:10.1001/jama.279.19.1566

Data Synthesis.— A total of 106 reviews were identified. Overall, 37% (39/106) of reviews concluded that passive smoking is not harmful to health; 74% (29/39) of these were written by authors with tobacco industry affiliations. In multiple logistic regression analyses controlling for article quality, peer review status, article topic, and year of publication, the only factor associated with concluding that passive smoking is not harmful was whether an author was affiliated with the tobacco industry (odds ratio, 88.4; 95% confidence interval, 16.4-476.5; *P*<.001).

Objectives

Reviews have various objectives

- Descriptive
  - Document what's been done
  - No synthesis
  - Scoping reviews & systematic maps

- Synthesis
  - "Summing up"
  - Describing patterns (averages, trends, variations) across studies

Review questions (Typology)

What do we know and how do we know it?

Possible topics include

- Rates and trends (e.g., incidence/prevalence, differences over time/place/subgroups)
- Correlates and causes (e.g., risk and protective factors)
- Prevention and treatment (e.g., outcomes, impacts, cost effectiveness, comparative effectiveness)
- Diagnosis (e.g., accuracy of various dx categories/tests)
- Prognosis (e.g., predict validity of categories/tests)
- Methods and measures (e.g., reliability, validity)

Types of reviews (Typology)

Review Type	Aim	Example
Effectiveness	To evaluate the effectiveness of a certain treatment/practice in terms of its impact on outcomes	A systematic review of the effectiveness of interventions to help older people adhere to medication regimes
Implementation	To evaluate the factors that are associated with successful/failure of implementation programs/projects/interventions	Implementation outcomes and strategies for depression interventions in low- and middle-income countries: a systematic review
Experiential (Qualitative)	To investigate the experience or meaningfulness of a particular phenomenon	Children's Experiences of Epilepsy: A Systematic Review of Qualitative Studies

Types of reviews (Typology)

Review Type	Aim	Example
Barriers and facilitators	To identify the factors that are barriers and/or facilitators for access/uptake of a program	Children and health eating: A systematic review of barriers and facilitators
Diagnostic Test Accuracy	To determine how well a diagnostic test works in terms of its sensitivity and specificity for a particular diagnosis	A systematic review of the diagnostic test accuracy of brief cognitive tests to detect amnestic mild cognitive impairment
Etiology and/or Risk	To determine the association between particular exposures/risk factors and outcomes	A systematic review and meta-analysis of risk factors for postherpetic neuralgia

Types of reviews (Typology)

Review Type	Aim	Example
Prevalence and/or Incidence	To determine the prevalence and/or incidence of a certain condition	A systematic review of prevalence studies of gender-based violence in complex emergencies
Psychometric	To evaluate the psychometric properties of a certain test, normally to determine how the reliability and validity of a particular test or assessment	Toward a consensus definition of pathological video-gaming: A systematic review of psychometric assessment tools
Costs/Economic Evaluation	To determine the costs associated with a particular approach/treatment strategy, particularly in terms of cost-effectiveness or benefit.	The Potential Cost-Effectiveness of HIV Vaccines: A Systematic Review

Types of reviews (Typology)

Review Type	Aim	Example
Prognostic	To determine the overall prognosis for a condition, the link between specific prognostic factors and an outcome and/or prognostic/prediction models and prognostic tests	A Systematic Review of Predictions of Survival in Palliative Care: How Accurate Are Clinicians and Who Are the Experts?
Methodology	To examine and investigate current research methods and potentially their impact on research quality	Applying systematic review methods to studies of people's views: an example from public health research
Predictors	To identify the factors associated with a certain condition	Childhood predictors of adult obesity: a systematic review

Types of reviews (Typology)

Review Type		Aim
Expert opinion/policy	To review and synthesize current expert opinion, text or policy on a certain phenomenon	A **systematic review** of national **policies** for the management of persons exposed to tuberculosis

There's more to a systematic review than meta-analysis

- Systematic search
- Systematic screening
- Systematic coding
- Systematic synthesis
- Systematic presentation of results

Not being systematic introduces bias

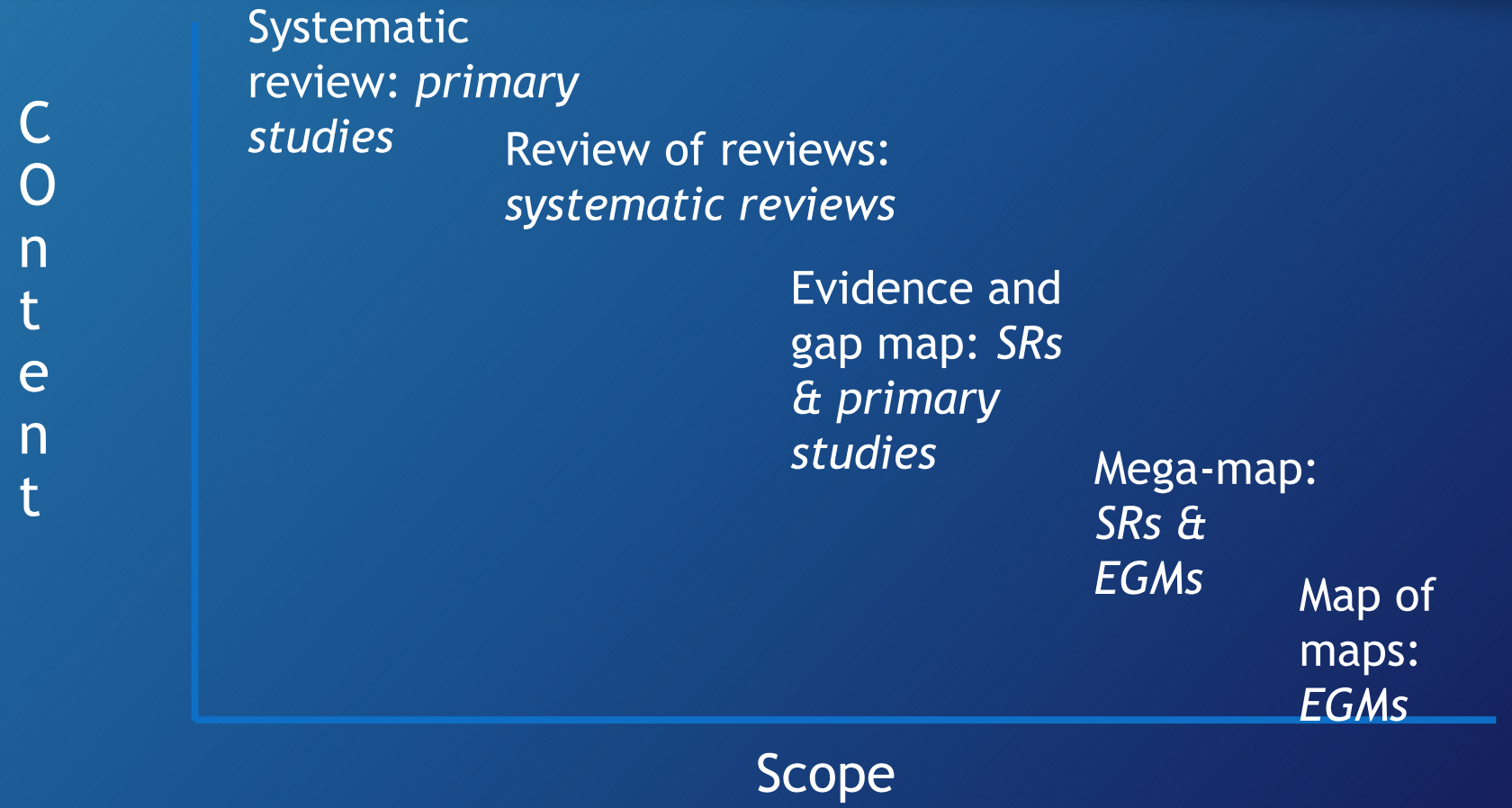
Questions & Methods

Different review questions call for

- Different types of evidence
- Different synthesis methods

“Evidence hierarchies” do not work across questions

Different types of evidence synthesis product: scope versus content



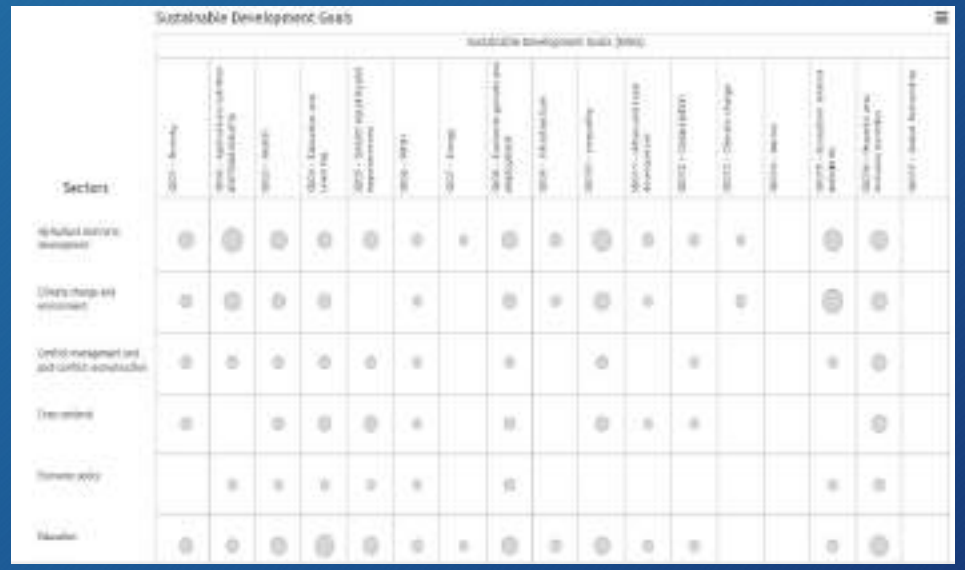
Review of reviews

- We identified 7272 reviews and included 15 in this overview, on: collection of funds (2 reviews), insurance schemes (1 review), purchasing of services (1 review), recipient incentives (6 reviews), and provider incentives (5 reviews).
- The reviews were published between 2008 and 2015; focused on 13 subcategories; and reported results from 276 studies: 115 (42%) randomised trials, 11 (4%)non-randomised trials, 23 (8%) controlled before-after studies, 51 (19%) interrupted time series, 9 (3%) repeated measures, and 67(24%) other non-randomised studies.
- Forty-three per cent (119/276) of the studies included in the reviews took place in low- and middle-income countries.

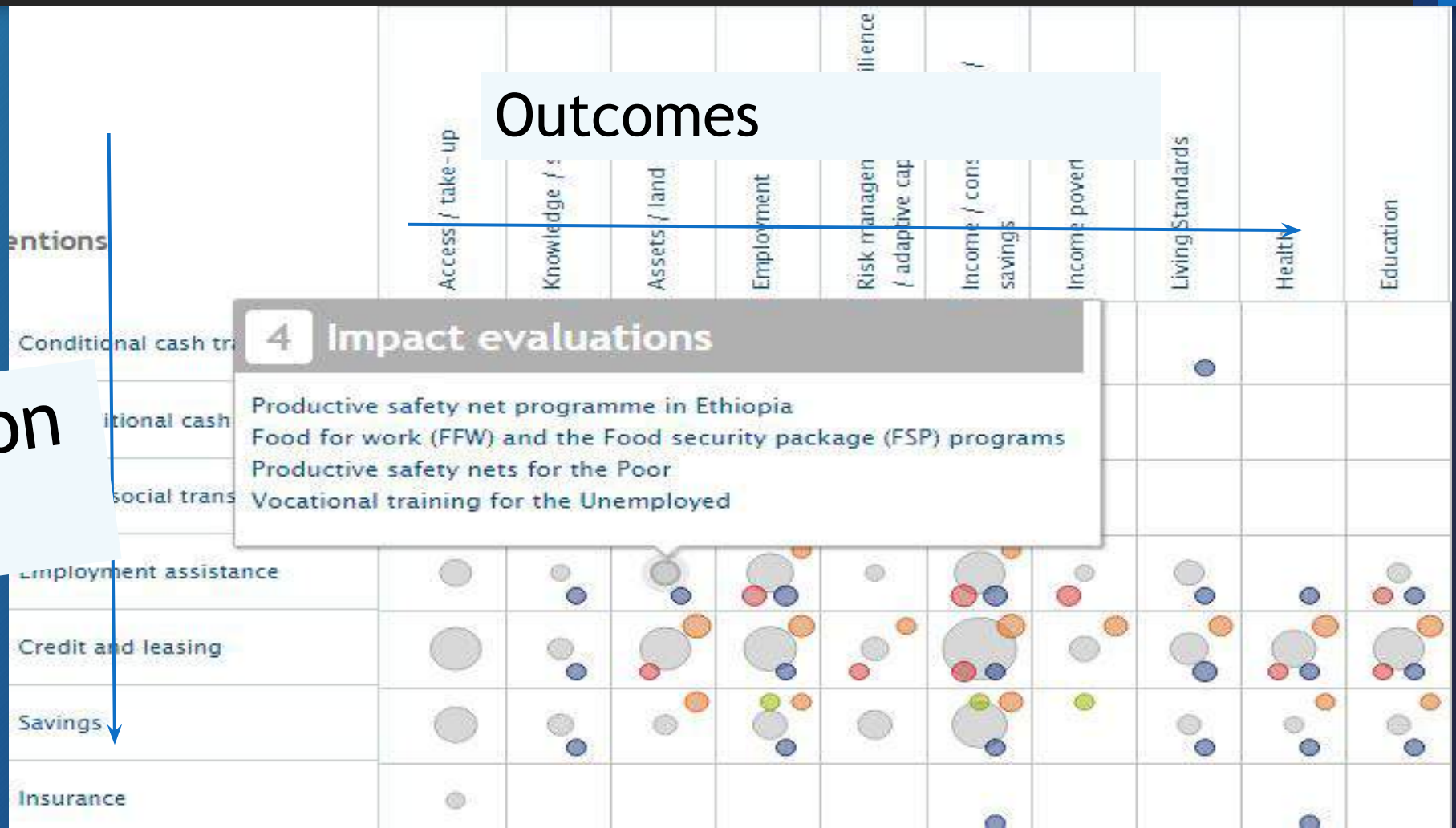
What are evidence and gap maps?

A systematic presentation of all available, relevant evidence for a particular sector or sub-sector.

A typical map is a matrix of intervention categories (rows) and outcome domains (columns).



What are Evidence and Gap Maps?



EGMs are systematic

- Have a pre-specified protocol
- Have a systematic search strategy
- Have clear inclusion and exclusion criteria which are systematically applied
- Systematically code and report all eligible studies
- May include critical appraisal

Construction of the framework is a critical stage: needs stakeholder buy-in

Effectiveness of interventions for people with disabilities in LMICs

Disability Evidence and Gap Map. (This includes 59 systematic reviews and 107 primary studies)

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Outcomes

Health

			Mental health and cognitive development	Access to health services	Immunization	Health check-up	Rehabilitation	Access to assistive devices
		Prevention						
		Rehabilitation						
		Medical care						

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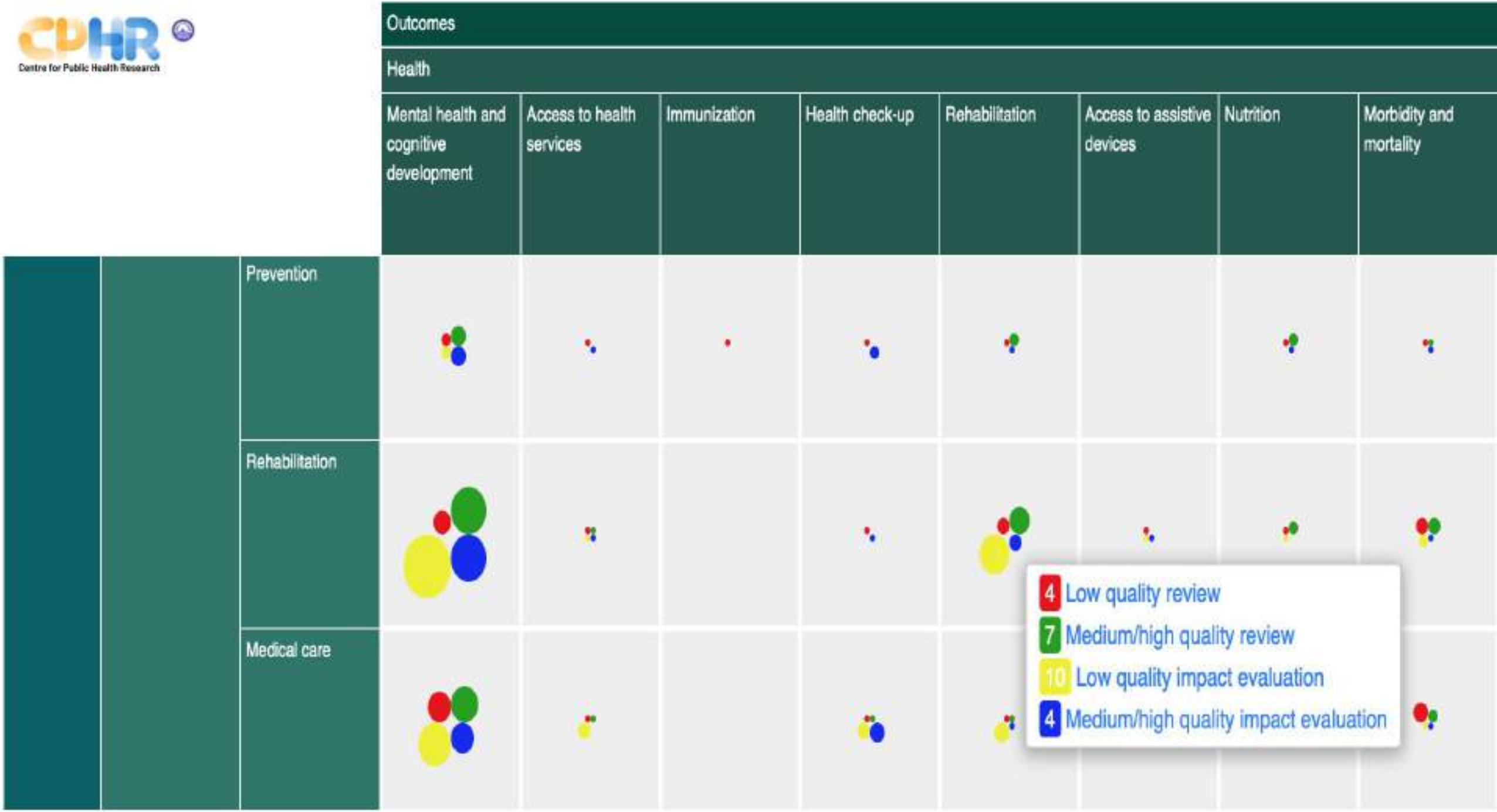


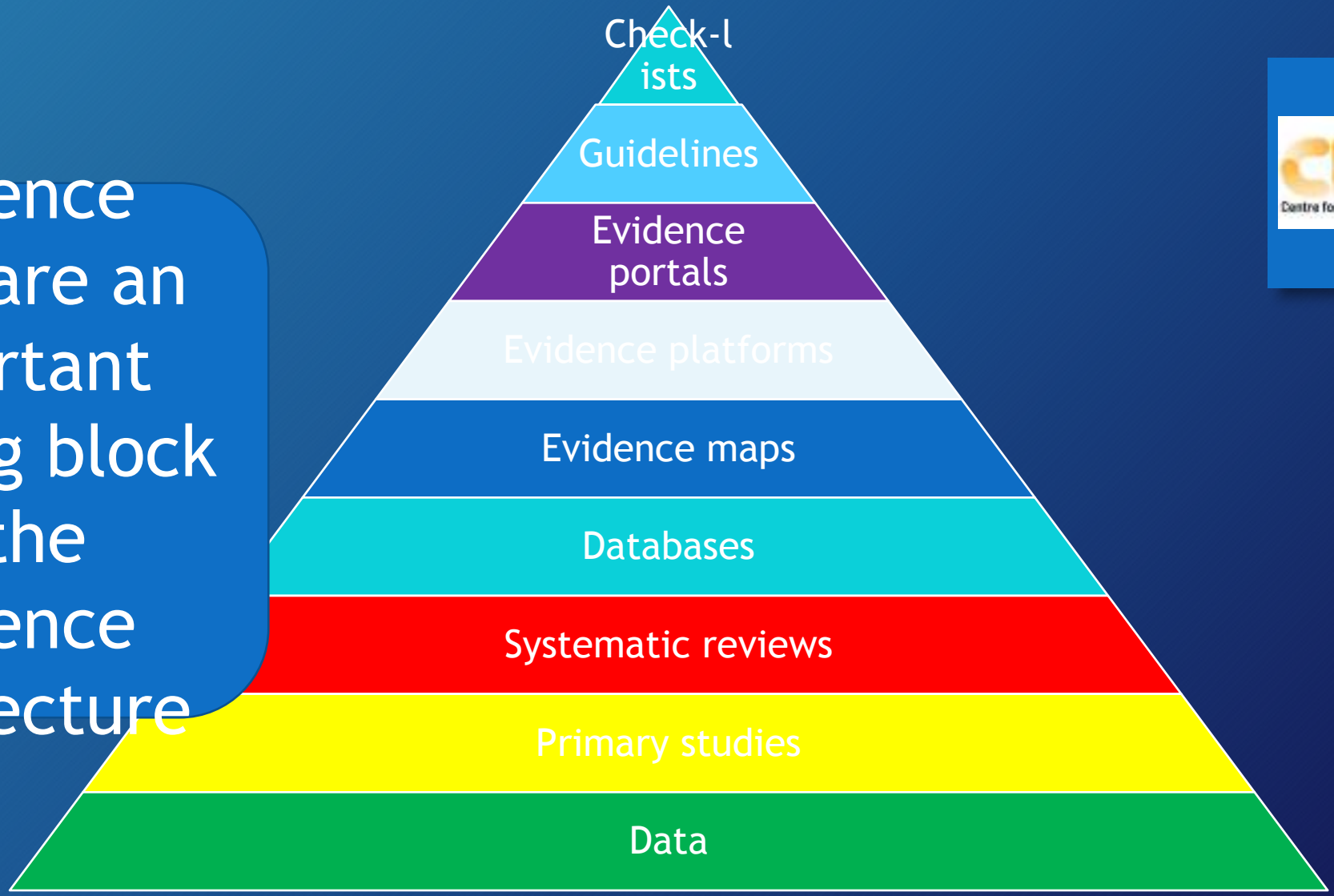
	Systematic review	Evidence and gap map	Comparison
Question setting	Often restricted to a single intervention, and a limited range of outcomes. A PICOS is specified to guide study inclusion criteria.	Broad scope of interventions across a sector or sub-sector, with full range of outcomes across causal chain. A PICOS is specified to guide study inclusion criteria.	**EGMs are broader** in scope than systematic reviews.
Search strategy	A comprehensive and systematic search for primary studies meeting the inclusion criteria (and not exclusion criteria)	A comprehensive and systematic search for systematic reviews and primary studies meeting the inclusion criteria (and not exclusion criteria)	**No difference** in approach. EGMs search for systematic reviews as well as primary studies.
Screening	Identified studies screened against inclusion and exclusion criteria	Identified studies screened against inclusion and exclusion criteria	**No difference** in approach
Coding and data extraction	Coding of study and intervention characteristics, moderators and data extraction of effect sized and related statistics	Coding of a limited number of study and intervention characteristics	EGMs require **coding of less data** than systematic reviews

	Systematic review	Evidence and gap map	Comparison
Critical appraisal	Assessment of quality of included studies using a critical appraisal instrument	Critical appraisal may not be done, but is recommended	Critical appraisal is mandatory for Campbell EGMs
Evidence synthesis	Statistical or narrative synthesis of the evidence	Not done	**EGMs do not synthesize the evidence**
Reporting	Systematic reporting of evidence	Graphical representation of map availability of evidence. Descriptive overview of map.	Systematic reviews summarize what the evidence says. **EGMs only summarize what evidence is available.**
Use	To inform policy and practice	To inform research priorities and research funding	Systematic reviews are to inform policy, and EGMS primarily to inform both research priorities.

Why do we want evidence and gap maps?

- Guide users to available high quality evidence to inform strategy and programme development
- Tell users where there is no high quality evidence (Yes Land and No Land)
- Identify gaps to be filled by evidence synthesis and new studies for researchers and research commissioners – and so more strategic, policy-oriented approach to research agenda
- Identify studies to be used in building the top levels of the evidence architecture

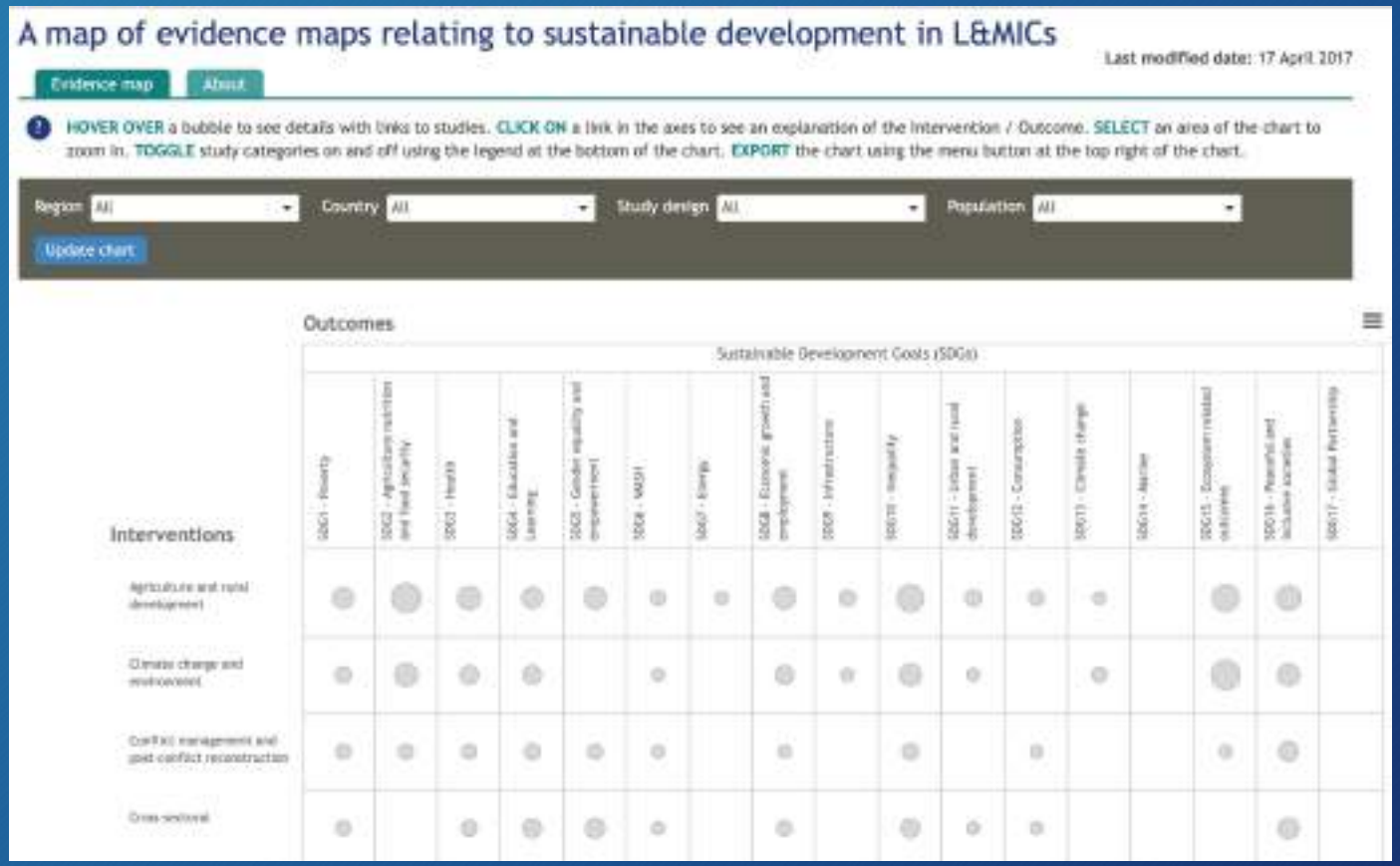
Evidence maps are an important building block in the evidence architecture



Mega-map

https://campbellcollaboration.org/better-evidence/evidence-gap-maps/child-welfare-mega-map.html

Map of Maps



http://gapmaps.3ieimpact.org/evidence-maps/map-evidence-maps-relating-sustainable-development-lmics

COVID-NMA
COVID-19 OPEN LIVING EVIDENCE SYNTHESIS TO INFORM DECISION

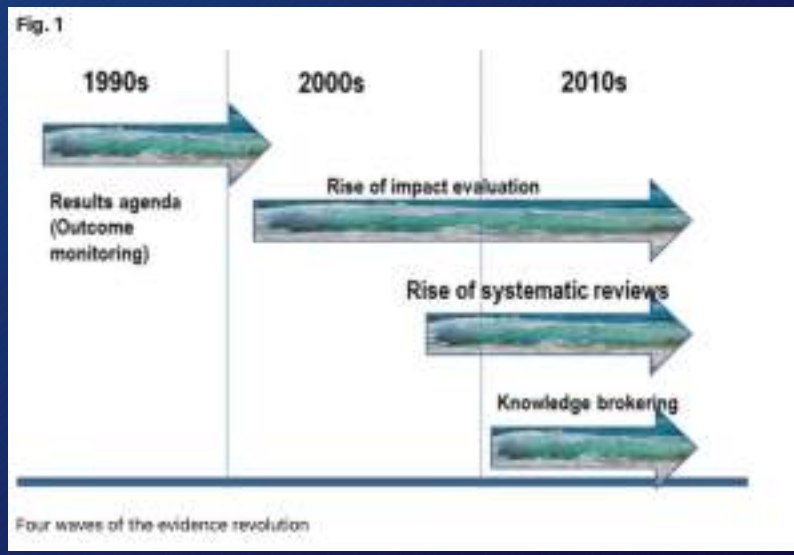
Therapeutics and COVID-19
LIVING GUIDELINE
World Health Organization

NIHR | Innovation Observatory

Epistemonikos

- Living Systematic Reviews, and Living Guidelines
- Horizon Scanning- NIHR Innovation Observatory
- Evidence and Gap Maps (EGMs)
- Epistemonikos database
- Evidence Architecture (Evidence o
- Knowledge brokering
- Newer guidelines (CHEERS 2020 checklist, GRADE for Trial-based and Model Based Economic Evaluations)

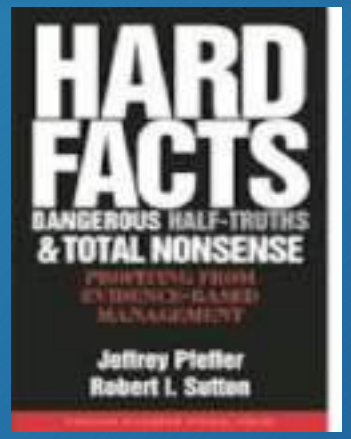
The evidence architecture

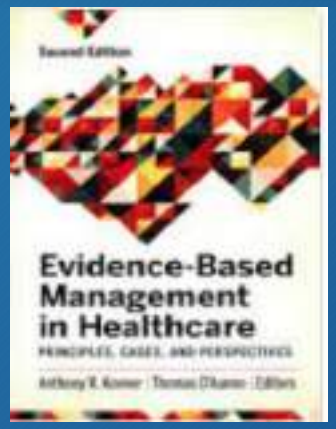


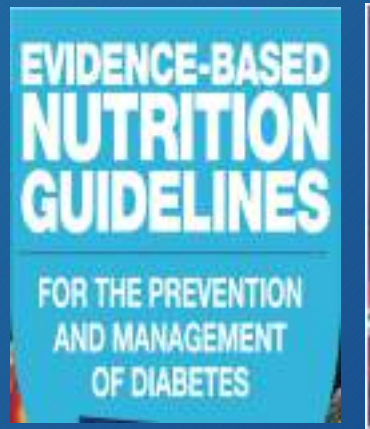
Four waves of the evidence revolution

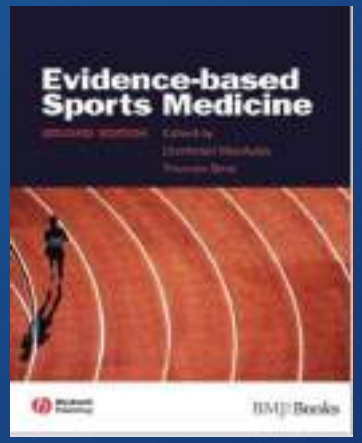
Evidence Revolution

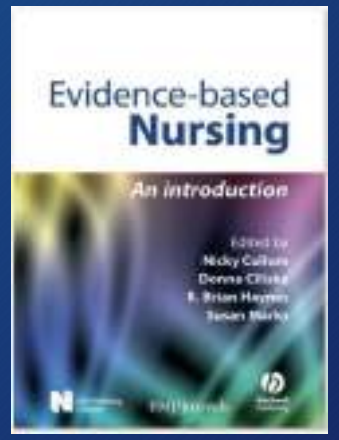
Campbell Collaboration

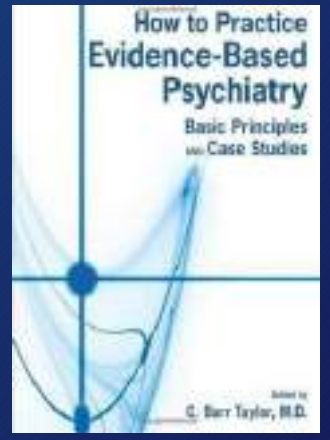


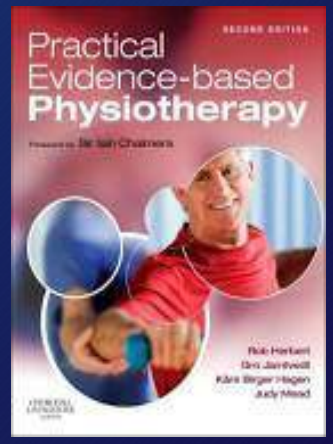












THANK YOU

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