

بِسْمِ اللَّهِ الرَّحْمَنِ
الرَّحِيمِ



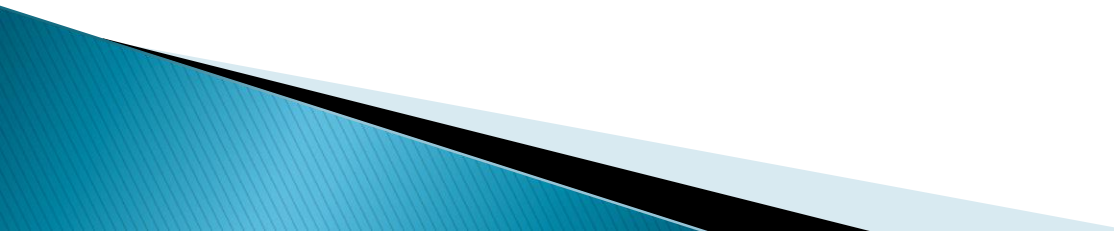
Systematic Reviews

An Overview

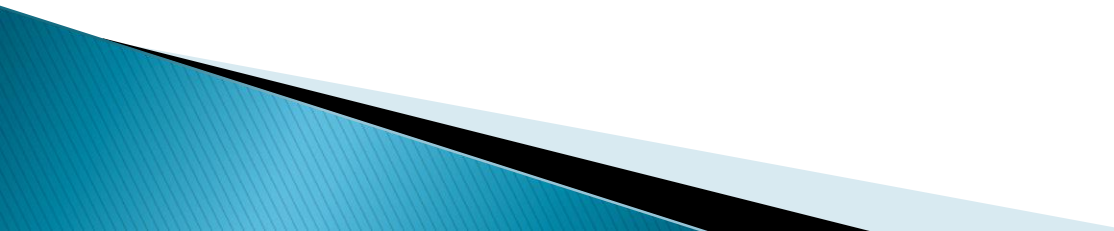
Mohammad Hosein Farzaei Pharm, D, PhD, Postdoc



Article structure

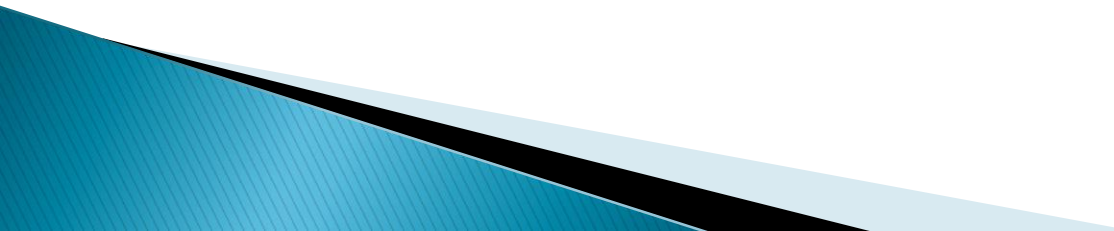
- ▶ Title
 - ▶ Authors name
 - ▶ Affiliation
 - ▶ Corresponding author
 - ▶ Abstract
 - ▶ Keywords
 - ▶ Abbreviation
 - ▶ Graphical abstract
 - ▶ Introduction
 - ▶ Method
 - ▶ Result
 - ▶ Discussion
- 

Article types

- ▶ **Editorial article:**
 - ▶ Individual idea
 - ▶ Mini article
 - ▶ Without abstract, method, result, discussion
 - ▶ Invitation
- 

Article type

- ▶ **Original article**
 - ▶ Or research article
 - ▶ Or research communication

 - ▶ IMRAD – non IMRAD
 - ▶ IMRAD: introduction, method, result, discussion
- 

Article type

- ▶ **Short communication**
- ▶ Or Brief report
- ▶ 2000–2500 words
- ▶ 3–4 pic and tables

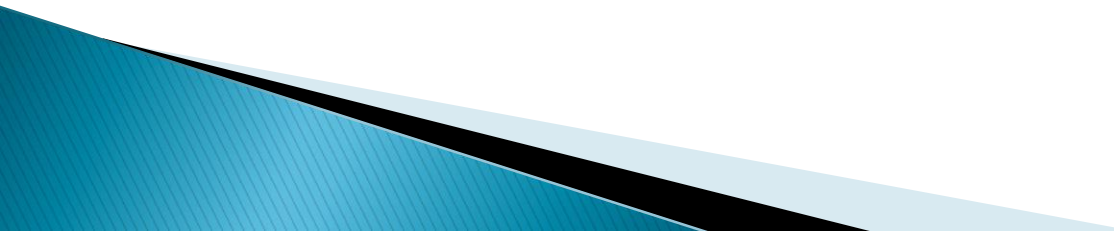
Article type

- ▶ **Case report**
- ▶ A rare symptom or outcome
- ▶ Has not previously reported
- ▶ Commonly without abstract
- ▶

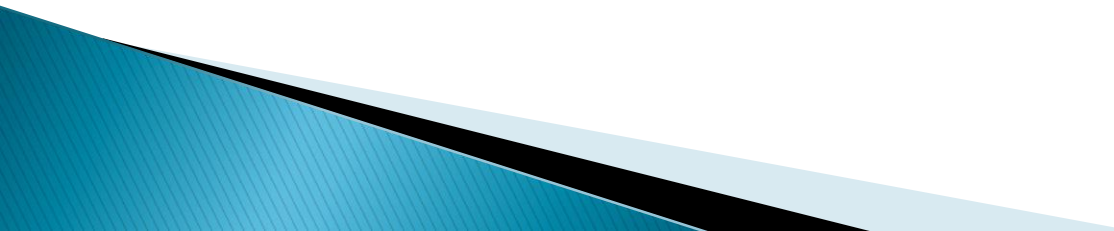
Article type

- ▶ Case series
- ▶ More than 4 case
- ▶ Structure similar to original paper

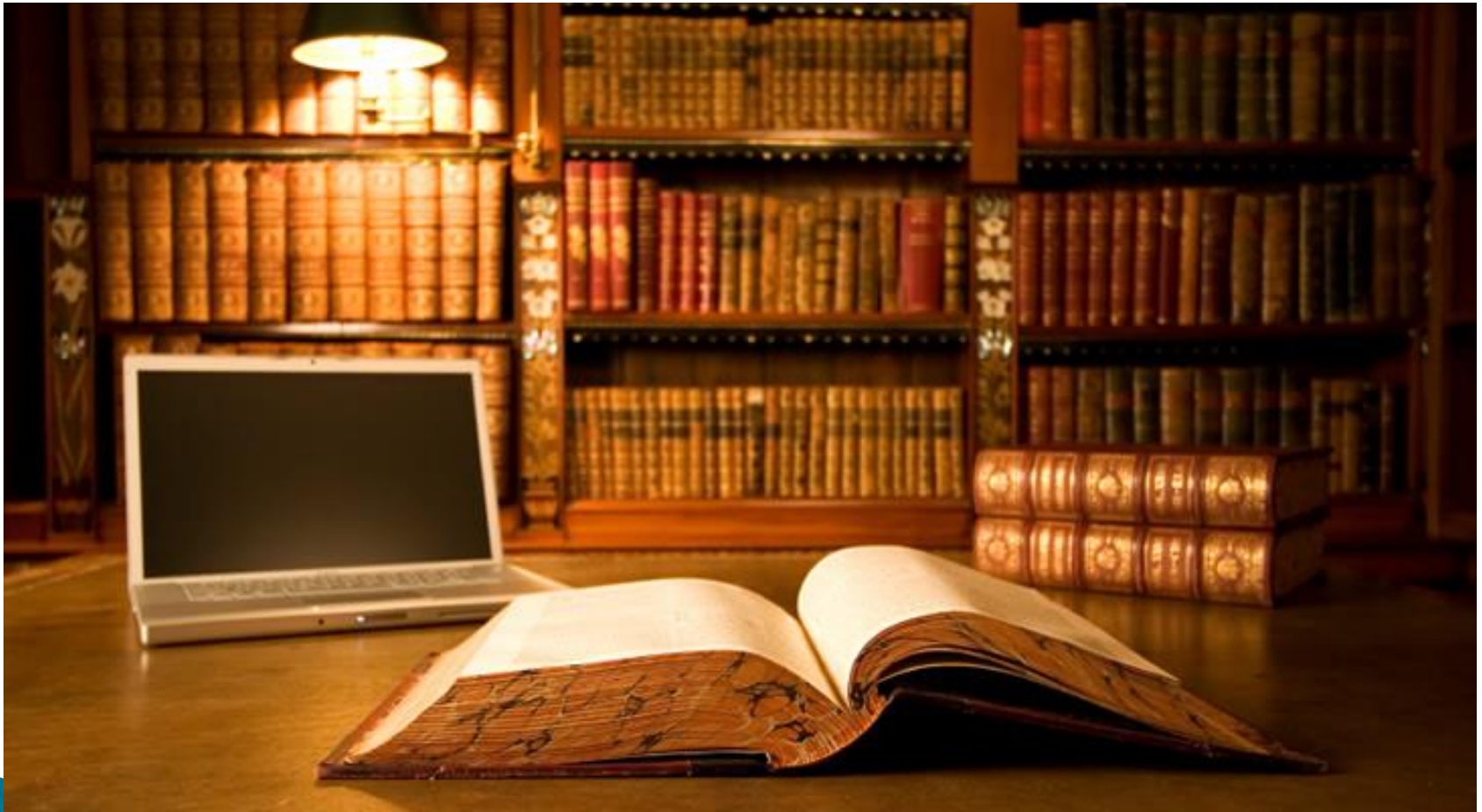
Article type

- ▶ **Letter to editor**
 - ▶ About a published article
 - ▶ Start with: “Dear editor “
 - ▶ Not more than 500 words
 - ▶ No peer-review
 - ▶ A very small research
 - ▶ Case report
- 

Review article types

- ▶ **Invited review**
 - ▶ **Expert person**
 - ▶ **By initial contact – proposal**
 - ▶ **Expert person**
 - ▶ **Submitted review article**
- 

Electronic Database

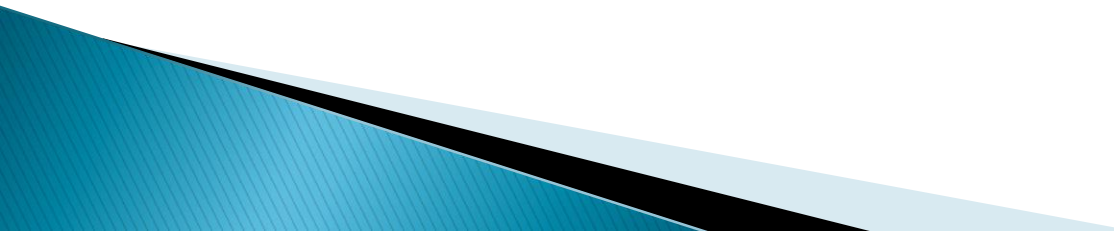


Electronic Database

- ▶ Pubmed
 - ▶ Scopus
 - ▶ Cochrane
 - ▶ www.thecochranelibrary.com
 - ▶ Science Direct
- 

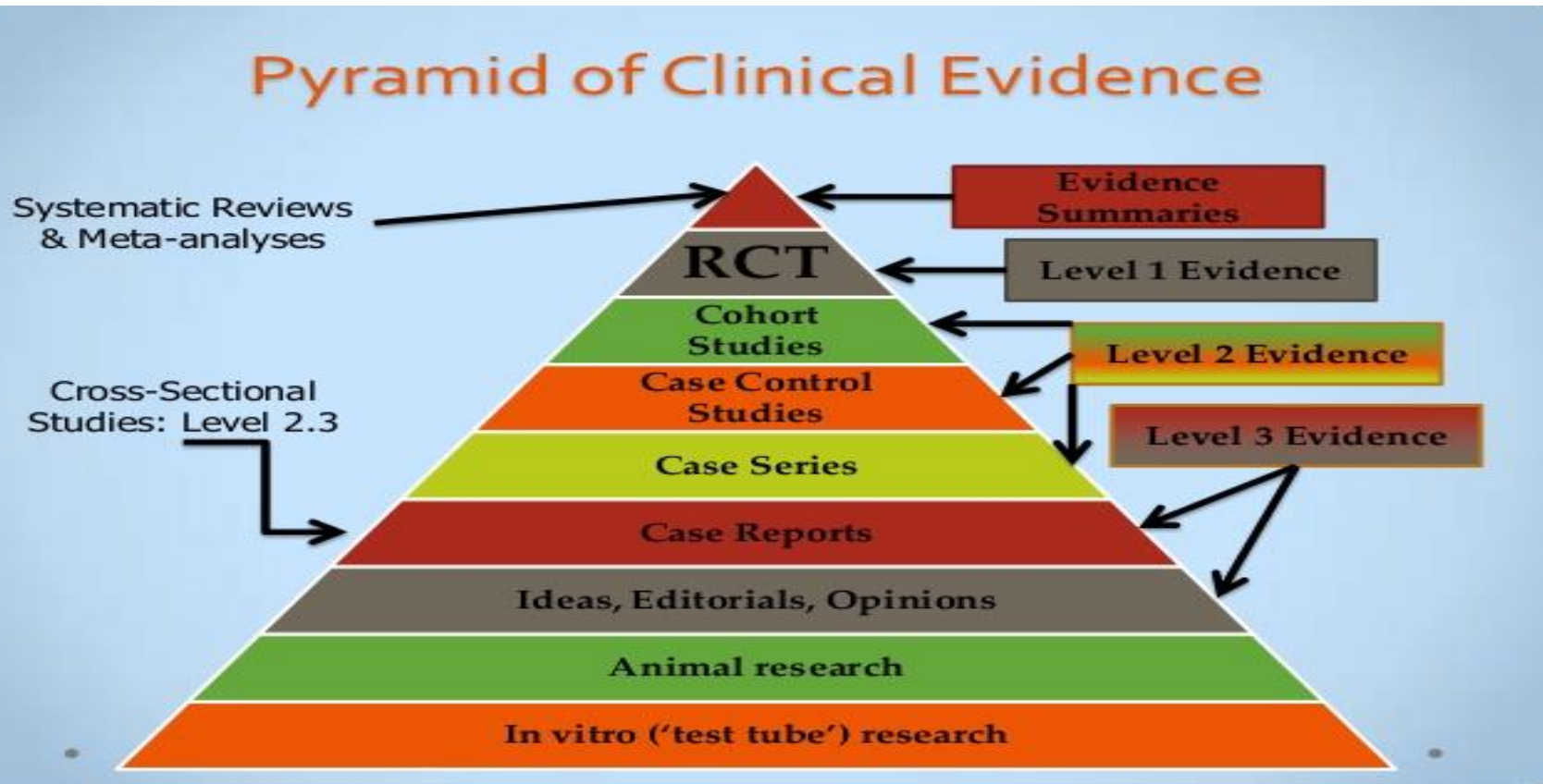
Article type

- ▶ ***Review article***
- ▶ Like:
 - ▶ Current opinions
 - ▶ Current reviews
 - ▶ Expert review

- ▶ **Narrative review**
 - ▶ **(specific)**
 - ▶ Expert persons
 - ▶ Without method, result, discussion
 - ▶ **Comprehensive review**
 - ▶ **CME review**
 - ▶ Without method, result, discussion
 - ▶ **Review**
 - ▶ **Systematic review**
 - ▶ **Meta-analysis**
- 

Systematic review and meta-analysis

- ▶ Higher level of evidence
- ▶ Mostly cited articles



Levels of Evidence

- ***National Guidelines Clearinghouse***
- **Ia** Evidence obtained from meta-analysis or systematic review of randomized controlled trials
- **Ib** Evidence obtained from at least one randomized controlled trial
- **IIa** Evidence obtained from at least one well-designed controlled study without randomization
- **IIb** Evidence obtained from at least one other type of well-designed quasi-experimental study, without randomization
- **III** Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies
- **IV** Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

What is a Systematic Review?

- ▶ “A review that is conducted according to clearly stated, scientific research methods, and is designed to minimize biases and errors inherent to traditional, narrative reviews.”

Margaliot, Zvi, Kevin C. Chung. Systematic Reviews: A Primer for Plastic Surgery Research. PRS Journal. 120/7 (2007)

systemic

throughout the whole system



systematic

methodic or according to a plan

What is the significance of Systematic Reviews?



- ▶ The large amount of medical literature requires clinicians and researchers alike to rely on systematic reviews in order to make an informed decision.
- ▶ Systematic Reviews minimize bias. “A systematic review is a more scientific method of summarizing literature because specific protocols are used to determine which studies will be included in the review.”

Kevin C. Chung, MD, Patricia B. Burns, MPH, H. Myra Kim, ScD, “Clinical Perspective: A Practical Guide to Meta-Analysis.” The Journal of Hand Surgery. Vol. 31A No.10 December 2006. p.1671

Why are Systematic Reviews Necessary?

- ▶ “The volume of published material makes it impractical for an individual clinician to remain up to date on a variety of common conditions. This is further complicated when individual studies report conflicting conclusions, a problem that is prevalent when
- ▶ small patient samples
- ▶ and retrospective designs are used.”

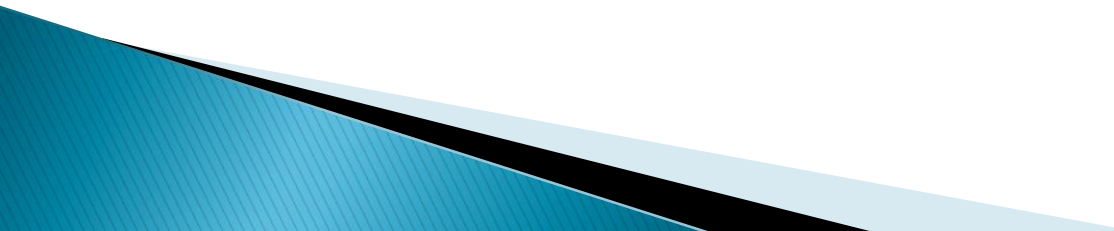
Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research”. PRS Journal. 120/7 (2007) p.1834



Key Characteristics of Systematic Reviews

- ▶ Clearly stated title and objectives
- ▶ Comprehensive strategy to search for relevant studies (unpublished and published)
- ▶ Explicit and justified criteria for the inclusion or exclusion of any study
- ▶ Clear presentation of characteristics of each study included and an analysis of methodological quality
- ▶ Comprehensive list of all studies excluded and justification for exclusion

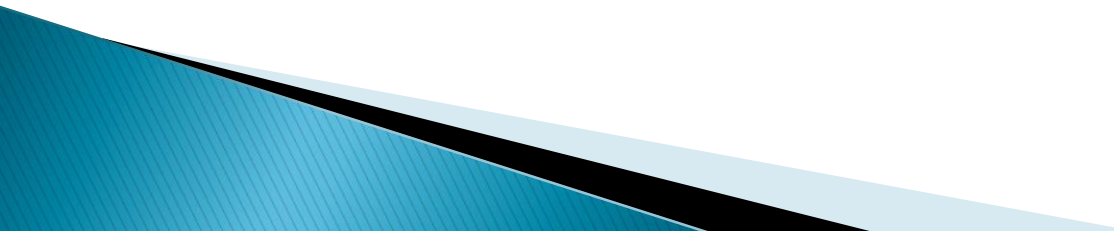
Linda N. Meurer, MD, MPH Department of Family and Community Medicine. "Systematic Synthesis of the Literature: Introduction to Meta-analysis". Power Point Presentation.



Characteristics of Systematic Reviews (cont.)

- ▶ Clear analysis of the results of the eligible studies
 - statistical synthesis of data (meta-analysis) if appropriate and possible;
 - or qualitative synthesis
- ▶ Structured report of the review clearly stating the aims, describing the methods and materials and reporting the results

Linda N. Meurer, MD, MPH Department of Family and Community Medicine. "Systematic Synthesis of the Literature: Introduction to Meta-analysis". Power Point Presentation.



An author of a good Systematic Review...

- ▶ Formulates a Question
- ▶ Conducts a Literature Search
- ▶ Refines the search by applying predetermined inclusion and exclusion criteria
- ▶ Extracts the appropriate data and assess their quality and validity
- ▶ Synthesizes, interprets, and reports data



Systematic review

- ▶ It is not necessary to be expert in the field
- ▶ Students are able to write it
- ▶ High levels of citation

Systematic review

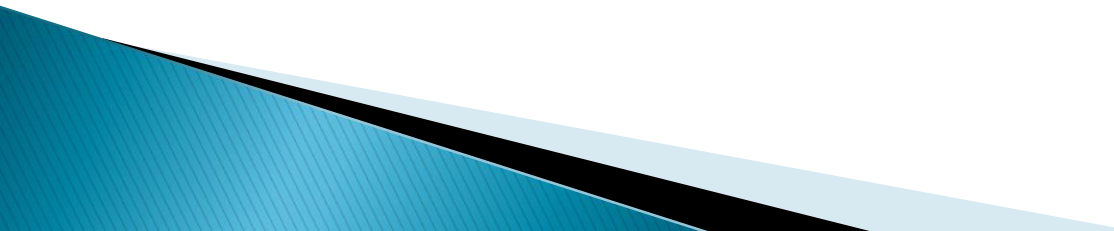
- ▶ Structured abstract
- ▶ Introduction
- ▶ Method
- ▶ Result
- ▶ Discussion
- ▶ Conclusion

Systematic Review Process



Centre for Health Communication and Promotion
<http://www.healthcommunication.org.au/explaining-prisma-reviews.html>

Idea & Title

- ▶ Read, read and read
 - ▶ Brand new articles
 - ▶ Ahead of print (in press)
 - ▶ Discussion of articles
 - ▶ Submit to journals
 - ▶ Choosing an area of focus
 - ▶ Congress and meeting
 - ▶ Interesting topics
 - ▶ Ability and availability (article, collaborator)
- 

Hypothesis

- ▶ “A systematic review should be based on principles of hypothesis testing, and the hypotheses must be conceived a priori.”

Margaliot, Zvi, Kevin C. Chung. Systematic Reviews: A Primer for Plastic Surgery Research. PRS Journal. 120/7 (2007) p. 1836

Focus of the Question

- ▶ The structured question will determine the inclusion and exclusion criteria:
 - What is the population of interest?
 - What are the interventions?
 - What are the outcomes of interest?
 - What study designs are appropriate?

Inclusion/Exclusion Criteria

- ▶ “Once the study question is formalized, the authors must compose a comprehensive list of inclusion and exclusion criteria.”
- ▶ “To avoid selection bias, inclusion and exclusion criteria should be agreed upon and formalized before data extraction and analysis.”

Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1836

Literature Search

► “A comprehensive and reproducible literature search is the foundation of a systematic review.”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1837

Systematic Review Process

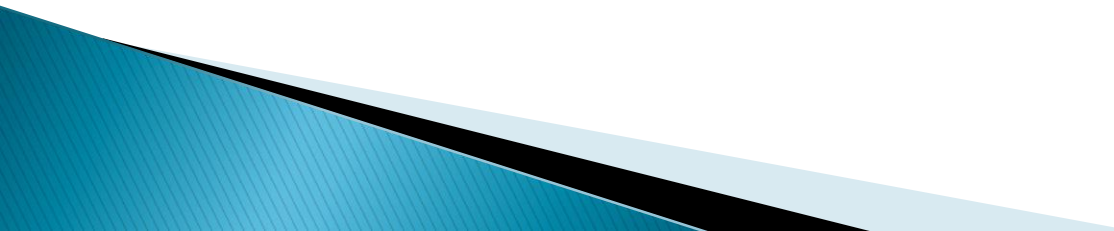


Centre for Health Communication and Promotion
http://www.healthcommunication.org.au/healthcomm/health_comm_what.shtml

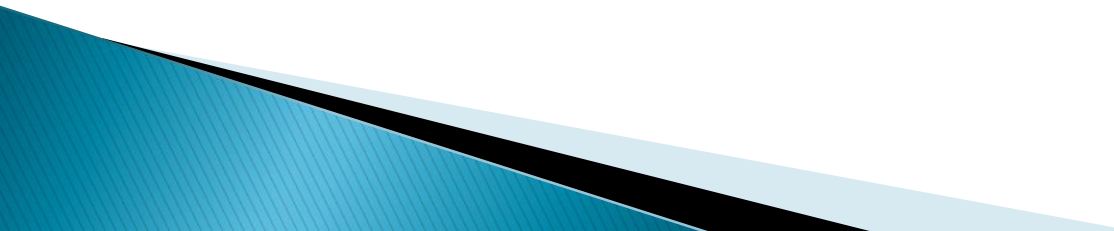
Literature Search Challenges

- ▶ **Database Bias** – “No single database is likely to contain all published studies on a given subject.”
- ▶ **Publication Bias** – selective publication of articles that show positive treatment of effects and statistical significance.
 - Hence, it is important to search for unpublished studies through a manual search of conference proceedings, correspondence with experts, and a search of clinical trials registries.

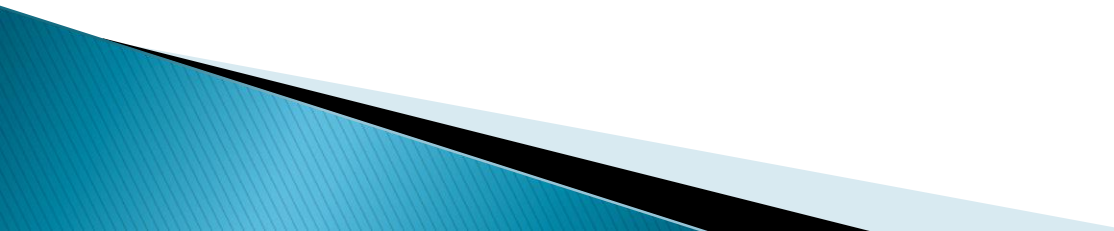
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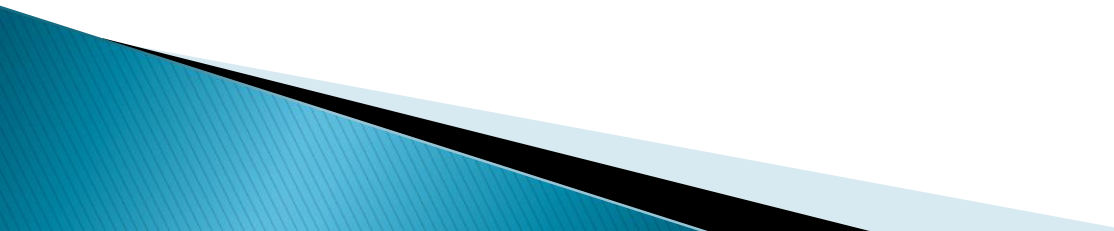
Literature Review Challenges (cont.)

- ▶ **English–language bias** – occurs when reviewers exclude papers published in languages other than English
 - ▶ **Citation bias** – occurs when studies with significant or positive results are referenced in other publications, compared with studies with inconclusive or negative findings
- 

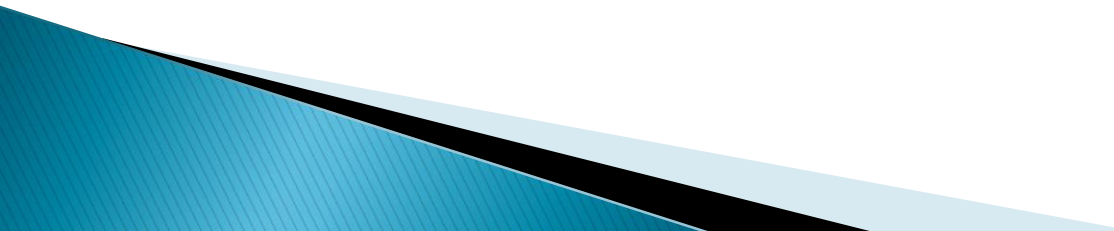
Method

- ▶ Keywords
 - ▶ Electronic Database
 - ▶ Search duration
 - ▶ Inclusion criteria
 - ▶ Exclusion criteria
 - ▶ Availability to full text
 - ▶ 20 –200 \$
- 

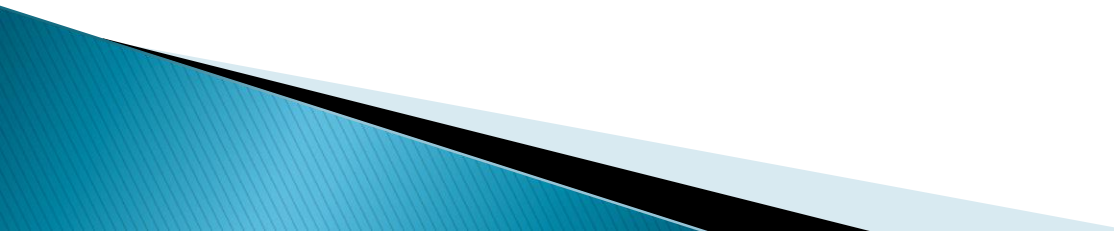
Search in Scientific Databases

- ▶ **Search for novelty**
 - ▶ Example :
 - ▶ Antidepressant effects of medicinal plants and their mechanisms of action
 - ▶ Search by
 - ▶ Antidepressant AND plants
 - ▶ Antidepressant AND herbal medicine
 - ▶ Depression AND herbal medicine
 - ▶ Depression AND plants
- 

Key words

- ▶ Depression, antidepressant
 - ▶ AND
 - ▶ Plant, extract, herb
 - ▶ So we must search in 6 way
 - ▶ Depression AND plant/ Antidepressant AND plant/ Depression AND extract/ Antidepressant AND extract/ Depression AND herb/ Antidepressant AND herb
- 

Key words

- ▶ Synonyms or abbreviations
 - ▶ inflammatory bowel disease
 - ▶ IBD
 - ▶ Irritable bowel syndrome
 - ▶ IBS
- 

Data Collection

- ▶ “The list of data to be extracted should be agreed upon a priori consensus during the design stage of the study.”

Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Data Collection (cont.)

- ▶ Collected data includes:
 - Study characteristics
 - Sample demographics
 - Outcome data

Data Collection (cont.)

- ▶ “It is necessary to design a review-specific data extraction form, so that the same data are extracted from each study and missing data are clearly apparent.”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Data Collection (cont.)

- ▶ “To ensure that data extraction is accurate and reproducible, it should be performed by **at least two independent readers.**”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Quality Assessment

- ▶ “The validity of a systematic review ultimately depends on the **scientific method** of the retrieved studies and the reporting of data.”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Quality Assessment (cont.)

- ▶ Randomized Controlled Trials (RCT):
 - RCT are considered to be more rigorous than observational studies
 - A review based on well-designed RCT will likely be more valid and accurate than a review based on observational studies or case reports

Margaliot, Zvi, Kevin C. Chung. "Systematic Reviews: A Primer for Plastic Surgery Research." PRS Journal. 120/7 (2007) p.1839

Quality Assessment (cont.)

- ▶ “The most common way to assess and report study quality has been using a composite, numerical scoring instrument.”

Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Quality Assessment (cont.)

- ▶ “More than 35 different quality assessment instruments have been published in the literature, and most are designed for randomized clinical trials.”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1839

Jadad score

- ▶ **Randomization (2 points possible)**
 - 1 point if study described as randomized
 - Add 1 point if randomization method described and appropriate (e.g. random numbers generated)
 - Deduct 1 point randomization described and inappropriate
- ▶ **Double-blinding (2 points possible)**
 - 1 point if study described as double-blinded
 - Add 1 point if method of double-blinding described and appropriate
 - Deduct 1 point if double-blinding described and inappropriate
- ▶ **Withdrawals (1 point possible)**
 - Give 1 point for a description of withdrawals and drop-outs

Jadad Score Example

Study	Randomization	Blinding	Drop-out
1	++	+	++
2	+	++	0
3	++	0	+
4	+	++	++
5	0	++	+

Data collection

- ▶ “Once the data have been extracted and their quality and validity assessed, the outcomes of individual studies within a systematic review may be pooled and presented as summary outcome or effect”

Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1840

Data collection (cont.)

- ▶ The authors summarize heterogeneous data qualitatively
 - “Data that are very conflicting and widely variable should not, under most circumstances, be combined numerically.”

Margaliot, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1840

Results

- ▶ Number of retrieved article
- ▶ Results of each eligible article
- ▶ Category of results of eligible article

Search diagram

- ▶ *Based on search strategy*
- ▶ *Eligible articles*

420 potentially relevant reports
identified and screened for
retrieval from electronic search
173 from PubMed
36 from Cochrane library
211 from Scopus

161 excluded because of duplication
35 excluded because they were reviews;
188 reports excluded on basis of title
and abstract

36 reports retrieved

8 reports excluded upon full text search:
 $n = 6$: reported the efficacy of plant
in functional gastrointestinal disorders
rather than IBS
 $n = 3$: reported the efficacy of other
complementary and alternative medicines
in IBS

27 eligible studies included:
 $n = 1$: *in vitro*
 $n = 3$: *in vivo*
 $n = 23$: human studies

When can data in a systematic review be analyzed numerically?

- ▶ When data are NOT too sparse, of too low quality or too heterogeneous
 - For example: the patients, interventions and outcomes in each of the included studies are sufficiently similar

Meta-Analysis

- ▶ “Meta-analysis is a statistical technique for combining the results of independent, but similar, studies to obtain an overall estimate of treatment effect.”

Margalioth, Zvi, Kevin C. Chung. “Systematic Reviews: A Primer for Plastic Surgery Research.” PRS Journal. 120/7 (2007) p.1840

Meta-analysis

- ▶ Meta-analyses are often, but not always, important components of a systematic review procedure.