



Systematic Reviews



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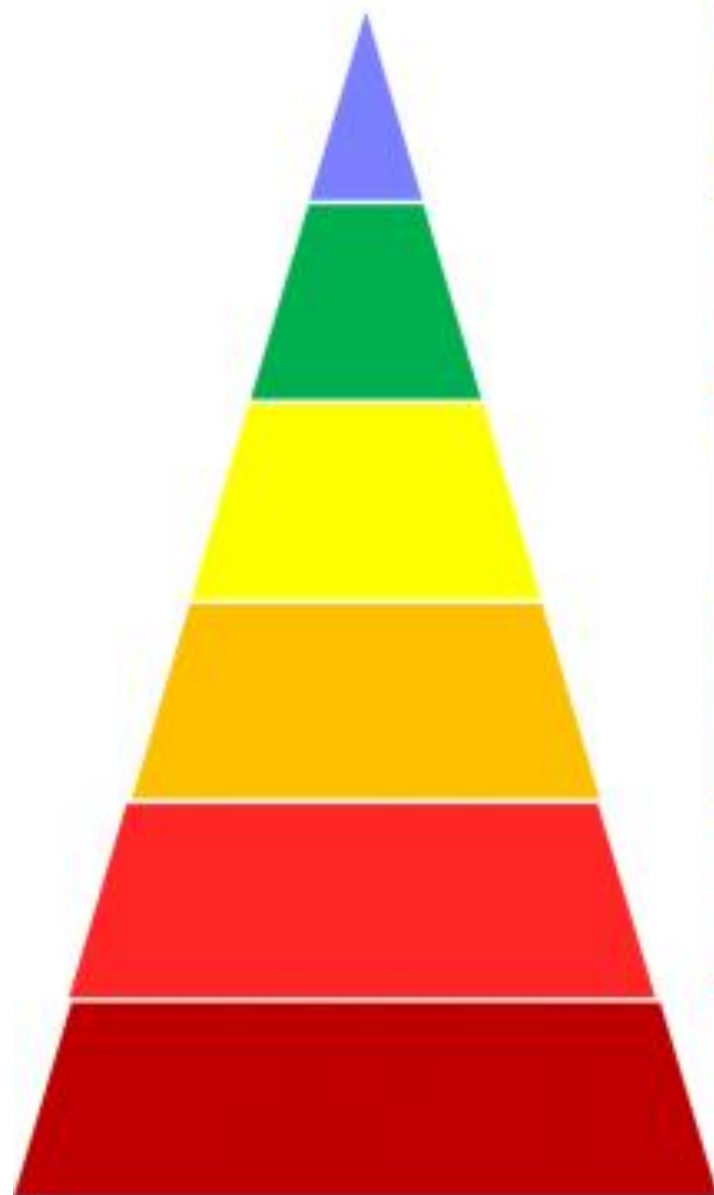
March 2023



● **Aims of this session....**

- Outline what a systematic review is
- Overview of systematic reviews
- Outline of The Cochrane Collaboration
- Role of the HPPH Field
- Function of systematic reviews in informing policy and practice
- Key elements of systematic reviews

Evidence-based Medicine



Evidence level

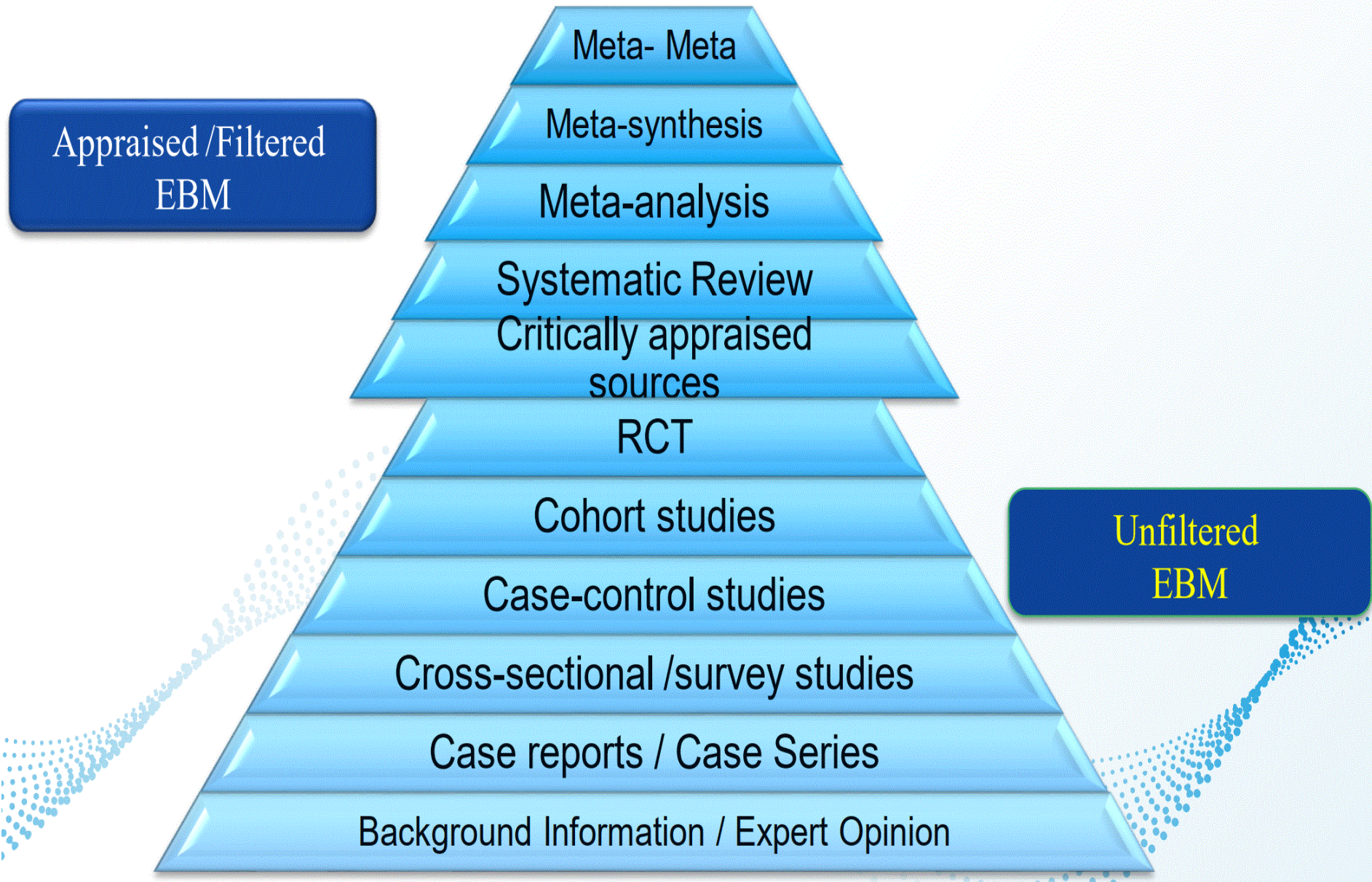
Objectives

Advantages

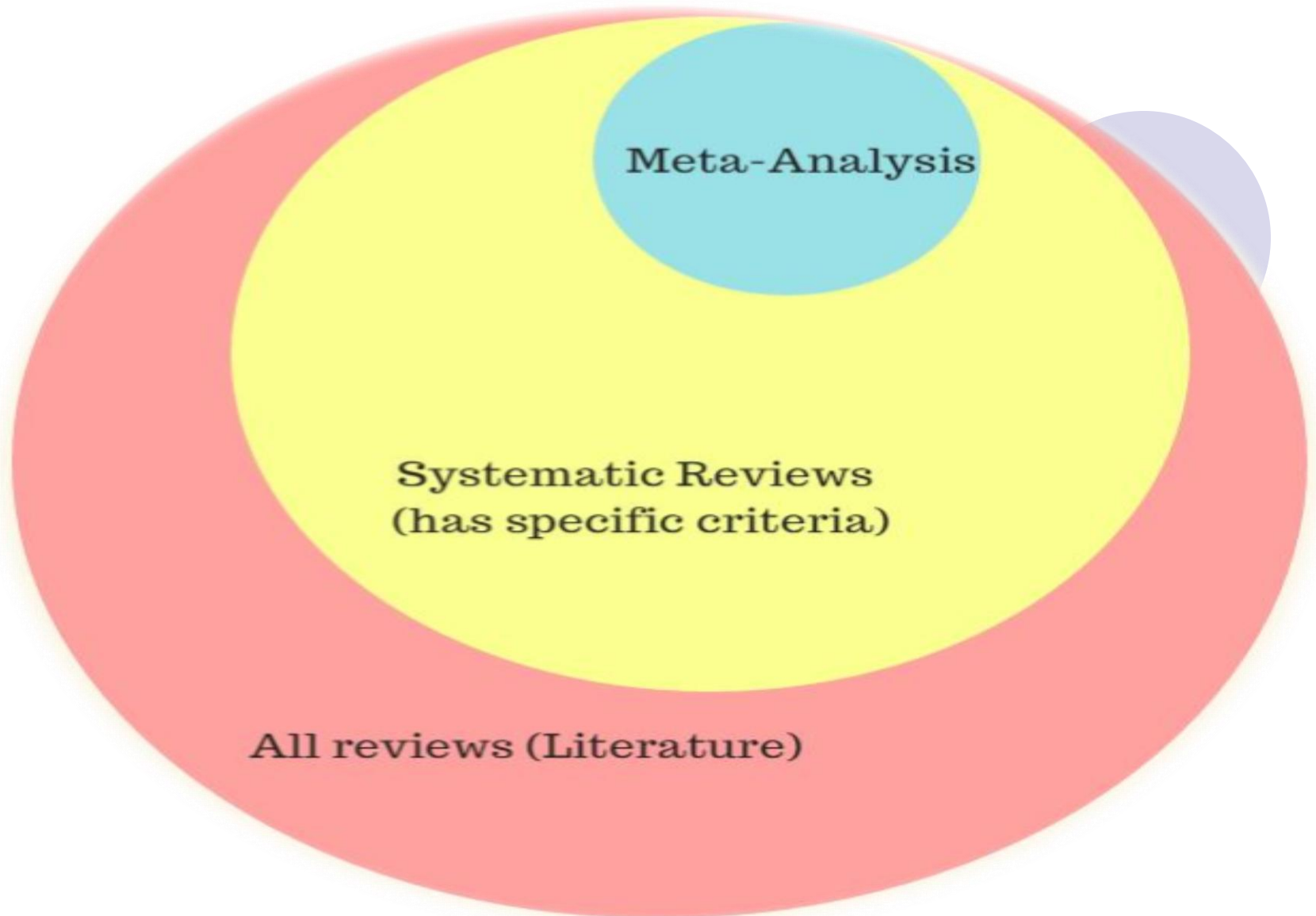
Disadvantages

Meta-analyses and Systematic reviews	Synthesize data from different studies	High quality and critical appraisal	Small amount of studies
Randomized-controlled trials	Reducing bias and confounding	High internal validity	Time, costs and ethical issues
Cohort studies	Observe an homogenous population	Prospective design	Long follow-up
Case-control studies	Study rare conditions	Small sample size	High bias probability
Case series and case reports	Describe a novelty	Peculiarity	Anecdotal
Expert opinion, in-vivo and in-vitro studies	Novel molecule or tool development	High internal validity	Costs and technical issues

The Evidence-Based Medicine Pyramid



Types of reviews



Narrative 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.

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.”



What is a systematic review?

A review of the evidence on a **clearly formulated question** that uses **systematic and explicit methods** to identify, select and **critically appraise** relevant **primary research**, and to **extract** and **analyse data** from the studies that are included in the review*

*Undertaking Systematic Reviews of Research on Effectiveness. CRD's Guidance for those Carrying Out or Commissioning Reviews. CRD Report Number 4 (2nd Edition). NHS Centre for Reviews and Dissemination, University of York. March 2001.

Systematic

vs.

Narrative reviews

- **Scientific approach** to a review article

- **Criteria** determined at outset

Comprehensive search for relevant articles

- Explicit methods of appraisal and synthesis

- **Meta-analysis** may be used to combine data

- Depend on authors' inclination (bias)

- Author gets to pick any criteria

- Search any databases

- Methods not usually specified

- Vote count or narrative summary

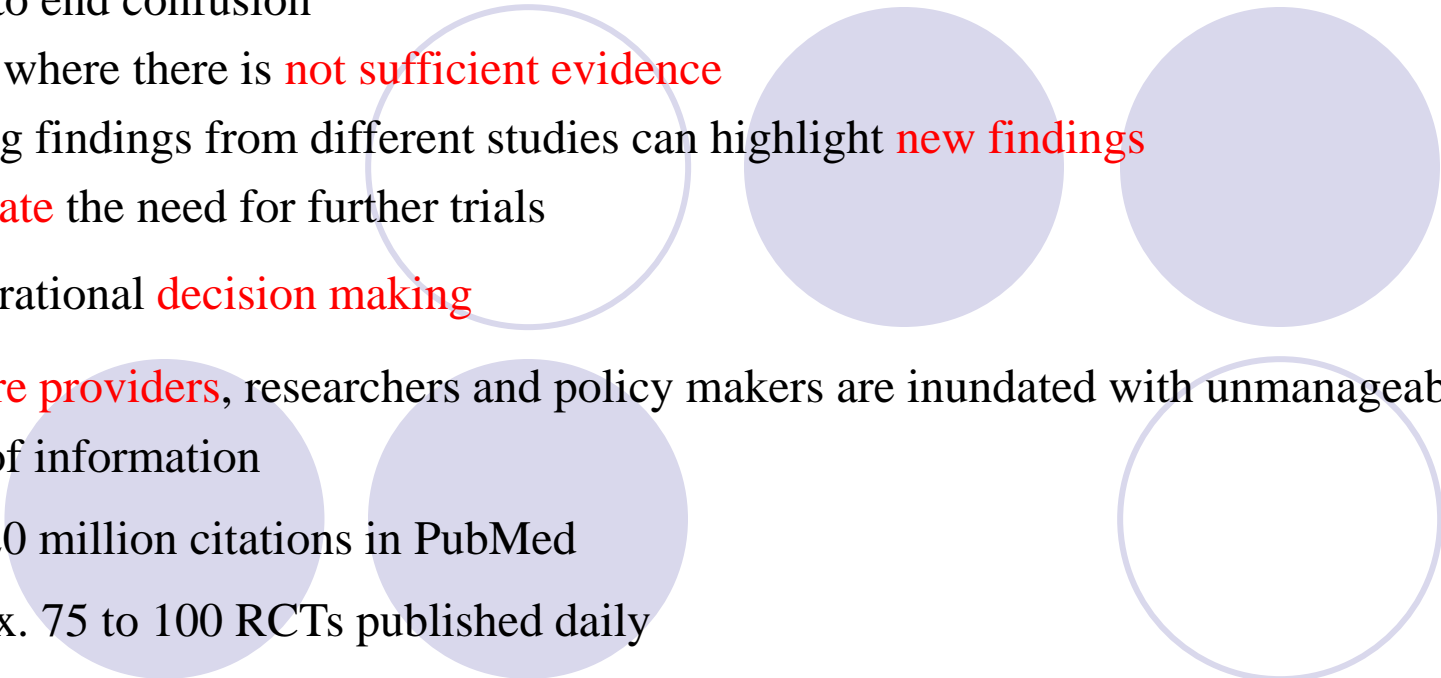
- **Can't replicate review**



Systematic review characteristics

- Reliability
- Sensitivity / Comprehensive coverage of resources
- Specificity /methodological quality

Why we need 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
 - 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 with evidence** accumulating in field and to practice evidence-based medicine
- 

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

Who undertakes systematic reviews?

- **Cochrane**/Campbell Collaboration
- NICE/Regulatory bodies
- Health Technology Assessment
- Academics/researchers/Clinicians
- MSc/PhD students
- Multidisciplinary teams
 - Clinicians
 - Health services researchers
 - Information scientists
 - Statisticians
 - Health Economists
 - Patient and public involvement – particularly for guidelines

The Cochrane Collaboration

International non-profit organisation that **prepares, maintains, and disseminates** systematic up-to-date reviews of **health care interventions**



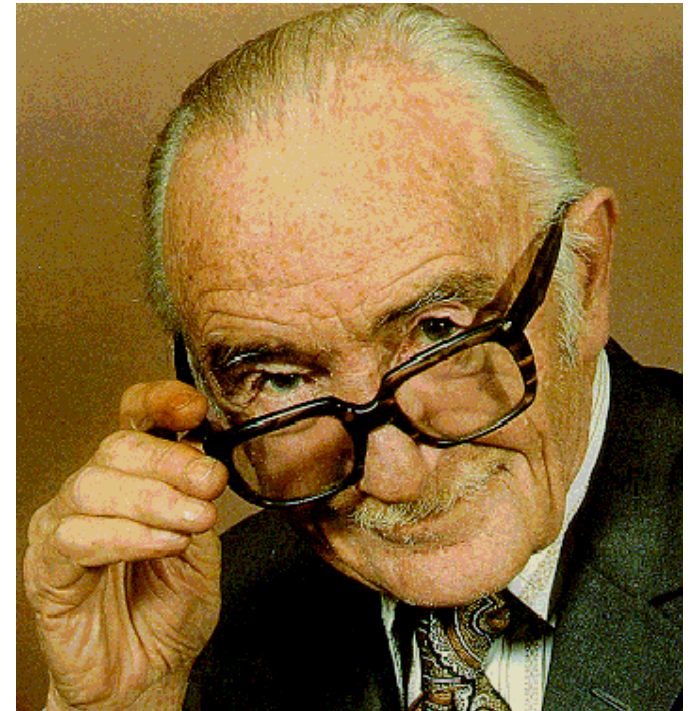
**THE COCHRANE
COLLABORATION®**

Cochrane Collaboration

Named in honour of Archie Cochrane, a British researcher

In 1979:

“It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials”





The Cochrane Library

- **Cochrane Systematic reviews :** Cochrane reviews and protocols
- **Database of Reviews of Effects:** Other systematic reviews appraised by the Centre for Reviews and Dissemination.
- **Cochrane Central Register of Controlled Trials:**
Bibliography of controlled trials (some not indexed in MEDLINE).
- **Health Technology Assessment Database:** HTA reports
- **NHS Economic evaluation database:**
Economic evaluations of health care interventions.

The Cochrane Library

www.thecochranelibrary.com

Wiley InterScience®

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the cochrane library

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SEARCH IN THIS TITLE

 Go

Cochrane Advanced Search

Search History

- Abstract
- Synopsis
- Background
- Objectives
- Criteria for considering studies for this review
- Search strategy for identification of studies
- Methods of the review
- Description of studies
- Methodological quality

Primary prevention for alcohol misuse in young people

DR Foxcroft, D Ireland, DJ Lister-Sharp, G Lowe, R Breen

The Cochrane Database of Systematic Reviews 2004 Issue 4

Copyright © 2004 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

DOI: 10.1002/14651858.CD003024 This version first published online: 22 July 2002 in Issue 3, 2002

Date of Most Recent Substantive Amendment: 29 May 2002

This record should be cited as: Foxcroft DR, Ireland D, Lister-Sharp DJ, Lowe G, Breen R. Primary prevention for alcohol misuse in young people. *The Cochrane Database of Systematic Reviews* 2004, Issue 4. DOI: 10.1002/14651858.CD003024

Cochrane HPPH Field



- Represent the **needs** and **interests** of those in health promotion and public health in Cochrane matters
- Represent Cochrane in health promotion and public health forums
- In transition from Field to Review Group
 - Will edit PH reviews for the Cochrane Library

Collaborative Review Groups (50)

- Produce **systematic reviews** relevant to a particular **disease or health issue** for inclusion in the Cochrane Library
- Examples
 - Airways Group
 - Drug and Alcohol Group
 - Heart Group
 - Injuries Group
 - Skin Group
 - Pregnancy and Childbirth Group
 - Stroke Group
 - Breast Cancer Group

Methods Groups (12)

- Provide advice and support in the development of the methods of systematic reviews:
- Examples
 - Non-Randomised Studies
 - Screening and Diagnostic Tests
 - Empirical Methodological Studies
 - Qualitative Methods

Cochrane Centres (14)

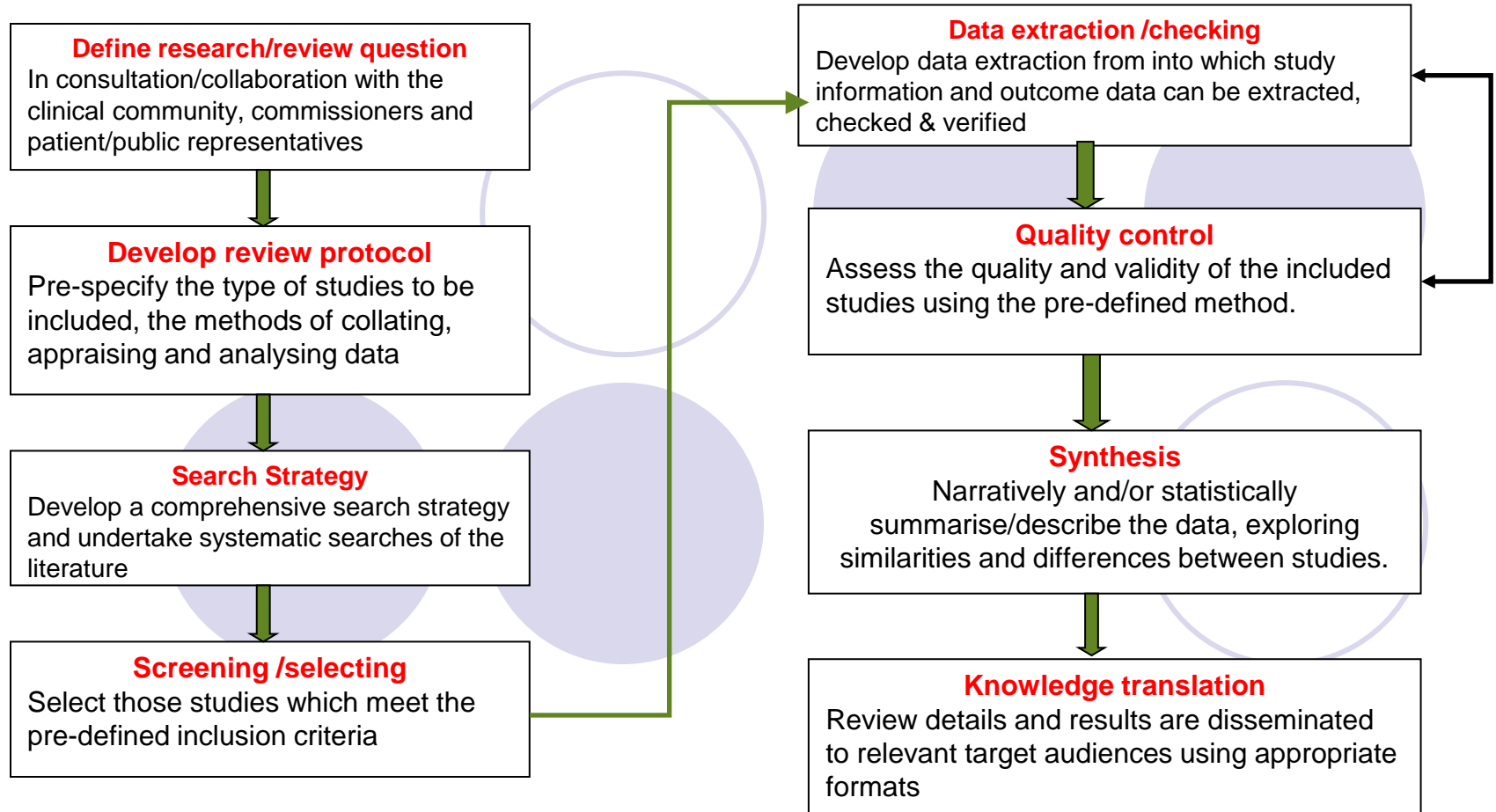
- Work to assist all Cochrane entities within a specific **geographical area**
- Examples
 - Australasian Cochrane Centre (at Monash)
 - South African Cochrane Centre
 - Italian Cochrane Centre
 - Chinese Cochrane Centre



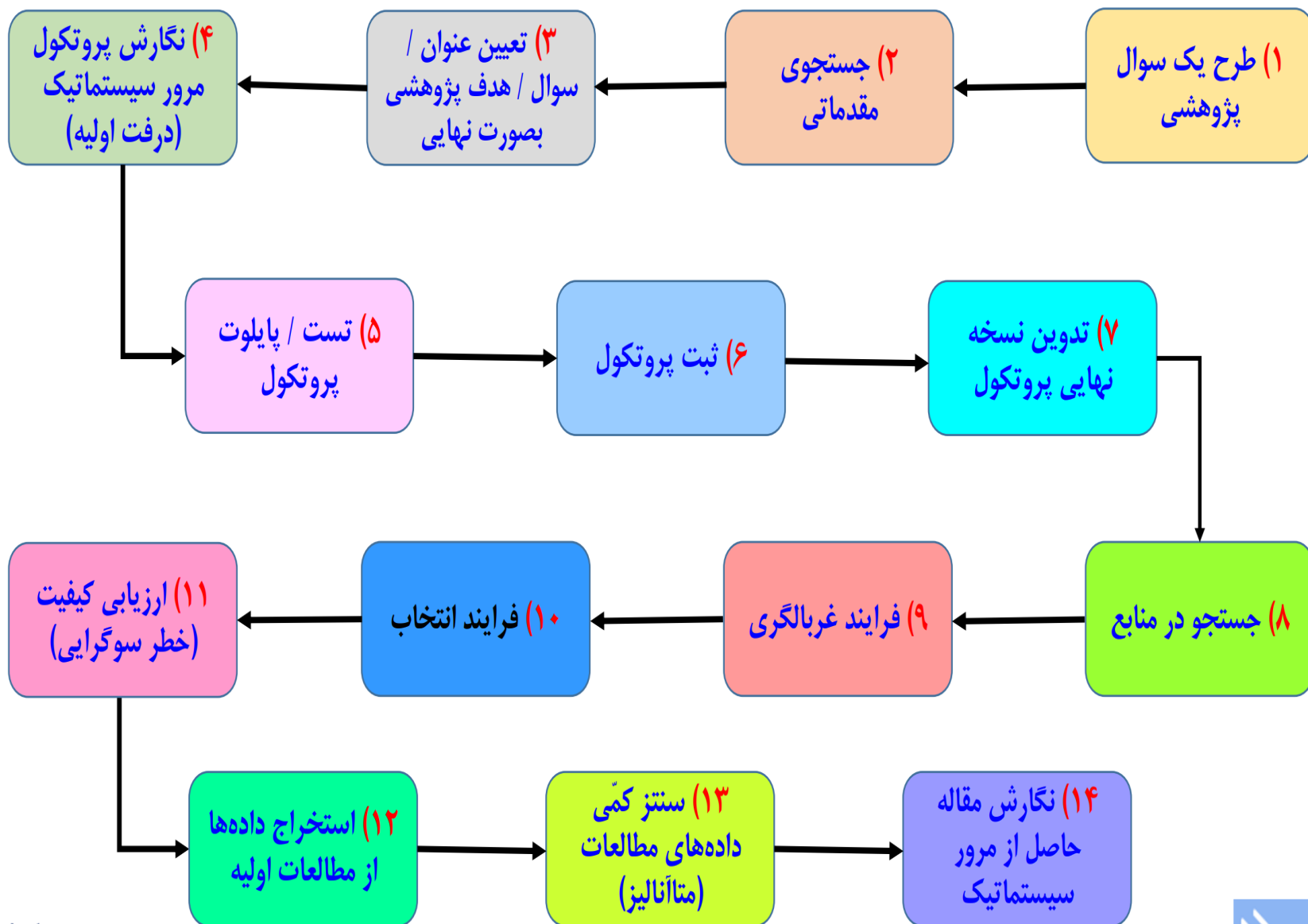
Cochrane Fields/Networks (9)

- Represent an area of interest which spans a number of health problems - and hence a number of Review Groups
- Examples
 - Health Promotion and Public Health Field
 - Primary Health Care Field
 - Cancer Network
 - Child Health Field

Key Stages in a Systematic Review- the process



گامهای اصلی یک مطالعه مرور سیستماتیک و متاآنالیز



Challenging Key Stages in a Systematic Review



1. Formulate the question (Narrow, novel, correlated with title, objective)
2. Comprehensive search strategy (three type of searches, inclusion criteria)
3. Methodological Quality control (Specific knowledge)
4. Metanalysis plan (Interpretation and diagnosis)

Different type of systematic review:

- 1. Systematic + Metanalysis
- 2. Only Metanalysis (Product of secondary study, insufficient search and quality assessment)
- 3. Only systematic (Justification, insufficient studies, high heterogeneous)



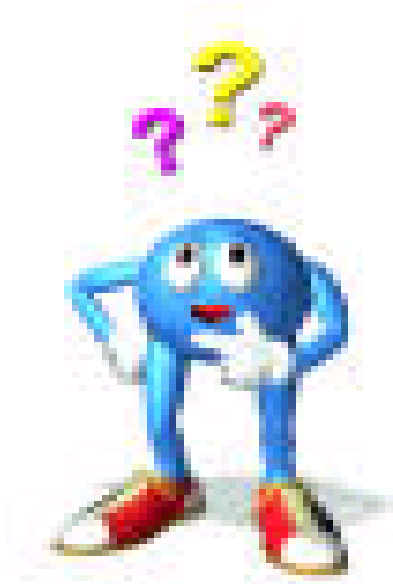
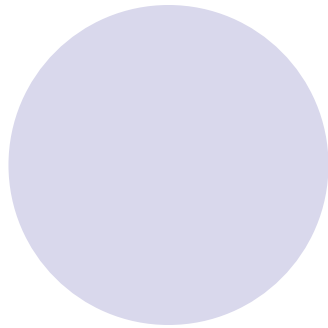
Key elements of a systematic review

Structured, systematic process involving several steps :

1. Formulate the question
2. Plan the review or develop protocol
3. Comprehensive search
4. Screening /selecting
5. Critical appraisal of data
6. Synthesis of data (may include meta-analysis)
7. Interpretation of results

All steps described explicitly in the review

Asking an answerable question





What is Questions of interest

1. What question will be answered
2. Primary (1,2) or secondary objective (2,4)
3. Title/objective/protocol

Main characteristics related research question:

- 1. FINER (Feasible, Interesting, Novel, Ethical, and Relevant)
- 2. Narrow, specific and focused (quality assessment, heterogenies, trade off)
- 3. Formulated question
- 4. Preliminary search

- Examples:
- 1. The prevalence of HIV among women: systematic analysis and metanalysis
- 2. Estimating the association between HIV and Sexual Behaviors Among the US Transgender Population: A Systematic Review and Meta-Analysis, 2006–2017
- (x and y pattern, primary objective)

- 3. Prevalence and factors associated with HIV among women in China: systematic analysis and metanalysis.
- 4. effect of theory –based models intervention on improving quality of life among pregnant women: systematic and metanalysis
- ** Location/justification in introduction

- 5. Association of Nitrate and Nitrite with digestive cancers: systematic and metanalysis
- 6. Effect of health promotion model on improving quality of life among pregnant women: systematic and metanalysis of Double-Blind Randomized Controlled Trial
- ** (study design on narrowing/outcomes)

3. Formulated question

EFFECTIVENESS

A description of the populations

P

An identified intervention

I

An explicit comparison

C

Relevant outcomes

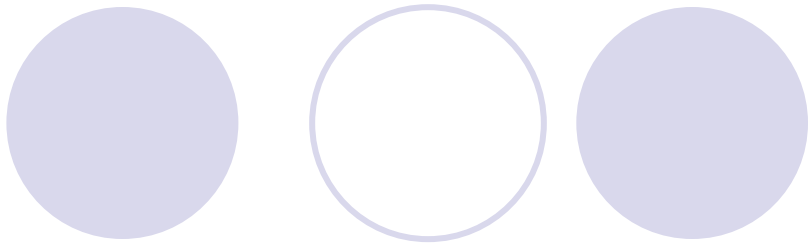
O

The PICO(T or S) chart

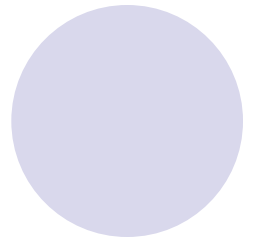
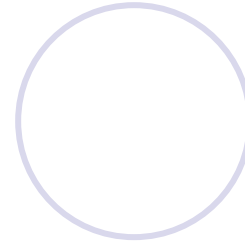
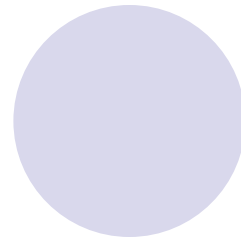
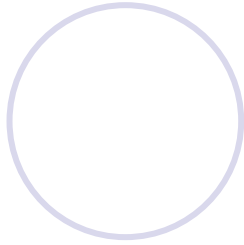
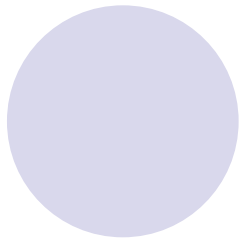
Problem, population	Intervention	Comparison (optional/3 groups)	Outcome	Types of studies
Young people under 25 years of age	a) Television b) Radio c) Newspapers d) Bill boards e) Posters f) Leaflets g) Booklets	a) School-based interventions b) No intervention	a) objective measures of smoking (saliva thiocyanate levels, alveolar CO) b) self-reported smoking behaviour c) Intermediate measures (intentions, attitude, knowledge, skills) d) Media reach	a) RCT b) Controlled before and after studies c) Time series designs



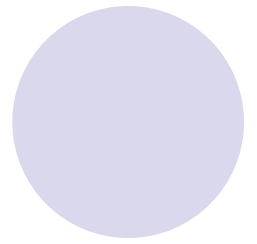
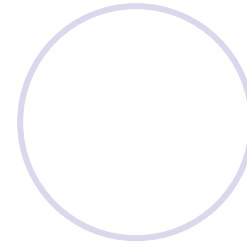
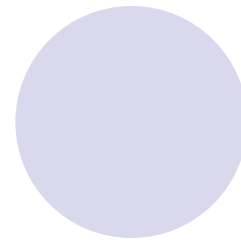
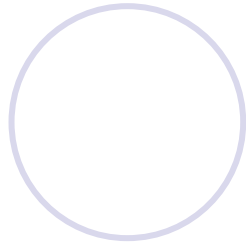
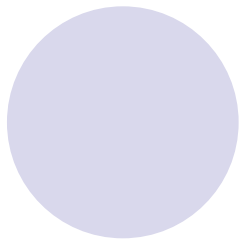
Example:



Are mass media (*or school-based or community-based*) interventions effective in preventing smoking in young people?



- Depression Prevalence in Intensive
Care Unit Nurses: Systematic review
and Metanalysis



Any condition and Wide

Question???

انواع سبکهای سوال مروری (شیوع)

سوال اولیه پیشنهادی بصورت فرموله، بدین صورت است :

POLIS:

- **P: Population** (جمعیت عمومی سالمندان / بالاتر از ۵۰ سال ؟؟؟)
- **O: Outcome** (سارکوپنی)
- **L: Location** (جهانی / منطقه‌ای ؟؟؟؟)
- **I: Indicator** (شیوع / بروز ؟؟؟)
- **S: Study Design(s)** (مطالعات مبتنی بر جمعیت / یا ...)

برای مرورهای سیستماتیک
توصیفی (شیوع، بروز و ...)

✓ مرور سیستماتیک شیوع / بروز سارکوپنی در میانسالان و سالمندان در مطالعات مبتنی بر جمعیت

✓ مرور سیستماتیک شیوع / بروز سارکوپنی در مطالعات مبتنی بر جمعیت منطقه خاور میانه

✓ مرور سیستماتیک شیوع افسردگی در بیماران دیابتی نوع ۲ ...

✓ مرور سیستماتیک فراوانی فرسودگی شغلی در پرستاران بخشهای مراقبت ویژه ...

انواع سبکهای سوال مروری (رابطه‌ای، علیتی)

سبکهای یک سوال فرموله، چگونه نوشته میشود؟

PECO / PECO-S:

- **P:** population / Patients / Participants
- **E:** Exposure
- **C:** Control group
- **O:** Outcome/ Disease
- **S:** Study design

برای مرورهای سیستماتیک
رابطه‌ای / علیتی

✓ مرور سیستماتیک ارزیابی رابطه مصرف سیگار با ابتلاء به سرطان پانکراس

✓ مرور سیستماتیک و متاآنالیز ارزیابی رابطه مصرف سیگار با ابتلاء به سرطان پانکراس، در مطالعات کوهورت آینده نگر

✓ مرور سیستماتیک و متاآنالیز ارزیابی رابطه بین چاقی کودکان یا نوجوانان با افسردگی در آنها

انواع سبکهای سوال مروری (مداخله‌ای)

سبکهای یک سوال فرموله، چگونه نوشته میشود؟

PICO / PICO-S:

- **P:** population / Patients / Participants
- **I:** Intervention
- **C:** Comparison / Control group
- **O:** Outcome (primary)
- **S:** Study design

برای مرورهای سیستماتیک
مداخله‌ای / درمانی

✓ مرور سیستماتیک اثربخشی متفورمین در مقایسه با ویتامین E در بهبود تستهای عملکردی کبد بیماران مبتلا به کبد چرب غیرالکلی

✓ مرور سیستماتیک اثربخشی متفورمین در مقایسه با ویتامین E در بهبود تستهای عملکردی کبد بیماران مبتلا به کبد چرب غیرالکلی، در کار آزمایه‌های

بالینی تصادفی شده دوسوکور

✓ مرور سیستماتیک و متاآنالیز اثربخشی بکارگیری نظام مدیریت دانش بر شاخصهای عملکردی سازمانهای صنعتی

انواع سبکهای سوال مروری (مداخلات غیر درمانی)

سبکهای یک سوال فرموله، چگونه نوشته میشود؟

CIAO:

- **C:** Clients
- **I:** Intervention
- **A:** Alternative Intervention
- **O:** Outcome(s)

برای مرورهای سیستماتیک
مداخله‌ای آموزشی،
مدیریتی، اجتماعی و ...

✓ مرور سیستماتیک و متاآنالیز اثربخشی آموزش برنامه مراقبت از پای دیابتی به روش الکترونیک در مقایسه با روش سخنرانی (مرسوم)، از

نظر تغییرات شاخصهای عملکردی در پرستاران شاغل در کلینیکهای دیابت

✓ مرور سیستماتیک اثربخشی آموزش «خود مراقبتی» بیماران دیابتی در مقایسه با مراقبت معمول (روتین) بر روی سطح HbA1c بیماران

انواع سبکهای سوال مروری (مداخلات غیردرمانی)

سبکهای یک سوال فرموله، چگونه نوشته میشود؟

CIAO:

- **C:** Clients
- **I:** Intervention
- **A:** Alternative Intervention
- **O:** Outcome(s)

برای مرورهای سیستماتیک
مداخله‌ای آموزشی،
مدیریتی، اجتماعی و ...

✓ مرور سیستماتیک و متاآنالیز اثربخشی آموزش برنامه مراقبت از پای دیابتی به روش الکترونیک در مقایسه با روش سخنرانی (مرسوم)، از

نظر تغییرات شاخصهای عملکردی در پرستاران شاغل در کلینیکهای دیابت

✓ مرور سیستماتیک اثربخشی آموزش «خود مراقبتی» بیماران دیابتی در مقایسه با مراقبت معمول (روتین) بر روی سطح HbA1c بیماران

انواع سبکهای سوال مروری (روانسجی ابزار)

سبکهای یک سوال فرموله، چگونه نوشته میشود؟

PIPO:

- **P:** Population (target)/ Participants
- **I:** Instrument(s) Name
- **P:** Measurement Property / Properties
- **O:** Outcome , Condition, ...

برای مرورهای سیستماتیک
روانسجی ابزارها، پیامدهای
گزارشی توسط بیمار و ...

✓ مرور سیستماتیک و متاآنالیز شاخصهای پایایی پرسشنامه کیفیت زندگی در کودکان آسمی

✓ مرور سیستماتیک خصوصیات روانسجی ابزارهای سنجش فرسودگی شغلی در پزشکان

✓ مرور سیستماتیک PROM (پیامدهای گزارشی توسط بیماران) در خودمراقبتی دیابت نوع ۲ در بالغین

انواع سبکهای سوال مروری (سبک عمومی)

اگر برای فرموله کردن سوال مرور سیستماتیک خود، سبک مورد نظر خود را نیافتید، نگران نباشید، یک مدل یا سبک عمومی یا ژنرال برای فرموله کردن سوال خود، استفاده از مدل زیر است:

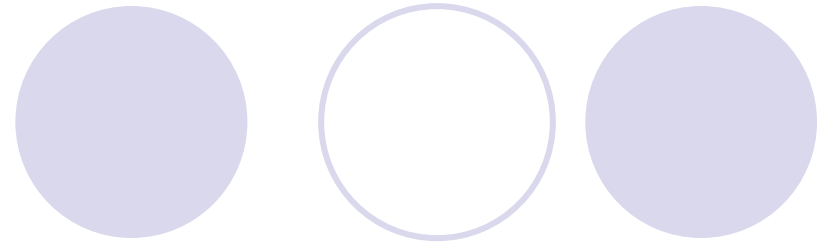
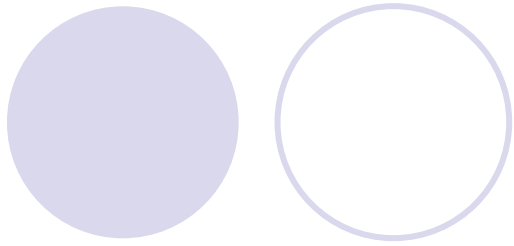
XY model:

- **X:** Independent Variable, Determinant
- **Y:** Dependent Variable, Outcome, Response

سبک مدل عمومی
مفید و کاربردی

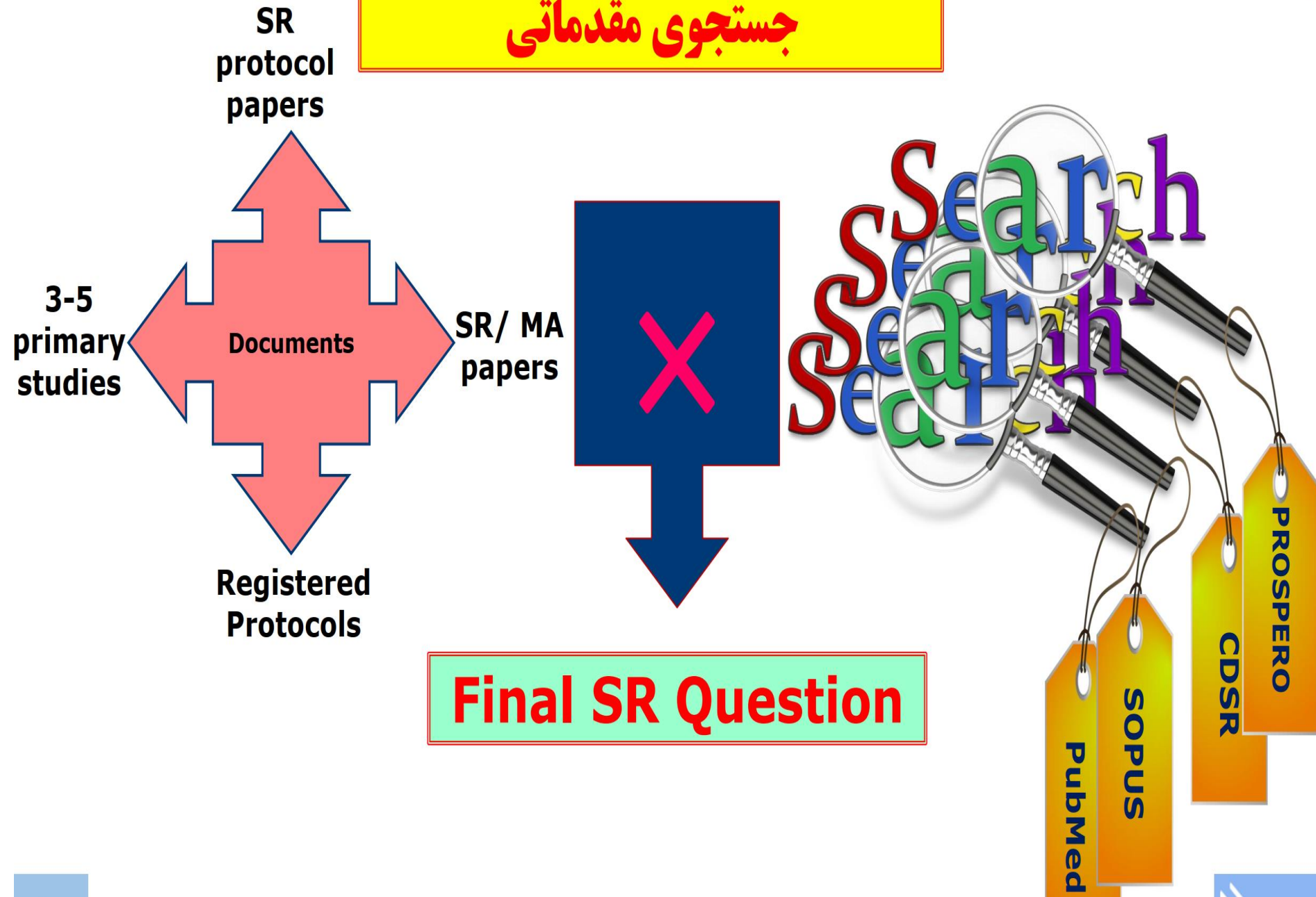
✓ مرور سیستماتیک ارزیابی رابطه بین ادراک عدالت سازمانی و فرهنگ کار

✓ مرور سیستماتیک اثر سامانه ثبت بیماری (EPR) بر ارتقاء وضعیت پژوهشهای متخصصین بالینی بیمارستانهای آموزشی



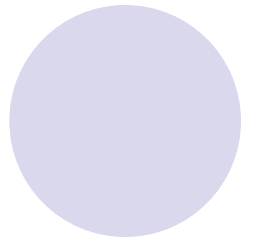
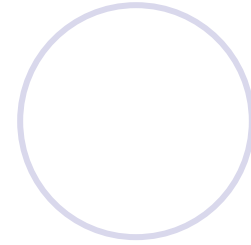
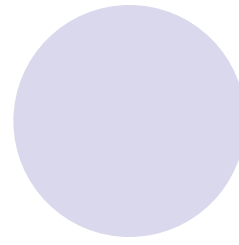
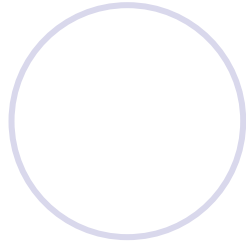
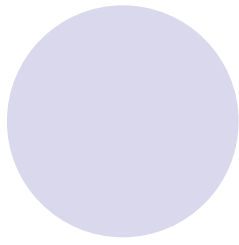
????????????????????????????????????

جستجوی مقدماتی



Main Point for Preliminary Search

- Components (only **P** or **I / I**, **O///// E**, **O**)
- Not used Measure (prevalence, risk, frequency...) , study design, Synonym
- Any Syntax/ Report / testing/
- Search based Title OR Abstract
- Used Google scholar (!!!!)



- Finding same Systematic is so
important ????????



Synonym:

- MESH/EMTREE: Biomedical
- Eric: Education and cognitive science
- Agrovov: Agriculture
- Irandoc: Multiple system

آشنایی با تکنیکهای چهار گانه جستجو در بانکهای اطلاعاتی

- Operators: AND , OR , NOT
- Tag / Field / Code: ti , tiab , all , ...
- Exact Phrase: " "
- Truncation: teen , teenager >>> teen*

2. Develop review protocol:

- 1. Priority
- 2. PROSPERO/ SYRCL/ Open access platform/
- 3. Prospective study
- 4. Reduce publication bias
- 5. 3 version (Cochran, Prospero/ PRISMA-p)
- 6. can publish as article (limitation)
-

What is research priority setting?

- Research priority setting (RPS) can be described as an **interpersonal** activity to decide the **key questions** or **research topics** which are agreed to be the priority.

1. Cochran

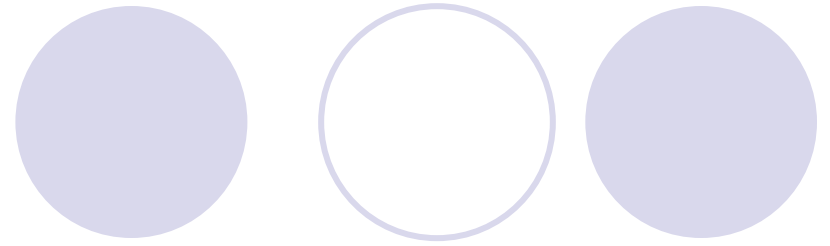
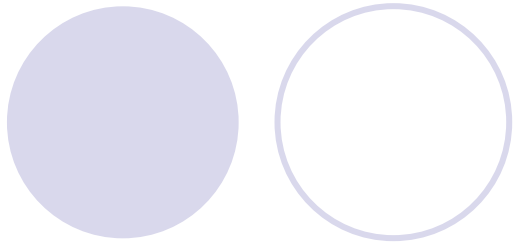
- Title
- Abstract
- Background
- Objectives
- Methods
 - *Inclusion and exclusion criteria*
 - *Search methods and sources (Search Strategy)*
 - *Data Collection and Analysis*
 - *Assessing study quality (Risk of Bias)*
 - *Data synthesis and analysis*
- Acknowledgement
- References
- Appendices:
 - *Search strategy (keywords, syntax)*
 - *History of SR*
 - *Contributions of authors/researchers*
 - *Conflict of interest*
 - *Sources of support/ grant*

2. Prospero

- Title
- SR question
- Sources of Search
- Types of study to be included
- Condition/Domain being studied
- Participants/ Population
- Intervention(s), Exposure(s)
- Comparator(s)/ Control
- Outcome(s):
 - *Primary outcome(s)*
 - *Secondary outcome(s)*
- Data extraction (selection & coding)
- Risk of bias (quality) assessment
- Strategy for data synthesis
- Analysis of subgroups / subsets
- Researchers information:
 - *Name, affiliation, contact information, conflict of interest*
- Stages of SR

چارچوب کلی پروتکول: یک مطالعه مرور سیستماتیک، دارای این اجزاء است:

- عنوان
- چکیده
- زمینه
- هدف / اهداف
- متد:
 - معیارهای ورود و خروج مطالعات اولیه
 - راهبرد جستجو (Search Strategy)
 - فرایندهای غربالگری و انتخاب
 - ارزیابی کیفیت (خطر سوگرایی) مطالعات اولیه
 - استخراج داده ها و تجزیه و تحلیل (متاآنالیز / متاسنتز)
- بخشهای تکمیلی / ضمایم پروتکول (سینتاکسهای استراتژی جستجو، سهم محققین و ...)



??

• عنوان پروتکول: مرور سیستماتیک شیوع، بروز و مورتالیتی سرطان پانکراس در سطح جهانی

★ عناوین مقالات اصلی حاصل پروتکول فوق:

1. مرور سیستماتیک و متاآنالیز شیوع سرطان پانکراس در سطح جهانی

2. مرور سیستماتیک و متاآنالیز نرخ بروز سرطان پانکراس در سطح جهانی

3. مرور سیستماتیک و متاآنالیز مورتالیتی سرطان پانکراس در جهان

Review question/Objectives

Interventions for improving health literacy in migrants

- To assess the effectiveness of interventions for improving health literacy in migrants.
- To assess whether female or male migrants may respond differently to the identified interventions

Systematic review and meta-analysis of magnitude and factors associated with mortality among hospitalized children in Nigeria

Primary questions

- What are the magnitudes of in-hospital child mortality in Nigeria?
- What are the main factors associated with child mortality in hospitalized children in Nigeria?

Secondary questions

- Do factors associated with child mortality differ between under 5, 5-9 and 10-18 years in Nigeria?
- Has there been a remarkable change in the main factors associated with child mortality over time?
- What protective factors may reduce child mortality during hospital admission for Nigerian children?

■ هدف اولیه: تعیین رابطه بین سطح نیترات آب آشامیدنی و وقوع سرطانهای معده

■ اهداف ثانویه:

- تعیین رابطه بین سطح نیترات آب آشامیدنی با وقوع سرطانهای معده به تفکیک جنس
- تعیین رابطه بین سطح نیترات آب آشامیدنی با وقوع سرطانهای معده به تفکیک انواع پاتولوژیک بدخیمی معده (آدنوکارسینوما،)
- تعیین رابطه بین سطح نیترات آب آشامیدنی با وقوع سرطانهای معده به تفکیک انواع طراحیهای مشاهده ای (مورد شاهدی، مقطعی، کوهورت)
- تعیین رابطه بین سطح نیترات آب آشامیدنی با وقوع سرطانهای معده به تفکیک سطوح مختلف نیترات آب (رابطه مقدار-پاسخ یا Dose Response Relationship)

3. Back ground: Cross-sectional

- Disease/ Outcome/ Behaviour importance
- Definition of Disease/ Outcome/ Behaviour
- Importance of Prevalence/ Incidence/ Mean / Frequency of the Disease, Outcome, Event, !!
- Past Systematic Review(s)/ Review(s) and the key finding(s)
- Why it is important to DO this Systematic Review???

مرور سیستماتیک شیوع کبد چرب غیر الکلی

- چرا بیماری «کبد چرب غیر الکلی» مهم است؟ (با استفاده از اطلاعات بار بیماری، شیوع و بروز، بار اقتصادی، از کار افتادگیها، بار اجتماعی و ...، بصورت مبتنی بر شواهد)
- تعریفی که برای این بیماری در منابع استفاده میشود، چیست؟ آیا تعاریف متنوع / متعدد داریم؟ اگر بلی، کدامیک معتبرتر / دارای توافق بیشتری است؟
- چرا شاخص «شیوع» در این بیماری (یا هر شاخص دیگری که یکی از اجزاء سبک سوال ماست)، مهم است؟ (فقدان اطلاعات معتبر، فقدان اطلاعات بهنگام یا جدید، برآوردهای معتبرتر و پایاتر بار بیماری و ...، مدیریت یا برنامه ریزی و یا سیاستگزاری و ...)
- وضعیت مطالعات مرور سیستماتیک مشابه / مرتبط در منابع چگونه است؟ یافته‌های کلیدی آنها به‌مراه ضعفهای متدولوژیک (مبتنی بر مزیت / مزیت‌های نسبی) چیست؟ اگر مرور سیستماتیک / متاآنالیز قبلی نداریم، اشاره شود. ضمناً بهتر است در این شرایط، به مطالعات مروری اشاره نماییم.
- چرا این مرور سیستماتیک مهم است و چرا باید آنرا طراحی و اجراء نمود؟ (با اشاره به موارد فوق)

Background: X-Y model



- Disease/ Outcome/ Behaviour importance
- Causation Web or Types of Determinants of Disease/ Outcome (Macro to Micro-level approach)
- Importance of the FACTOR (Risk vs Protective factor) & the Outcome
- The evidences on FACTOR-OUTCOME relation / causation; (molecular, preclinical, clinical, ...)
- Past Systematic Review(s)/ Review(s) and the key finding(s)
- Why it is important to DO this Systematic Review???

مرور سیستماتیک رابطه بین بیهوشی عمومی و وقوع بیماری آلزایمر

- چرا بیماری آلزایمر مهم است؟ (با استفاده از اطلاعات بار بیماری، شیوع و بروز، بار اقتصادی، از کار افتادگیها، بار اجتماعی و ...، بصورت مبتنی بر شواهد)
- شبکه علّیتی بیماری آلزایمر شامل چه عوامل کلی است؟ جایگاه فاکتور یا عامل تعیین کننده مورد نظر، در این شبکه کجاست؟
- چرا این فاکتور در ارتباط با پیامد / بیماری مورد مطالعه، مهم است؟ (چرا این فاکتور خطر / فاکتور محافظتی، بنظر مهمتر از بقیه است؟)
- چه شواهدی در مورد رابطه بین بیهوشی عمومی و ابتلاء به بیماری آلزایمر موجود است؟ سطوح این شواهد را به تفکیک شواهد مولکولی، مطالعات حیوانی، مطالعات بالینی و ...، بیان نمایید. اگر در این شواهد، ناهمخوانی یا تناقض وجود دارد، اشاره نمایید.
- به مطالعات مرور سیستماتیک/متاآنالیز قبلی (در صورت وجود) اشاره گردد. همچنین در بیان شواهد حاصل از مطالعات ثانویه، به موضوع مزیت نسبی / مزایای نسبی نیز توجه نموده و به شکل مطلوبی به آنها اشاره شود.

Background: Intervention



- Disease/ Outcome/ Behaviour importance
- Types of Intervention categories & the related Components (drug, surgery, behaviour change, consult, ...) using Macro to Micro-level approach
- Importance of the INTERVENTION in term of the OUTCOME
- The evidences on the INTERVENTION effectiveness; (molecular, preclinical, clinical, ...)
- Past Systematic Review(s)/ Review(s) and the key finding(s)
- Why it is important to DO this Systematic Review???

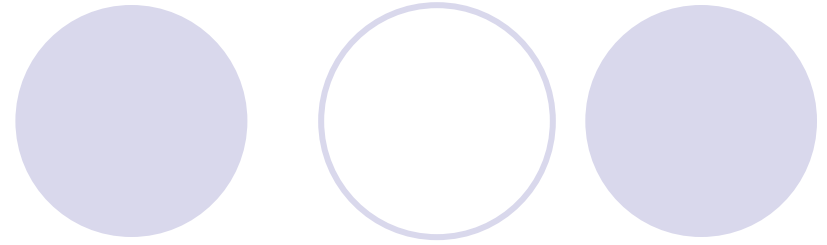
مرور سیستماتیک اثر مهارکننده‌های SGLT-2 بر روی پیامدهای میکرواز کولار دیابت نوع ۲

- چرا عوارض / پیامدهای میکرواز کولار دیابت نوع ۲ مهم است؟ (با استفاده از اطلاعات بار بیماری، شیوع و بروز، بار اقتصادی، از کار افتادگیها، بار اجتماعی و ...، بصورت مبتنی بر شواهد)
- انواع مداخلات (دست بندیها) در درمان دیابت نوع ۲ کدامند؟ جایگاه مهارکننده های SGLT-2 کجاست؟
- چرا این مداخله (دارو، فراورده بیولوژیک) در ارتباط با عوارض میکرواز کولار دیابت، مهم است؟ (چرا این درمان / مداخله از دیگر مداخلات مهمتر است؟)
- چه شواهدی در مورد اثر یا اثربخشی این مهارکننده ها بر روی عوارض میکرواز کولار دیابت موجود است؟ سطوح این شواهد را به تفکیک شواهد مولکولی، مطالعات حیوانی، مطالعات بالینی و ...، بیان نمایید. اگر در این شواهد، ناهمخوانی یا تناقض وجود دارد، اشاره نمایید.
- به مطالعات مرور سیستماتیک/متاآنالیز قبلی (در صورت وجود) اشاره گردد. همچنین در بیان شواهد حاصل از مطالعات ثانویه، به موضوع مزیت نسبی / مزیت‌های نسبی نیز توجه نموده و به شکل مطلوبی به آنها اشاره شود.

چارچوب کلی پروتکول: یک مطالعه مرور سیستماتیک، دارای این اجزاء است:

- عنوان
- چکیده
- زمینه
- هدف / اهداف
- متد:
 - معیارهای ورود و خروج مطالعات اولیه
 - راهبرد جستجو (Search Strategy)
 - فرایندهای غربالگری و انتخاب
 - ارزیابی کیفیت (خطر سوگرایی) مطالعات اولیه
 - استخراج داده ها و تجزیه و تحلیل (متاآنالیز / متاسنتز)
- بخشهای تکمیلی / ضائم پروتکول (سینتاکسهای استراتژی جستجو، سهم محققین و ...)

Eligibility Criteria:



- 1. Type of Participants (population based of other population)
- 2. Sampling Method (Randomized or nonrandomized)
- 3. Sample size ($30 > n$ or $30 < n$)
- 3. Type of Study
- 4. number of Study in preliminary search

Eligibility Criteria: Cross-sectional

Prevalence childhood obesity in the Middle East region: A systematic review and meta-analysis

■ Types of studies:

- Descriptive vs Analytical design
- Cross-sectional (population based vs clinic based, ...)
- Case series (Included or Excluded??)
- Special design (COHORT baseline, RCT/ CT baseline, ...)

■ Types of Participants

- Characteristics of eligible participants / subjects
- Age group, sex, race or ethnicity, SES, job and

■ Disease/ Outcome/ Behaviour Definition

- Only specific Definition vs different types of Definition
- Measurement method(s): specific method vs different methods
- Measurement tool/ instrument (questionnaire): specific vs different

■ Sampling Method & Sample Size

- Random sampling vs Non-random sampling
- Specific random sampling vs any random sampling methods
- Need to determine for minimum sample size (25-30)

■ Exclusion based on; Study design or Methodological quality

Eligibility Criteria: Intervention

■ Types of studies:

- 2 optimum features in clinical trials; randomization, concurrent control
- High quality designs (parallel RCT, Cross-over RCT) vs Low quality designs (Non-randomized CT, One group before-after trial, ...)
- Need to include observational design (Cohort or follow-up study)

■ Types of Participants

- Characteristics of eligible patients / subjects
- Age group, sex, race or ethnicity, severity, staging and

■ Intervention & Comparison

- Types of interventions (drug, surgery, educational package, ...)
 - Drug/ intervention Dose, Duration, Frequency, Route, ...
- Types of comparison groups (Internal vs Concurrent)
 - No intervention/ Placebo / Standard treatment

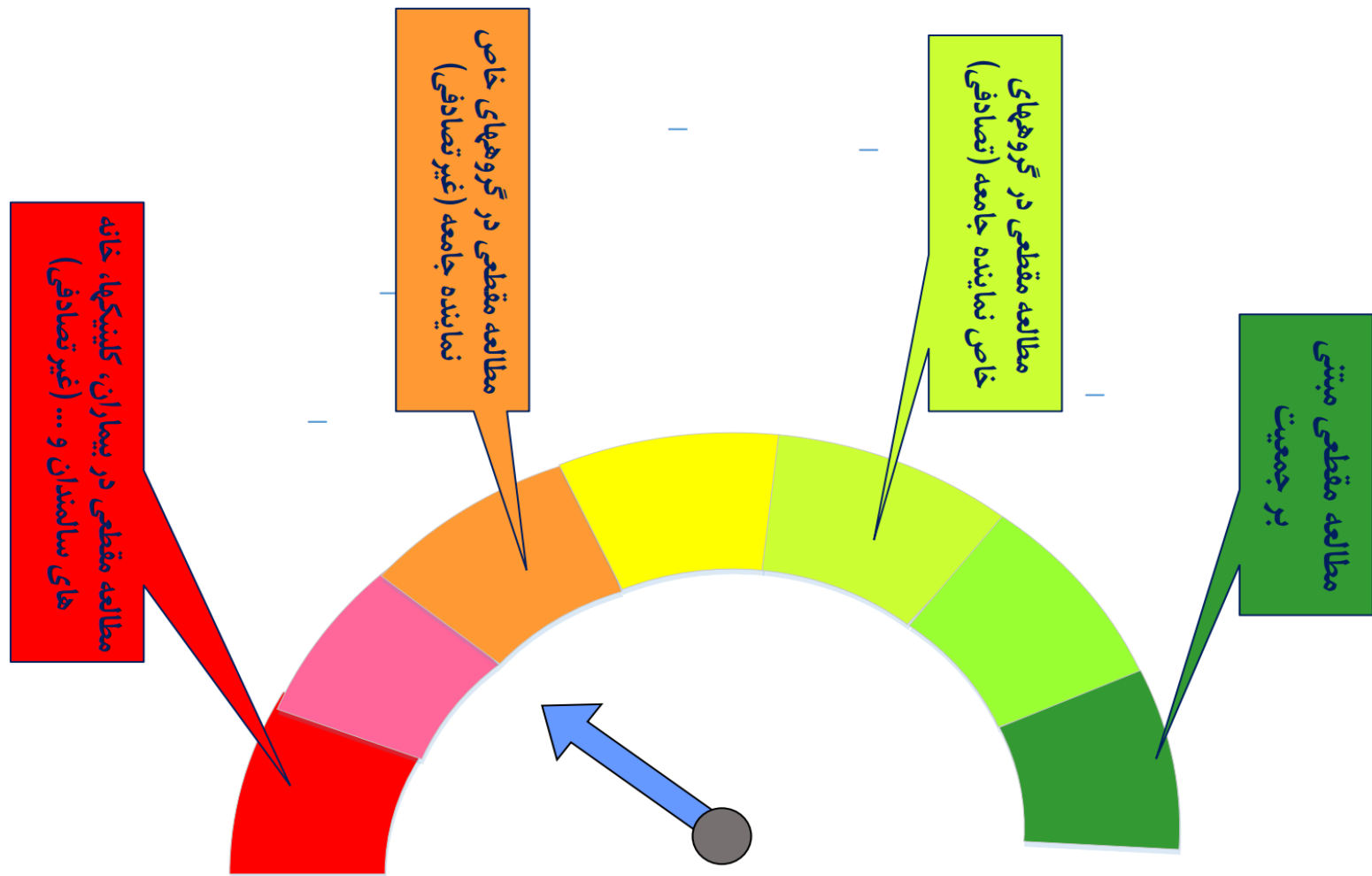
■ Outcome

- Types of outcome(s):
 - Primary vs Secondary (usually 1 primary, 2-4 secondary outcomes)

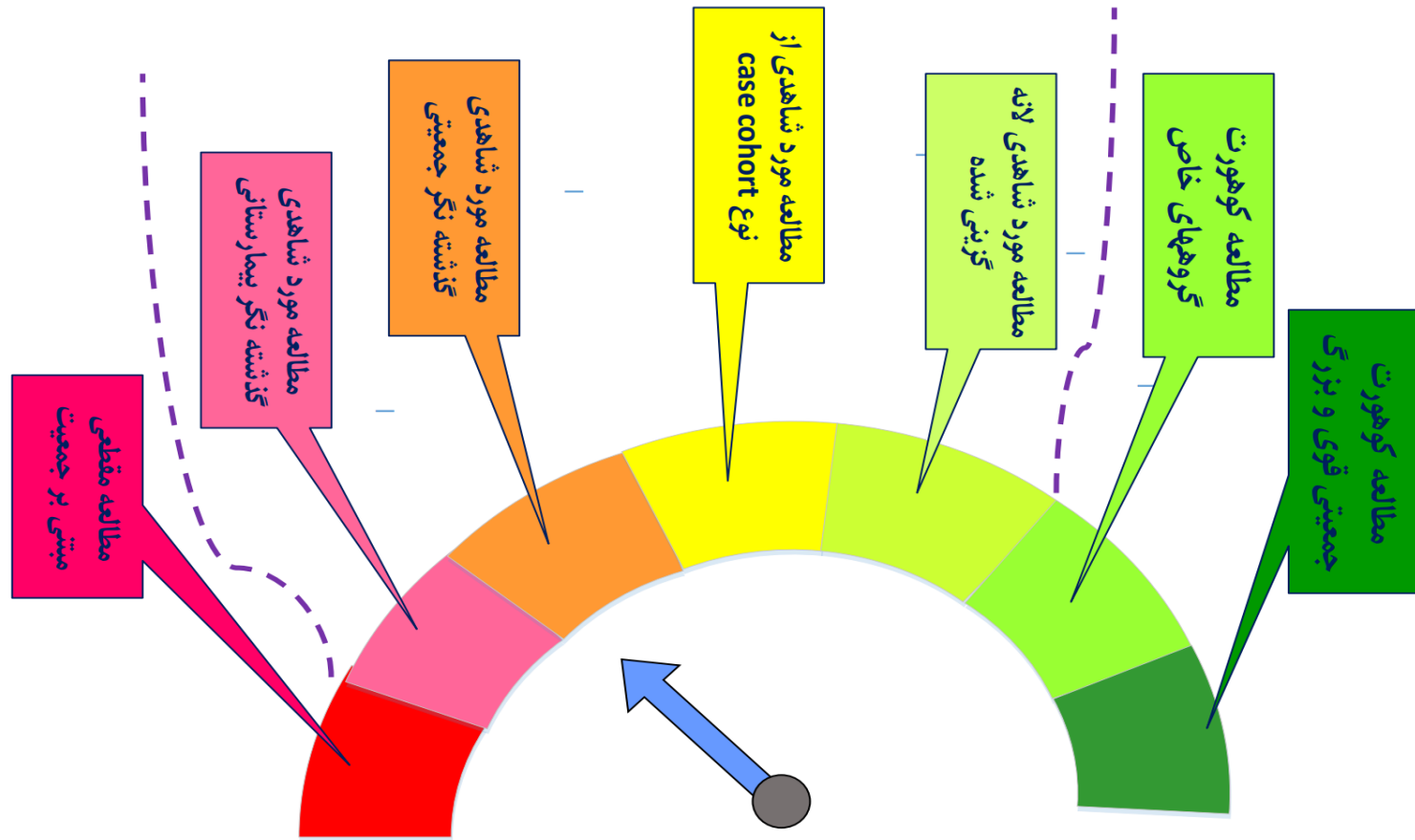
■ Exclusion based on; Study design or Methodological quality



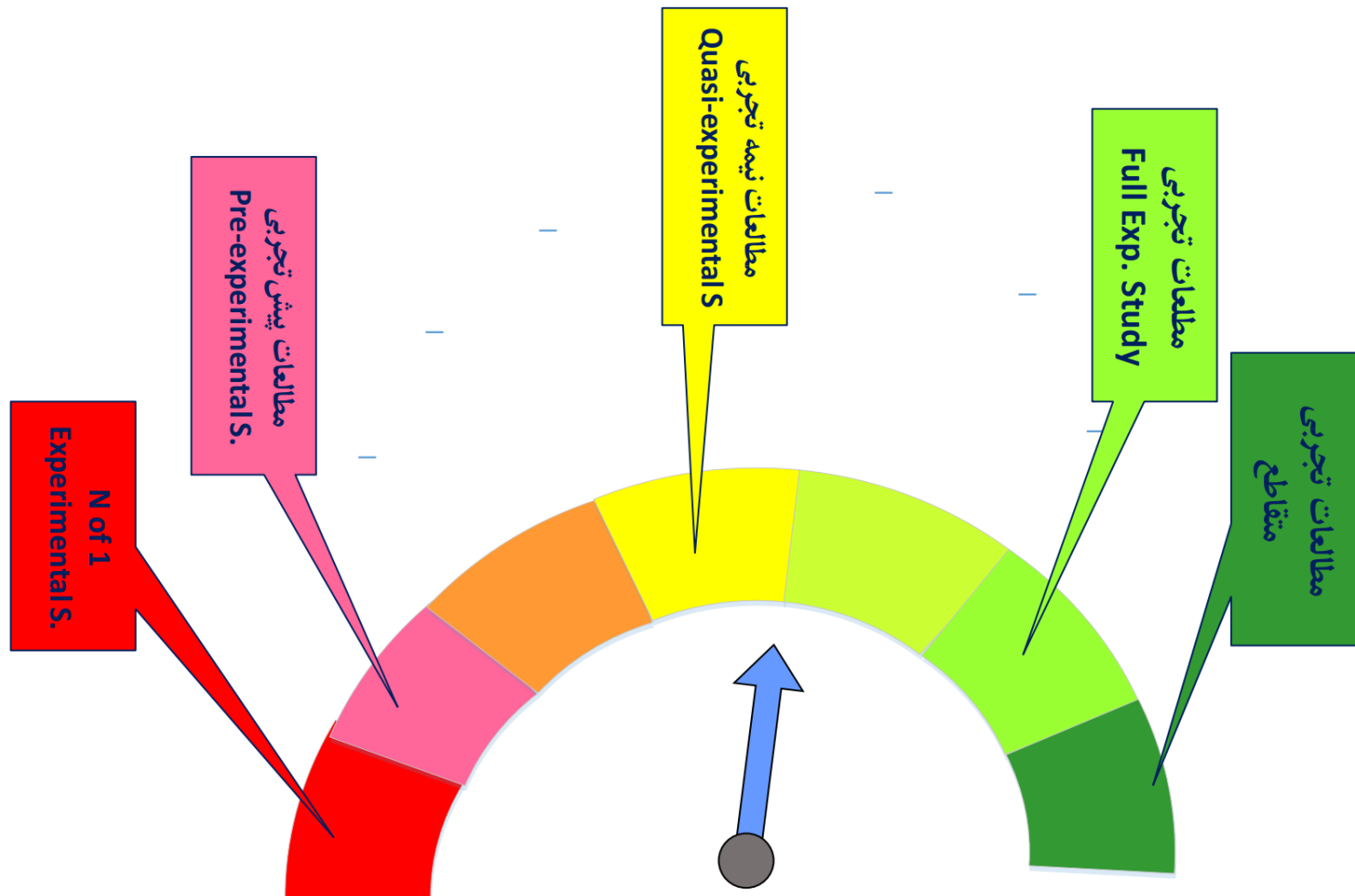
1. Cross-sectional (Type population, sampling)



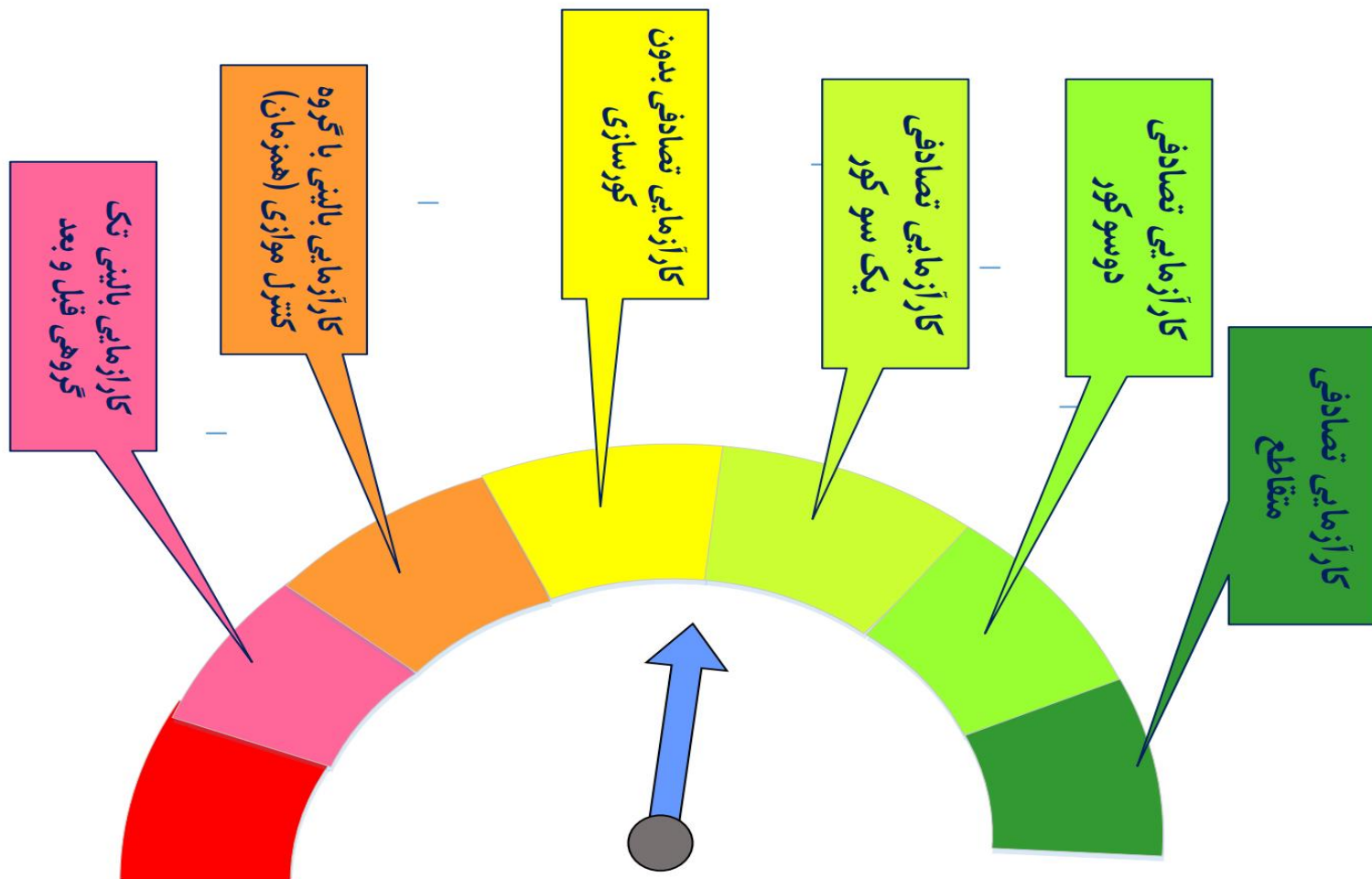
Type of Cross-Sectional and population



Experimental



IRCT



Search Strategy



1. Sources of Primary Research:

- a. Electronic Databases*
- b. Gray Literatures*
- c. Key Journals*
- d. References of Included Research/ Papers*
- e. Other Sources*

2. Time Interval of SEARCH

3. SEARCH terms/ Keywords

4. SEARCH syntax: come soon

SS-1) General Guideline for SR Sources

Source Type	Minimum no.	Examples / Subtypes / Criteria	Search Method*
Bibliographic DB	4-5	PubMed, SCOPUS, WoS, EMBASE, PsycINFO, ERIC, Scholar Google, CENTRAL, PEDro, AGRICOLA, ...	E
Gray Literature	2 from 3 essential	3 Main subtypes: Conferences Papers, Thesis, Research Reports	E / H
Key Journals	1-2	Based on SEARCH in SCOPUS	H
References of Included/ Final Papers / Researches	-	Maximum 1-2 relevant researches > 2 relevant researches: insufficient SEARCH in previous sources	H
Other Sources	-	Organizational Website(s) , Contact to Relevant Expert(s) , Registration Systems (IRCT, PROSPERO, US-FDA, relevant Books/ Chapters , ...	E / H

***E: Electronic Search, H: Hand-searching**

Optimum DB Combination for SRs



Best Optimal Database Combination:

- ✓ **MEDLINE / PubMed**
- ✓ **EMBASE**
- ✓ **Web of Science (WoS)**
- ✓ **Scholar Google**

• **This combination achieved 98.3% Search Recall**

SEARCH terms/ Keywords

1. Describe each **PICO** component
2. Start with **primary** concept
3. Find **synonyms**
4. Add other components of PICO question to narrow citations (*may use study filter*)
5. Examine abstracts



Points:

- 1. Language limitation (S: 40%/P: 25%/W: 15%)
- 2. Reference Hand Check
- 3. Type of Database (General, Specific)

Time Interval of SEARCH

- 1. Limit based on start/end, (Justification)
- 2. End (from inception to 2020)
- 3. Any time border
- 4. 1990 ???
- 5. First and end of month
- 6. tools/quality of method/ Gold Standard
(Subgroup analysis)

The Cochrane Library: www.thecochranelibrary.com

Wiley InterScience: Reference Work: The Cochrane Library 2005, Issue 3 - Microsoft Internet Explorer provided by VicHealth

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The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases. The databases and the current numbers of records are:

Database	Total Records
The Cochrane Database of Systematic Reviews (Cochrane Reviews) *	4041
Database of Abstracts of Reviews of Effects (DARE) **	5340
The Cochrane Central Register of Controlled Trials (CENTRAL)	454449
The Cochrane Database of Methodology Reviews (Methodology Reviews) ***	20
The Cochrane Methodology Register (Methodology Register)	7059
Health Technology Assessment Database (HTA)	4620
NHS Economic Evaluation Database (NHS EED)	15884
About The Cochrane Collaboration and the Cochrane Collaborative Review Groups (About) §	90

* Comprises 2435 Complete Reviews and 1606 Protocols
** Comprises 4540 Abstracts and 800 other reviews
*** Comprises 11 Reviews and 9 Protocols
§ The Cochrane Collaboration: 1; Collaborative review groups (CRGs): 50; Fields: 11; Methods Groups: 11; Networks: 1; Centres: 12; Possible Cochrane entities: 4

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Cochrane HPPH Field

Cochrane Health Promotion and Public Health Field - Welcome - Microsoft Internet Explorer provided by VicHealth

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Cochrane entities >

Cochrane Health Promotion and Public Health Field

Welcome

The Cochrane Health Promotion and Public Health (CHPPH) Field seeks to represent the needs and concerns of health promotion and public health professionals in the work of the Cochrane Collaboration. The CHPPH Field aims to increase the profile of Health Promotion and Public Health issues in the public arena. It seeks to increase the quantity and quality of systematic reviews of health promotion and public health interventions to ensure the evidence needs of decision makers with government and non-government organisations are met. This site provides updates of the Field's activities and provide opportunities for participation in the Field's work.

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 **Cochrane Colloquium**
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[Ireland, 2006](#) and [earlier](#)

A FIELD OF THE COCHRANE COLLABORATION*

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Latest News

The Field's 5 year funding proposal to VicHealth has been accepted and commenced in May 2007. A key part of our plans for the next 5 years is to transition from a Cochrane Field to a Collaborative Review Group. This will eventually enable us to edit and publish Public Health reviews within a predetermined scope (still in draft form and open to discussion). Keep updated on our progress by regularly checking this site

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 **health-evidence.ca**
Promoting evidence based decision making



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- addiction/drug use
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- adult health
- child health
- chronic diseases
- communicable disease & infection
- community health
- dental health
- elderly health
- environmental health
- food safety & inspection
- infant health
- injury prevention & safety
- mental health
- nutrition
- parenting/infants & children
- physical activity
- pregnancy
- sex education
- stds
- women's health

evidence based nursing practice workshop

Evidence-Based Nursing Practice Workshop

One-week intensive course at McMaster University, Hamilton Ontario, June 10-15, 2007.

- To advance your skills in critical appraisal of research literature
- To learn strategies for teaching evidence-based nursing practice

The format will be small groups led by nursing faculty at McMaster. There will be specific tutorial groups for nurses in advanced practice, oncology, public health and gerontology, in addition to groups for nursing faculty and other clinical nursing areas. For more information contact [Dr. Maureen Dobbins](#)

[Click here to view the PDF](#)

Most Popular References...

Q15783 - Day care for pre-school children	modified: 6/2/2005
Q15782 - The health and welfare effects of day-care: A systematic review of randomized controlled trials	modified: 6/2/2005
Q15329 - Interventions for preventing obesity in children	modified: 6/2/2005
Q16121 - Effectiveness of physical activity enhancement and obesity prevention programs in children and youth	modified: 11/10/2005
Q15345 - Effectiveness of community-based interventions to increase fruit and vegetable consumption	modified: 6/2/2005

Latest Additions...

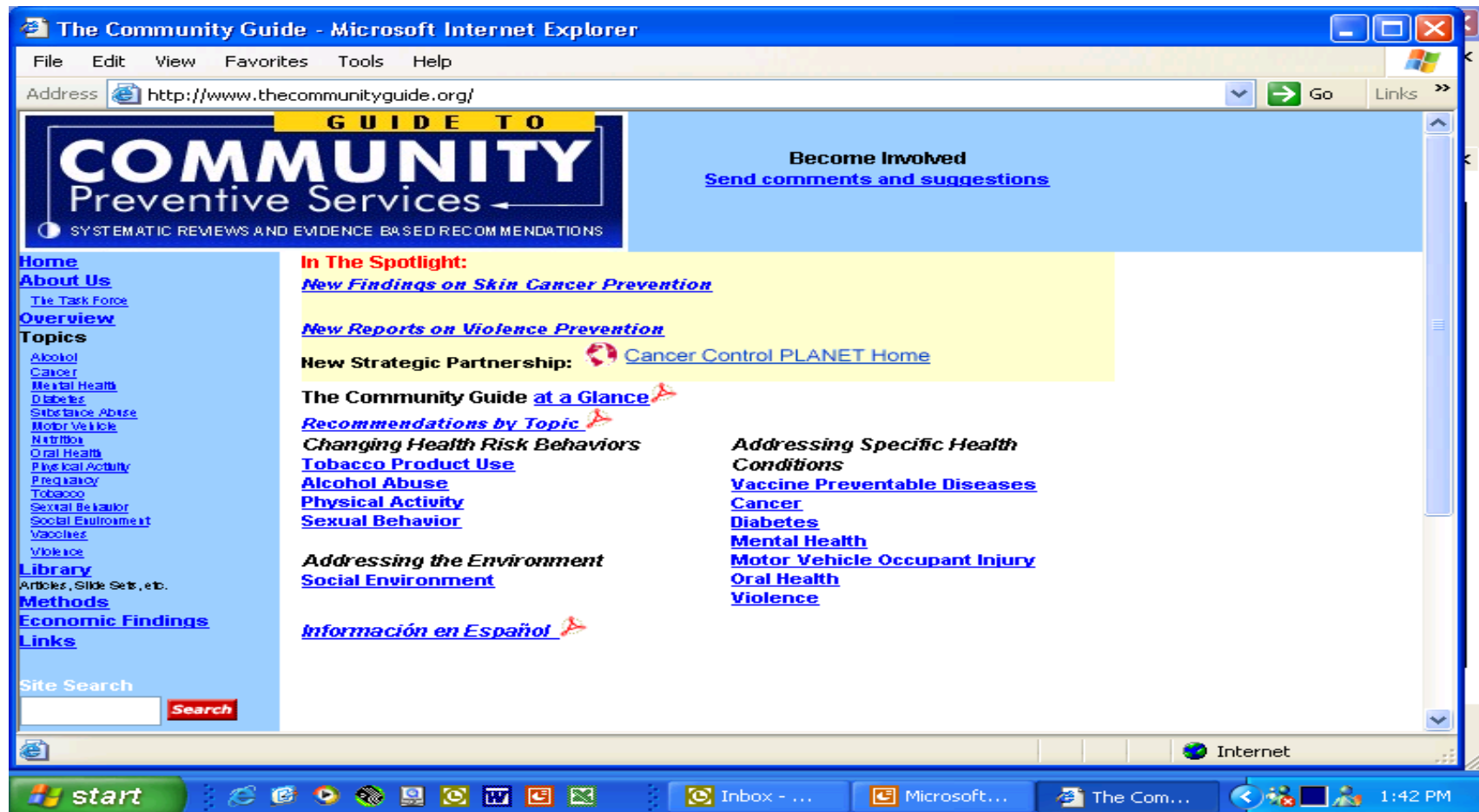
Q15561 - Do condoms prevent genital HPV infection, external genital warts, or cervical neoplasia? A meta-analysis	modified: 11/2/2006
Q16136 - The effectiveness of public health strategies to reduce or prevent the incidence of low birth weight in infants born to adolescents: A systematic review	modified: 6/30/2006
Q15330 - Effectiveness of environmental awareness interventions	modified: 11/10/2005
Q16120 - Effectiveness of school-based interventions in reducing adolescent risk behaviour: a systematic review of reviews	modified: 11/10/2005
Q16121 - Effectiveness of physical activity enhancement and obesity prevention programs in children and youth	modified: 11/10/2005

(15 items remaining) Downloading picture http://health-evidence.ca/images/header_pics.gif...

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The Guide to Community Preventive Services

<http://www.thecommunityguide.org/>



National Institute for Health and Clinical Excellence

<http://www.publichealth.nice.org.uk/page.aspx?o=home>

The screenshot shows the NICE website in a Microsoft Internet Explorer browser window. The address bar displays the URL: <http://www.publichealth.nice.org.uk/page.aspx?o=home>. The website header includes the NICE logo and the text "National Institute for Health and Clinical Excellence". The main navigation menu consists of links: Home, Evidence, Practice, Our Guidance, Publications, News & Events, and About Us. The "Publications" link is highlighted.

Public health excellence at NICE

The new National Institute for Health and Clinical Excellence (NICE) has taken on the functions of the Health Development Agency to create a single excellence-in-practice organisation responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health. Our guidance is for those working in the NHS, local authorities and the wider public, private and voluntary sectors.

New on this site:

- Publications:**
 - 17/08/05 Helping smokers to stop: advice for pharmacists in England
 - 12/07/05 Update on Public Health Evidence
 - 20/06/05 Making the case for sustainable procurement: the NHS as a good corporate citizen
 - 17/06/05 Public health interventions for the prevention and reduction of exposure to second-hand smoke: a review of reviews. Evidence briefing summary - Word version
 - more publications...
- Events:**
 - 12/09/05 Health Protection Agency conference 2005
 - 07/12/05 NICE 2005: Health and Clinical Excellence Conference
 - more events...

Latest news:

- 16/08/05 Draft Scope, Stakeholders response comments and potential stakeholders published for Preventing Sexually Transmitted Infections and Reducing Under 15 Conceptions
- 12/08/05 NICE is recruiting lay members for the group that will be developing public health guidance on Maternal and Child Nutrition
- 03/08/05 Advertisement: The NICE Research and Development Advisory Committee is recruiting new members with a public health background
- 28/07/05 Final Scope and Stakeholder response comments table published for Physical Activity
- 28/07/05 Final Scope and Stakeholder response comments table published for Smoking Cessation
- 05/07/05 News item: Closure of the HealthPromis and Evidence Base websites
- 28/06/05 Press release: NICE's Citizen's Council to debate social issues linked to Public Health measures
- 14/06/05 News item: Creating Healthier Communities resource pack published
- more news...

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Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI-Centre)

<http://eppi.ioe.ac.uk>

The screenshot shows a Microsoft Internet Explorer browser window displaying the EPPI-Centre website. The address bar shows the URL <http://eppi.ioe.ac.uk/EPPIWeb/home.aspx?page=/hp/reviews.htm>. The website has a blue header with the EPPI logo and navigation links: EPPI-Centre, Research Evidence in Education Library, Health Promotion, and Perspectives & Participation. A left sidebar contains a list of links including Health Promotion Introduction, Reviews (highlighted), EPPI-Centre Staff, Databases, Tools, Comments, Links, EPPI-Centre Home, Social Science Research Unit, and Institute of Education. The main content area is titled 'Health promotion reviews' and includes a breadcrumb trail 'You are in: Health Promotion - Reviews'. It features a paragraph about recent reviews focusing on young people, a link to contact for paper copies, and two columns of links to online reports and protocols. The bottom of the browser window shows the Windows taskbar with the start button and several open applications.

Health promotion reviews - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Address <http://eppi.ioe.ac.uk/EPPIWeb/home.aspx?page=/hp/reviews.htm> Go Links

ePPI

EPPI-Centre Research Evidence in Education Library Health Promotion Perspectives & Participation

Health Promotion Introduction

Reviews

EPPI-Centre Staff

Databases

Tools

Comments

Links

EPPI-Centre Home

Social Science Research Unit

Institute of Education

Health promotion reviews

You are in: [Health Promotion](#) - Reviews

[About the recent series of EPPI-Centre reviews focusing on young people](#)

To order paper copies of both online and offline reports, please [contact us](#).

Reports available online	Protocols available online
Children and healthy eating: a systematic review of barriers and facilitators (October 2003)	HIV health promotion and men who have sex with men (MSM): a systematic review of research relevant to the development and implementation of effective and appropriate interventions August 2003
Children and physical activity: a systematic review of barriers and facilitators (April 2003)	Reports available offline

Internet

start

Inbox - ... Microsoft... Health pr... 1:44 PM

Effective Public Health Practice Project (EPHPP)

<http://www.myhamilton.ca/myhamilton/CityandGovernment/HealthandSocialServices/Research/EPHPP/>

Effective Public Health Practice Project - Microsoft Internet Explorer provided by VicHealth

File Edit View Favorites Tools Help

Back Forward Stop Home Search Favorites

Address <http://www.myhamilton.ca/myhamilton/CityandGovernment/HealthandSocialServices/Research/EPHPP/> Go Links

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Culture and Recreation
Public Health & Social Services

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- Public Health
- Social Services
- Long-term Care
- Teachers
- Research
 - Effective Public Health Practice Project
 - 2005 Social and Health Issues Report (SHIR)
 - Rapid Risk Factor Surveillance System (RRFSS)

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City of Hamilton Effective Public Health Practice Project

[Print](#)

The Effective Public Health Practice Project (EPHPP) is a key initiative of the [Public Health Research, Education and Development Program \(PHRED\)](#). It is jointly funded by the Ministry of Health and Long-Term Care and the City of Hamilton Public Health Services.

Public Health Literature Reviews:

[Public Health Reviews](#)
Final systematic reviews summaries and highlights for practitioners and managers for policy development.

[Notification of new reviews](#)
Send us an email to let us know if you would like to be notified when a new review is posted.

[Health-Evidence.ca](#)
Health-evidence.ca is an external site which features a comprehensive online registry of published systematic reviews on the effectiveness of public health and health promotion interventions. Developed by Dr. Maureen Dobbins at McMaster University, health-evidence.ca is the product of a program of research that promotes evidence-based public health decision making.

Tools Used:

[Dictionary for the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies](#) (pdf)
[Quality Assessment Tool for Quantitative Studies](#) (pdf)

More about EPHPP:

[About the EPHPP](#)
[The Hamilton EPHPP Team](#)

Contact Information:

Email: ephpp@hamilton.ca

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start Microsoft Office Microsoft Office Microsoft Excel Microsoft PowerPoint Windows Media Center EndNote 6 Published Interventions Effective Public Health 1:22 PM

Centre for Reviews and Dissemination


<http://www.york.ac.uk/inst/crd>

The screenshot shows the website of the Centre for Reviews and Dissemination (CRD) in a Microsoft Internet Explorer browser window. The address bar shows the URL <http://www.york.ac.uk/inst/crd/crddatabases.htm>. The website features a navigation menu on the left with links to Home, About CRD, Databases, Publications, Research & Projects, Enquiry Service, Dissemination, Review Methods & Resources, Training, Cochrane Library, Links, Contact Us, and CRD staff only. A search bar is located below the menu. The main content area displays a search button labeled "Search the CRD databases now" and a list of databases: DARE (Database of Abstracts of Reviews of Effects), NHS EED (NHS Economic Evaluation Database), and HTA (Health Technology Assessment Database). Each database entry is accompanied by a small graphic of three colored circles (yellow, red, and dark red) on a horizontal line. The browser's taskbar at the bottom shows the Start button and several open applications, including an email client and a document titled "CRD Dat...". The system clock indicates the time is 1:43 PM.

CRD Databases - Microsoft Internet Explorer


File Edit View Favorites Tools Help

Address <http://www.york.ac.uk/inst/crd/crddatabases.htm> Go Links

 Centre for Reviews and Dissemination

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Research & Projects
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Dissemination
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Search
Search Help

 Search the CRD databases now

Click the banners below for more details of the CRD databases

DARE
Database of Abstracts of Reviews of Effects

NHS EED
NHS Economic Evaluation Database

HTA
Health Technology Assessment Database

<http://www.york.ac.uk/inst/crd/nhsdhp.htm> Internet

start | Inbox - ... | Microsoft... | CRD Dat... | 1:43 PM

Other sources of primary research

The Campbell Collaboration - Microsoft Internet Explorer

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THE CAMPBELL COLLABORATION

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THE CAMPBELL COLLABORATION

Preparing, maintaining, and promoting the accessibility of systematic reviews of the effects of social and educational policies and practices

C2-SPECTR

The Campbell Collaboration's
Social, Psychological, Educational, and Criminological Trials Register

[SEARCH SPECTR](#)

http://geb9101.gse.upenn.edu/default.htm

start | Internet

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Screening

A decorative graphic consisting of two groups of three circles. The group on the left has a solid light purple circle on the left and an outlined light purple circle on the right. The group on the right has a solid light purple circle on the left, an outlined light purple circle in the middle, and a solid light purple circle on the right.

- 1. Title / Abstract
- 2. Criteria (, 3-6/ primary or Secondary)
- 3. Check list based on PICO

Study no	Cr. 1 RCT-1 st bl/+	Cr. 2 T2-DM	Cr. 3 Age>=18	Cr. 4 DRD	Cr. 5 Psych. Int	Final Decision
101	+	+	+	+	-	Exclude
102	+	+	+	+	+	Selection p.
103	-	+	+	+	+	Exclude
104	+	*	+	+	+	Selection p.
105	-	+	*	+	+	Exclude
106	-	-	-	-	-	Exclude
107	+	*	*	+	+	Selection p.

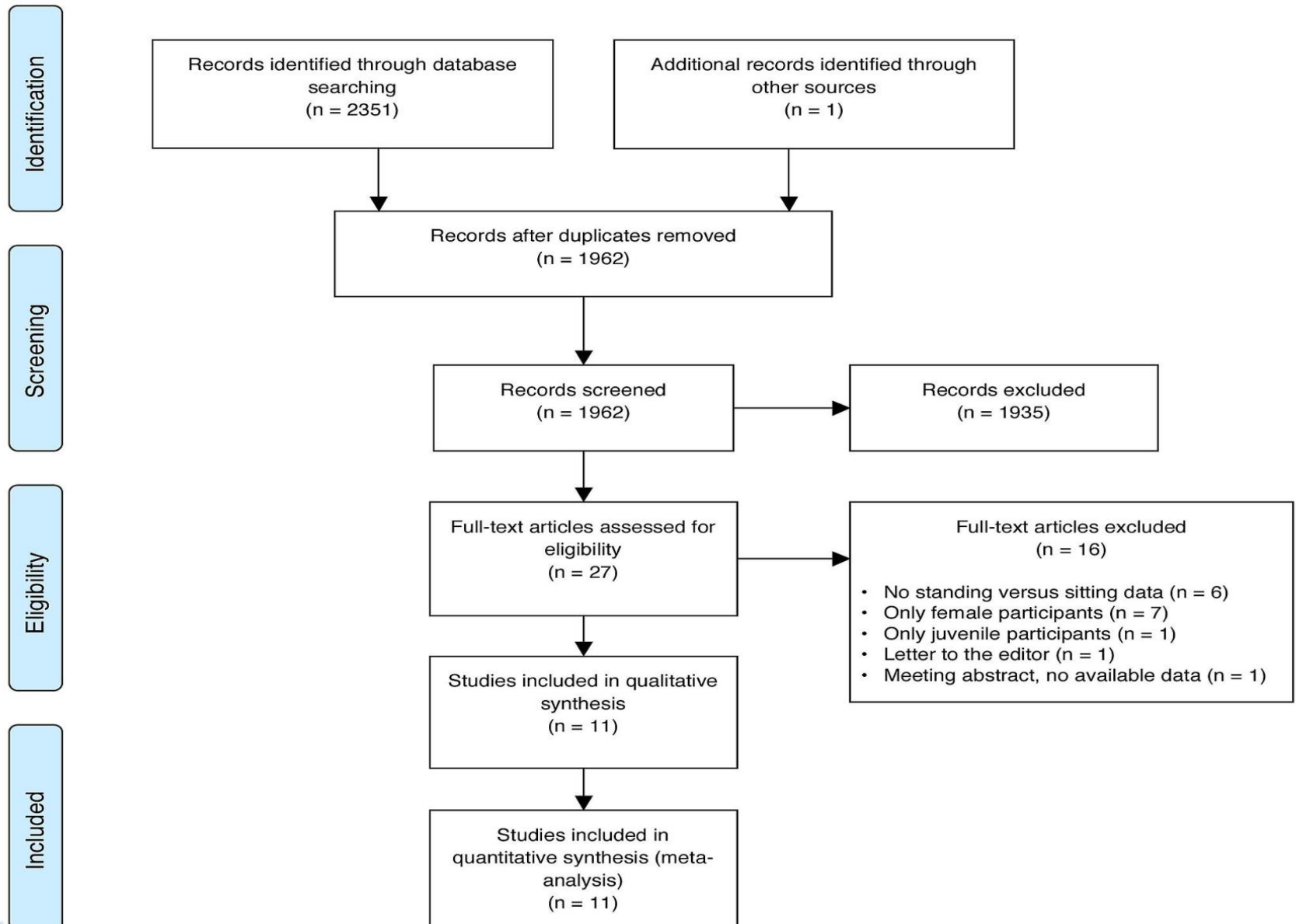


Selecting

- 1. Insufficient data
- 2. Effect size
- 3. Any full text
- 4. Conflict in Method/sampling/study design/ tools/population.... (Eligibility Criteria)



PRISMA flowchart



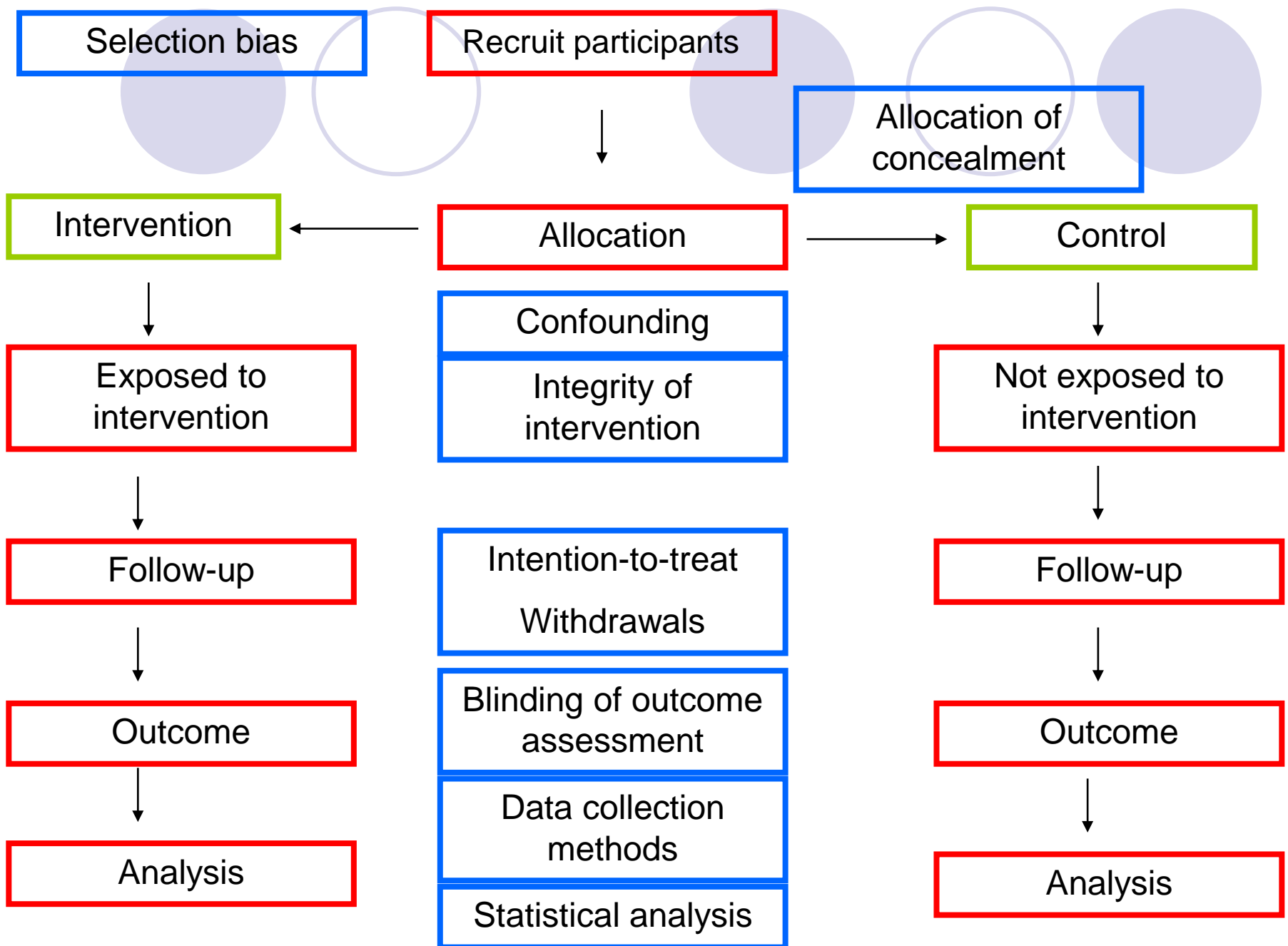
Quality Control



- 1. Bias/Method quality assessment/controls (primary studies)
- 2. Process assessment (Systematic Review)
- 3. differences (tools/time/background)
- 4. Score based or categorized based

Bias – quality assessment tool

1. Selection bias
2. Allocation bias
3. Confounding
4. Blinding (detection bias)
5. Data collection methods
6. Withdrawals and drop-outs
7. Statistical analysis
8. Intervention integrity



Critical appraisal tools

- RCTs

- The Quality Assessment Tool for Quantitative Studies
(<http://www.city.hamilton.on.ca/PHCS/EPHPP/>).

- Non-RCTs

- Cochrane Effective Practice and Organisation of Care Group (<http://www.epoc.uottawa.ca/>).
- The Berkeley Systematic Reviews Group
(<http://www.medepi.net/meta/>)

Qualitative research



- ... explores the subjective world. It attempts to understand why people behave the way they do and what meaning experiences have for people.
- Qualitative studies of experience
- Process evaluation

CASP appraisal checklist



1. Clear aims of research (goals, why it is important, relevance)
2. Appropriate methodology (what, how, why)
3. Sampling strategy
4. Data collection
5. Relationship between researcher and participants
6. Ethical issues
7. Data analysis
8. Findings
9. Value of research (context dependent)

Other qualitative checklist

- Quality framework
 - Government Chief Social Researcher's Office, UK
 - http://www.strategy.gov.uk/files/pdf/Quality_framework.pdf
- 19 question checklist for process evaluations (EPPI-Centre)

Quality assessment tools/guideline/checklist

SR categories	♣♣ Specific (SR) Tool ♣♣	Writing Guideline	CAT
SR of Descriptive /prevalence St.	Hoy et al Tool JBI tool	STROBE (modified)	CASP SIGN ...
SR of Relational St.	Newcastle-Ottawa Scale (NOS) JBI (Relational Studies)	STROBE	CASP SIGN ...
SR of Trials	JADAD scale/ tool ??? Cochrane tool Verhagen et al tool	CONSORT-2010 / Different Extensions	CASP SIGN ...
SR of DA St.	QUADAS-1 QUADAS-2	STARD	CASP SIGN ...

quality assessment of the included studies using the **QUADAS** tool



Extraction:

- 1. Study ID (author, time/location/ citation/ publication type)
- 2. Study characteristics (sample size, sampling, data source, population demographic,
- 3. outcomes (control/ group/before/after)
- 4. missing data ??? (Plot Digitizer)