Assessing effectiveness

Montarat Thavorncaroensap, Ph.D.
1: Faculty of Pharmacy, Mahidol University
2. HITAP, Thailand
Outline

- Role of Systematic Review (SR) and meta analysis in health care decision making

- Overview of SR/ Meta-analysis
  - Searching for the evidence
  - Quality appraisal
  - Interpretation of meta-analyses
Evidence-based health care decision making process

- Request for inclusion in benefit package
- Evidences on efficacy/effectiveness
  - Systematic review/Meta analysis
- Cost consideration
  - Economic evaluation
- Decision making
  - Other factors: Political, ethical, budget impact
Systematic review

- Systematic review: is a summary of the medical literature that
  - Use explicit methods
  - Is based on a through literature search
  - Performs a critical appraisal of individual studies
  - Synthesize the world literature on a specific issue
  - Use statistical techniques to combine data from valid studies (meta-analyses)

- Systematic review may or may not include meta-analysis

- Meta-analysis: A quantitative approach for systematically combining the results of previous research in order to arrive at conclusion about the body of research

# Systematic review VS Narrative review

<table>
<thead>
<tr>
<th>Narrative (Traditional) review</th>
<th>Systematic review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not always conduct extensive search</td>
<td>Extensive search</td>
</tr>
<tr>
<td>Rarely explicit about how they select the study. (Informal &amp; subjective, tend to be selective in citing reports that reinforce their preconceived idea)</td>
<td>Use explicit method with clear and reproducible eligibility criteria to select the study for review</td>
</tr>
<tr>
<td>Less rigorous critical appraisal</td>
<td>Rigorous critical appraisal</td>
</tr>
<tr>
<td>High risk of bias</td>
<td>Minimal bias</td>
</tr>
</tbody>
</table>
Literature review VS Systematic review VS Meta-analysis

- Literature review
- Systematic review
- Meta-analysis
Steps in conducting a systematic review

1. Formulating review question
2. Searching & Selecting study
3. Study quality assessment
4. Extracting data from studies
5. Data analysis and interpretation

PICO
- P: Patient or problem
- I: Intervention
- C: Comparison
- O: Outcome
Example

Mass media interventions for smoking cessation in adults (Review)

Bala MM, Strzeszynski L, Topor-Madry R, Cahill K

Formulate review question: Example

**Background:** Much of the literature is focused on the effects of tobacco control advertising on young people, but there are also a number of evaluations of campaigns targeting adult smokers, which show mixed results.

**Review question:** Whether mass media interventions can reduce smoking among adults?

- **P:** Current smoker
- **I:** Mass media Intervention
- **C:** No intervention
- **O:** Reduce smoking (measured by cigarette consumption, quit attempts, and quit rates)
Steps in conducting a systematic review

1. • Formulating review question
2. • Searching & Selecting study
3. • Study quality assessment
4. • Extracting data from studies
5. • Data analysis and interpretation

PICO
- P: Patient or problem
- I: Intervention
- C: Comparison
- O: Outcome
search method for identification of studies

- Only one database such as MEDLINE is not enough!
- Use multiple sources and start with the highest yield
  - Electronic databases and trial registers such as MEDLINE, EMBASE, The Cochrane Controlled Trials Register (CCTR), ClinicalTrials.gov, PsycINFO, Scopus
  - Checking of reference lists
  - Handsearching of key journal and conferences
  - Identify un-published study
  - Personal communication with experts in fields.
    - The searching electronic databases may uncover only half of all relevant studies and that contacting other experts is an important method!
- Use appropriate keywords & MeSH terms
How to search for unpublished clinical trial evidence?

*Out of sight but not out of mind*

A key challenge in conducting systematic reviews is to identify the existence and results of unpublished trials, and unreported methods and outcomes within published trials. An-Wen Chan provides guidance for reviewers on adopting a comprehensive strategy to search beyond the published literature.
Publication bias

- Positive results more likely to be published
- More likely to be published in English
- More likely to be published more than one
- More likely to be cited by others
Example: search method for identification of studies

Search methods for identification of studies

The Cochrane Tobacco Addiction Group search strategy was combined with ad hoc searches for any studies that referred to tobacco/smoking cessation, mass media and adults. We also searched the Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, PsycINFO, Dirline, Hstat, Healthstar, Science Direct, EIFL Direct, IBZ, IDEAL, Addiction Abstracts, ASSIA, ISI, ERIC, IBSS, Sociological Abstracts, Conference Paper Index, ProQuest, Springer Link, Swetsnet, and the ASH (Action on Smoking and Health) Database. In addition, we searched the reference lists of identified studies and checked the web sites of included mass media campaigns for additional data. The most recent search was carried out in February 2013.

Study selection process

- Decide if studies meet inclusion criteria and record reasons for exclusion
- Done by two independent review authors
- Beware of duplicate
- Define inclusion/exclusion criteria
  - Participants
  - Interventions and comparisons
  - Outcome
  - Study designs and methodological
Example: Study selection

**P:** Adults, 25 years or older who regularly smoke cigarettes

**I:** Mass media Intervention

- Channels of communication such as television, radio, newspapers, billboards, posters, leaflets or booklets intended to reach large numbers of people, and which are not dependent on person-to-person contact

- The purpose of the mass media intervention must be primarily to encourage smokers to quit.
Example: Study selection

**C:** No intervention

**O:** Tobacco cessation (measured by prevalence rates, quit rate) and/or tobacco reduction (measured by number of cigarette purchased or smoked, prevalence of daily smoking, quit attempts), measured at the longest follow-up, and at least 6 months from the beginning of the intervention.

Type of studies:

- RCT or quasi-RCT allocating communities, regions or states to intervention or control conditions.
- Control trials without randomization allocating communities, regions or states to intervention or control conditions.
- Interrupted time series
Example: Study selection

Figure 1. Prisma flow diagram of search results

Update search results: 1443 studies

Selected based on titles and abstracts: 136 papers;
Handsearching and websites: 10 papers;
Acquired as full-text papers: 146

Included in update: 3 papers (updating 1 existing included study)

Excluded based on titles and abstracts: 1307

Excluded based on full papers: 143;
10 new studies added to Excluded Studies table

Steps in conducting a systematic review

1. Formulating review question
2. Searching & Selecting study
3. Study quality assessment
4. Extracting data from studies
5. Data analysis and interpretation

PICO
- P: Patient or problem
- I: Intervention
- C: Comparison
- O: Outcome
Assess study quality

- Peer review does not guarantee the validity of published research
- Consider assessment by more than one observer
- Use simple checklists rather than quality scales
  - JADAD Score
  - Cochrane risk of bias tool
  - Newcastle-Ottawa Scale (NOS) – for observational study
  - Etc.
- Always assess concealment of treatment allocation, blinding, and handling of patient attrition
Example: Cochrane risk of bias tool

Cochrane handbook for systematic reviews of interventions

http://www.cochrane-handbook.org/

If the methodological quality of trials is inadequate then the findings of reviews of this material may also be compromised.

Solution: Assess study quality
Steps in conducting a systematic review

1. Formulating review question
2. Searching & Selecting study
3. Study quality assessment
4. Extracting data from studies
5. Data analysis and interpretation

PICO
- P: Patient or problem
- I: Intervention
- C: Comparison
- O: Outcome
Extract data

- Design and pilot data extraction form
- Consider data extraction by more than one observer
- Information from included study
  - Bibliographic details
  - Study characteristics
    - Design/method
    - Participants
    - Interventions
    - Outcome measures
  - Study results
    - Continuous outcome: Mean, SD, and/or SE
    - Dichotomous outcome: Number of events and N
Steps in conducting a systematic review

1. Formulating review question
2. Searching & Selecting study
3. Study quality assessment
4. Extracting data from studies
5. Data analysis and interpretation

PICO
- P: Patient or problem
- I: Intervention
- C: Comparison
- O: Outcome
Example: Data analysis

Data collection and analysis

Two authors independently assessed all studies for inclusion criteria and for study quality (MB, LS, RTM). One author (MB) extracted data, and a second author (LS) checked them.

Results were not pooled due to heterogeneity of the included studies and are presented narratively and in table form.
Heterogeneity

Issue: Are the studies combinable?

- Heterogeneity is variation between the results of a set of studies due to differences between studies with respect to
  - Participants (Condition, eligibility criteria, etc)
  - Interventions (Type of drug, dose, duration, mode of administration, etc)
  - Outcome (Type, follow-up duration, ways of measuring outcome, definition)
Test of Heterogeneity

- Chi-square test (Q statistics)
- $I^2 = \text{Percentage of total variation across studies that is due to heterogeneity rather than chance}$
  - $I^2 < 25\% = \text{low}$
  - $I^2 25-75\% = \text{moderate}$
  - $I^2 > 75\% = \text{high}$
- Visual inspections
Descriptive synthesis

- Describe studies
- Highlight similarity and differences
- Identify patterns of factors
Example: SR Results

Main results

Eleven campaigns met the inclusion criteria for this review. Studies differed in design, settings, duration, content and intensity of intervention, length of follow-up, methods of evaluation and also in definitions and measures of smoking behaviour used. Among nine campaigns reporting smoking prevalence, significant decreases were observed in the California and Massachusetts statewide tobacco control campaigns compared with the rest of the USA. Some positive effects on prevalence in the whole population or in the subgroups were observed in three of the remaining seven studies. Three large-scale campaigns of the seven presenting results for tobacco consumption found statistically significant decreases. Among the seven studies presenting abstinence or quit rates, four showed some positive effect, although in one of them the effect was measured for quitting and cutting down combined. Among the three that did not show significant decreases, one demonstrated a significant intervention effect on smokers and ex-smokers combined.

**Example: Meta analysis results**

**Figure 3. Analysis 3.1 Motivational enhancement versus brief interventions, cessation at 6 months or longer.**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Intervention Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown 2003</td>
<td>15</td>
<td>116</td>
<td>6</td>
<td>75</td>
<td>6.6%</td>
<td>1.62 [0.86, 3.98]</td>
<td></td>
</tr>
<tr>
<td>Colby 2005</td>
<td>3</td>
<td>43</td>
<td>1</td>
<td>42</td>
<td>0.9%</td>
<td>2.93 [0.32, 27.06]</td>
<td></td>
</tr>
<tr>
<td>Greenberg 1978</td>
<td>6</td>
<td>25</td>
<td>1</td>
<td>25</td>
<td>0.9%</td>
<td>6.00 [0.70, 46.29]</td>
<td></td>
</tr>
<tr>
<td>Hollis 2005 (1)</td>
<td>40</td>
<td>226</td>
<td>23</td>
<td>222</td>
<td>21.0%</td>
<td>1.71 [1.06, 2.76]</td>
<td></td>
</tr>
<tr>
<td>Horn 2007</td>
<td>1</td>
<td>40</td>
<td>1</td>
<td>34</td>
<td>1.0%</td>
<td>0.85 [0.06, 13.08]</td>
<td></td>
</tr>
<tr>
<td>Kelly 2006</td>
<td>7</td>
<td>30</td>
<td>4</td>
<td>26</td>
<td>3.9%</td>
<td>1.52 [0.50, 4.60]</td>
<td></td>
</tr>
<tr>
<td>Lipkus 2004</td>
<td>44</td>
<td>209</td>
<td>37</td>
<td>193</td>
<td>34.8%</td>
<td>1.10 [0.74, 1.62]</td>
<td></td>
</tr>
<tr>
<td>Myers 2005</td>
<td>4</td>
<td>26</td>
<td>1</td>
<td>28</td>
<td>0.9%</td>
<td>4.31 [0.51, 36.08]</td>
<td></td>
</tr>
<tr>
<td>Peterson 2009</td>
<td>36</td>
<td>414</td>
<td>20</td>
<td>398</td>
<td>19.1%</td>
<td>1.60 [0.94, 2.71]</td>
<td></td>
</tr>
<tr>
<td>Project EX Russia 2013</td>
<td>4</td>
<td>76</td>
<td>1</td>
<td>88</td>
<td>0.8%</td>
<td>4.63 [0.53, 40.55]</td>
<td></td>
</tr>
<tr>
<td>Project EX-1 2001</td>
<td>44</td>
<td>259</td>
<td>6</td>
<td>76</td>
<td>8.4%</td>
<td>2.16 [0.95, 4.96]</td>
<td></td>
</tr>
<tr>
<td>Sherbo 2005</td>
<td>5</td>
<td>13</td>
<td>2</td>
<td>13</td>
<td>1.8%</td>
<td>2.50 [0.59, 10.64]</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**

<table>
<thead>
<tr>
<th>Intervention Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>100.0%</th>
<th>1.60 [1.28, 2.01]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1477</td>
<td>1190</td>
<td>103</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 8.38, df = 11 (P = 0.68); I² = 0%
Test for overall effect: Z = 4.11 (P < 0.0001)

(1) At two years

---

**Citation:** Stanton A, Grimshaw G. Tobacco cessation interventions for young people. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD003289. DOI: 10.1002/14651858.CD003289.pub5.
How to report SR/Meta-analysis?

- PRISMA Statement (Preferred Reporting Items for Systematic Reviews and Meta-analyses)
Thank you