Evidence-Based Medicine Summarizing Evidence

Component 2 / Unit 5

Summarizing evidence

- For many tests and treatments, there are multiple studies such that one study does not tell the whole story
- As such, there has been a growing trend towards "systematic reviews" or "evidence reports" to bring all the evidence on a treatment or test together
- Per the Haynes 4S model (2001), syntheses bring primary data together while synopses make it available to users in highly digested form
- Summarizing the evidence has many methodological challenges (Helfand, 2005)

Steps in creating a systematic review (Guyatt, 2008)

- Define the question – population, intervention, comparison, outcome(s)
- Conduct literature search – define information sources and searching strategy
- Apply inclusion and exclusion criteria – for articles retrieved and measure reproducibility
- Abstract appropriate data
- Conduct analysis – determine method of pooling, explore heterogeneity, and assess for publication and other bias

Results from a systematic review

- Often use meta-analysis, which combines results of multiple similar studies
- Systematic review ≠ meta-analysis
  - Studies may be too heterogeneous in terms of patient characteristics, settings, or other factors, e.g., telemedicine outcomes and diagnosis (Hersh, 2001; Hersh, 2002; Hersh, 2006)
- When meta-analysis is done, summary measures employed usually include odds ratio (OR) or weighted mean difference (WMD)

Usual meta-analysis summary statistics

- Odds ratio (OR)
  - Used for binary events, e.g., death, complication, recurrence, etc.
  - Usually configured such that OR < 1 indicates treatment benefit
  - If CI does not cross OR=1 line, then results are statistically significant
  - Can calculate NNT from OR
- Weighted mean difference (WMD)
  - Used for numeric events, e.g., measurements
  - Usually configured such that WMD < 0 indicates treatment benefit
  - If CI does not cross WMD=0 line, then results are statistically significant

Systematic reviews of treatment of cardiac risk factors

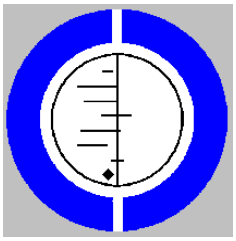
- A series of meta-analyses found benefits for lowering cholesterol (Law, 2003) blood pressure (Law, 2003), and homocysteine (Wald, 2002)
- Leading to a proposal for development of a "polypill" (six medications: statin, three blood pressure lowering drugs in half standard dose, beta blocker, folic acid, and aspirin) that could potentially reduce cardiovascular disease by 80% (Wald, 2003)
- Though a "polymeal" may be natural, safer, and tastier, with wine, fish, dark chocolate, fruits and vegetables, garlic, and almonds (Franco, 2004)
- Initial clinical trial in India found lowering of blood pressure and cholesterol but has not gone on long enough to assess outcomes (Lancet, 2009)

More recent meta-analyses

- Continued benefits for lipid reduction with statins
  - Meta-analysis of 20 trials found reduced cardiovascular and all deaths with no increased adverse events (Mills, 2008)
  - Meta-analysis of 10 trials of people with cardiovascular risk factors (no disease) found reduced risk and improved survival (Brugts, 2009)
  - Though some concerns: risk of diabetes (Sattar, 2009) and high NNT (Hadler, 2008; Wilson, 2010)
- Continued benefits for lowering blood pressure
  - Meta-analysis of 147 RCTs show reduction of coronary heart disease and death from all categories of antihypertensive drugs (Law, 2009)
- Walds continue to promote polypill (Wald, 2010)
- But is healthy living the "best revenge" (Ford, 2009)?
  - Never smoking, BMI < 30, 3.5 hours/week of exercise, and healthy diet associated with 78% lowered risk of developing a chronic disease (myocardial infarction, stroke, cancer, diabetes)

The Cochrane Collaboration

- An international collaboration with the aim of preparing and maintaining systematic reviews of the effects of health care interventions
- Largest producers of systematic reviews, limited to interventions
- www.cochrane.org
- Levin, 2001



The Cochrane Database of Systematic Reviews (CDSR)

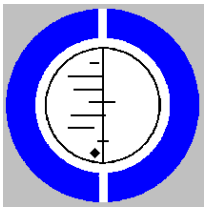
- It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials.
  - Archie Cochrane, 1972
- CDSR embodies Cochrane's vision
- About 2,000 reviews done but many more needed to cover medicine comprehensively

Elements of Cochrane reviews

- Statement of clinical problem or question
- Sources of evidence
  - Literature search
  - Non-experimental data, if included
- Inclusion/exclusion criteria
- Results in tabular and graphical form
- Conclusions
- Date of last update
  - Last update and last substantive update

Cochrane logo embodies content of reviews

- Most reviews include meta-analysis
  - This one: steroids in preterm labor
- Each horizontal line represents a single RCT
  - Span of line indicates CI
- All study questions configured relative to vertical line
  - Line represents OR=1 or WMD=0
  - Treatment benefit is to left of line
  - CI not touching line indicates statistical significance



Other sources of summarized evidence

- Meta-analyses scattered about the medical literature
- Evidence reports from Evidence-Based Practice Centers of AHRQ (www.ahrq.gov) (Atkins, 2005)
- Synopses
  - Clinical Evidence – "evidence formulary" published by BMJ
  - InfoPOEMS – "patient-oriented evidence that matters"
  - Physician's Information and Education Resource (PIER) from ACP (pier.acponline.org, also in Stat!-Ref)

Limitations of systematic reviews

- Not everyone accepts use of meta-analysis; Feinstein (1995) calls it “statistical alchemy”
- Meta-analyses on same topic sometimes reach different conclusions due to methodologic reasons (Hopayian, 2001)
- “Truth” determined by meta-analysis has the shortest “half life” of all knowledge (Poynard, 2002)
- Effect of publication bias may be exacerbated in systematic reviews (Dickersin, 1997)