Poll Everywhere intro: Enter a few words to describe your research interests
Evidence Synthesis
Topics to be introduced

1. Importance of evidence syntheses
2. What are some types of evidence syntheses?
3. Steps to a systematic review
4. Tools for evidence syntheses
Review Summary

Import references

Title and abstract screening

TEAM PROGRESS

246 DONE
0 ONE VOTE
0 CONFLICTS
755 NO VOTES

113 irrelevant
755 studies to screen

ROBIN, YOU CAN STILL
SCREEN
755
Continue

You’ve screened 247 studies so far

Full text screening

0 excluded
133 studies to select

Extraction

0 extracted
0 studies to extract
Do you have a Covidence account? Enter the email associated with your account here and I will invite you to this test review.
What we ARE NOT covering today:

• Statistics – how to do a meta-analysis
• In-depth training for creating comprehensive search strategies
• Basics covered in the earlier Literature Review sessions in the Bootcamp series
• ALL of the content on these slides! They are for your reference, but we won’t have time for all the details included here.
Did you attend any research bootcamp sessions last week or another year?

<table>
<thead>
<tr>
<th>Core Skills, Part 1 (Getting Started and Lit Review/Searching)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core Skills, Part 2 (Writing Lit Review and RefWorks)</td>
</tr>
<tr>
<td>Both Core Skills sessions</td>
</tr>
<tr>
<td>Core Skills + other sessions</td>
</tr>
<tr>
<td>Other research bootcamp session(s)</td>
</tr>
<tr>
<td>No, this is my first session</td>
</tr>
</tbody>
</table>
Evidence Informed Decision-Making

Use of current best evidence

– Health care policy
– Clinical practice

Importance

– Quality care
– Limited resources
Evidence for Decision-making

The LD₅₀ of toxicity data is 2 kilograms per kilogram.

http://xkcd.com/1260/
Evidence Synthesis

- **Single studies**: Original journal articles and studies. Examples: RCTs.
- **Synopses of studies**: Very brief descriptions of single articles, like a literature review. Example: critically-appraised topics.
- **Syntheses**: Provide an overview and analysis of multiple studies. Examples: systematic reviews, meta-analyses.
- **Synopses of syntheses**: Very brief descriptions of original reviews, often with recommendations for best practice. Example: Cochrane Summaries.
- **Summaries**: Integrate best evidence addressing all management options for a health problem. Example: evidence-based textbooks.
- **Systems**: Often patient-specific, linking between patient's condition and current best practices; not yet very common.
Knowledge Syntheses

- Evolving science
- Varying terminology
- Basic types reflect objectives and methods
- Scoping reviews: Map the literature to clarify boundaries & identify gaps
- Research syntheses: Studies are analyzed and summarized

What types of reviews (syntheses) have you heard of?
Systematic Reviews: A How-To Guide

Overview of systematic review steps and resources to assist researchers conducting reviews

Types of Reviews

Systematic reviews, while common in the health sciences field, are not the only type of review that exist. In their widely cited article entitled “A Typology of Reviews: An Analysis of 14 Review Types and Associated Methodologies,” Grant and Booth (2009) outline several major types of reviews, including the following (adapted from pages 94-95 in their article - see link below):

<table>
<thead>
<tr>
<th>Label</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical review</td>
<td>Aims to demonstrate the writer has extensively researched literature and critically evaluated its quality. Goes beyond mere description to include degree of analysis and conceptual innovation. Typically results in hypothesis or model.</td>
</tr>
<tr>
<td>Literature review</td>
<td>Generic term: published materials that provide examination of recent or current literature. Can cover wide range of subjects at various levels of completeness and comprehensiveness. May include research findings.</td>
</tr>
<tr>
<td>Mapping review/systematic map</td>
<td>Map out and categorize existing literature from which to commission further reviews and/or primary research by identifying gaps in research literature.</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>Technique that statistically combines the results of quantitative analyses.</td>
</tr>
</tbody>
</table>

Is a systematic review the right choice for my research team?

- I Want to Do a Systematic Review
  - This blog post by the Mayo Clinic Libraries outlines what makes a systematic review different from a traditional literature review. It also suggests some questions for your research team that can help you decide whether or not to embark on a systematic review.
- Quiz: What kind of review

Types of Reviews: More Resources

Websites
- The RAMESES Project
  - A guide to producing realist and...
A few methods…

http://libguides.utoledo.edu/litreview/types
# Types of Literature Reviews

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Systematic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Question</strong></td>
<td>Often broad in scope</td>
<td>Often a focused clinical question</td>
</tr>
<tr>
<td><strong>Sources &amp; Searches</strong></td>
<td>Not usually specified Potentially biased</td>
<td>Comprehensive source and strategy explicitly stated</td>
</tr>
<tr>
<td><strong>Selection</strong></td>
<td>Not usually specified Potentially biased</td>
<td>Criterion-based uniformly applied</td>
</tr>
<tr>
<td><strong>Appraisal</strong></td>
<td>Variable</td>
<td>Rigorous critical appraisal</td>
</tr>
<tr>
<td><strong>Synthesis</strong></td>
<td>Qualitative summary common</td>
<td>Qualitative summary +/- Meta Analysis</td>
</tr>
<tr>
<td><strong>Inferences</strong></td>
<td>Sometimes evidence-based</td>
<td>Evidence-based</td>
</tr>
</tbody>
</table>
Systematic Reviews:

What is a Systematic Review? - National Library of Medicine - PubMed Health
Which review type(s) would you like to learn more about? Rank in order of your interest

| Qualitative reviews | Rapid reviews | Realist reviews/syntheses | Scoping reviews | Systematic reviews | Evidence Synthesis |
Example: “Traditional” Review

Treatment of toxic epidermal necrolysis by a multidisciplinary team. A review of literature and treatment results


Abstract

Background

Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are mucocutaneous hypersensitivity reactions, usually to drugs or their metabolites. TEN is the most severe involving greater than 30% of the total body surface area (TBSA). Management of these patients usually benefits from a large multidisciplinary team for both wound and medical management. Treatment of these patients varies between centers and physicians and there is lack of a standardized treatment protocol in the medical literature.

Objectives

To review the literature and complete a retrospective review of patients treated at Vancouver General Hospital over a 11-year period.

Methods

A retrospective chart review of all patients diagnosed with SJS/TEN and treated at Vancouver General Hospital from 2001 to 2011 was completed. Data collected include patient demographics, time to transfer to a burn center, SCORTEN calculation, suspected cause of TEN, %TBSA involved, length of stay in hospital and ICU, medications, dressings, infections/cultures, fluids, mucosal involvement, teams involved, associated complications, morbidity and mortality. Data is reported quantitatively.
Example: Systematic Review

**How does tillage intensity affect soil organic carbon? A systematic review**

Several reviews and meta-analyses have shown both beneficial and null effects on SOC due to no tillage relative to conventional tillage, hence there is a need for a comprehensive systematic review to answer the question: what is the impact of reduced tillage intensity on SOC?

**Methods**

We systematically reviewed relevant research in boreo-temperate regions using, as a basis, evidence identified within a recently completed systematic map on the impacts of farming on SOC. We performed an update of the original searches to include studies published since the map search. We screened all evidence for relevance according to predetermined inclusion criteria. Studies were appraised and subject to data extraction. Meta-analyses were performed to investigate the impact of reducing tillage [from high (HT) to intermediate intensity (IT), HT to NT, and from IT to NT] for SOC concentration and SOC stock in the upper soil and at lower depths.
Example: Scoping Review

The state of the science on sensory factors and their impact on daily life for children: A scoping review

The objective of this study was to identify and synthesize research about how sensory factors affect daily life of children. We designed a conceptual model to guide a scoping review of research published from 2005 to October 2014 (10 years). We searched MEDLINE, CINAHL, and PsycINFO and included studies about sensory perception/processing; children, adolescents/young adults; and participation.
Example: Rapid Review

The value of the use of participatory arts activities in residential care settings to enhance the well-being and quality of life of older people: A rapid review of the literature

This rapid review of the literature explores the value of using participatory arts activities in residential care settings to enhance the health and well-being of older people. A rapid review of the literature published between 2000 and 2013 was undertaken and focused on participants aged 65 years and over living in residential care settings participating in arts activities such as music, dance, singing and the visual arts.
Example: Rapid Review

Due to time constraints, a rapid review was undertaken; this is a systematic literature review conducted within a limited time period (Petticrew & Roberts, 2006). The database search adopted a strategy similar to that followed by Daykin et al. (2008), but encompassed a wider range of participatory arts activities and focused on those aged 65 years and over living in residential care settings. The literature search took place during July–August 2013 and was conducted systematically. It was limited to English language publications from 2000 onwards. Google and Google Scholar were also used to track any grey literature. The Boolean search keyword groupings are shown in Table 1, and the searches were conducted on 26 different databases, as shown in Table 2...
Example: Integrative Review

Social Work Practices for Young People with Complex Needs: An Integrative Review

The aim of this integrative review is to investigate research of social work practices for adolescents and young adults with complex needs. The research questions are: What are the major themes in studies of practices for young people with complex needs? How do studies suggest that complex needs can be met in ways that are beneficial for young people? A young person with complex needs is in this review defined as an adolescent or young adult who, due to mental ill-health in combination with different types of social vulnerabilities, is receiving assistance from multiple welfare services. Searches were conducted in seven databases. These searches resulted in a sample of 1677 records, published 2007–2016, which in the screening process were reduced to 24 publications, all peer-reviewed articles.
Example: Integrative Review, cont’d

Social Work Practices for Young People with Complex Needs: An Integrative

…The articles were analyzed with qualitative summative content analysis. Three empirically generated themes were found in studies of work practices targeting young people with complex needs: collaboration-, relationship- and empowerment-oriented practices. In conclusion, the practices contain a wide variety of features, but with the joint aim of acknowledging young people’s needs. The results can be used by practitioners and policymakers to further the development of services for youth with mental ill-health and social vulnerabilities, who use multiple welfare services.
A research agenda that flows logically from the critical analysis of the literature. The research agenda should pose provocative questions (or propositions) that give direction for future research.

A taxonomy or other conceptual classification of constructs is often developed as a means to classify previous research. They, in turn, lay the foundation for new theorizing (Doty & Glick, 1994).

Alternative models or conceptual frameworks—new ways of thinking about the topic addressed by the integrative review. Alternative models or conceptions proposed by the author should be derived directly from the critical analysis and synthesis provided.

Metatheory—The integration and synthesis of a literature review can provide the basis for developing metatheory across theoretical domains through future research.
Example: Realist Review

Experiences with integrative Indigenous and Western knowledge in water research and management: A systematic realist review of literature from Canada, Australia, New Zealand, and the United States

The implementation of Indigenous and Western knowledge systems in integrative water research and management is gaining prominence in the realm of academia, particularly in four countries with a shared, albeit different, history of British colonialism: Canada, Australia, New Zealand, and the United States. While integrative water research in particular is gaining popularity, currently there is a gap in our understanding regarding where, when, why, how, and for whom this type of research has been successful. …
Example: Realist Review, cont’d

Experiences with integrative Indigenous and Western knowledge in water research and management: A systematic realist review of literature from Canada, Australia, New Zealand, and the United States

...A systematic review method was used to identify peer-reviewed literature from each of the four countries and to understand where and when integrative water research projects were taking place. Then, we used a realist review method to synthesize and analyze the included peer-reviewed literature to determine why, how, and for whom this type of research has been successful, or not.
Marijuana and College Students: A Critical Review of the Literature

Background: Marijuana represents the most widely used illicit drug on college campuses. Repeated use can impair students’ academic, emotional, and physical success and can lead to chronic diseases.

Purpose: The purpose of this study was to evaluate existing literature on the associated effects of marijuana use on U.S. college students’ academic success, including conduct/legal issues, negative outcomes, normative perceptions, and physical/mental health.
Marijuana and College Students: A Critical Review of the Literature

Method: A critical review was conducted in January 2015 using the PubMed, Academic Search Complete, Electronic Journal Center, ProQuest, and Google Scholar databases. Studies were included if they focused on epidemiological outcomes of marijuana use on U.S. undergraduate college students aged 17–24. Results: Overall, studies lacked scientific rigor. In several studies, researchers relied on convenience samples, used small sample sizes, did not report response rates, or did not report the psychometrics of the instrument. The majority of the studies were conducted at single institutions, limiting external validity.
Examples in other disciplines:

Review #1 Question

Question: What makes community programmes for children and youth with disabilities work?

PURPOSE:
To synthesise research literature describing elements of community recreation and leisure activities that create meaningful participation experiences for children and youth with disabilities.
What kind of review? Review #1

**METHOD:** Database searches of Medline, Embase, PsycINFO, ERIC, SportDiscus, CINAHL, Scopus and Web of Science were conducted. Studies describing the experience of participating in a community-based programme or activity from the perspectives of children and youth with a disability aged 0-21 or their parents, and published in English were included. Meta-ethnography was used to synthesise qualitative data, and resulting themes were conceptualised in the International Classification of Functioning, Disability and Health-Child and Youth version. Consultation with stakeholders occurred throughout the review process.
Review #1: What type of review?

- Meta-synthesis
- Integrative review
- Scoping review
- Meta-analysis
Review #2

The aim of this study was to examine how nurse-led interventions that support self-management of outpatients with chronic conditions work and in what contexts they work successfully.
What kind of review? Review #2

**Review Methods:** For each study, we described how the intervention was supposed to improve self-management and compared this with the empirical evidence. Next, we described the context-mechanism-outcome strings for each separate study, explored patterns and integrated the findings.
# Review #2: What kind of review?

<table>
<thead>
<tr>
<th>Type of Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic review</td>
</tr>
<tr>
<td>Realist review</td>
</tr>
<tr>
<td>Critical theory review</td>
</tr>
<tr>
<td>Scoping review</td>
</tr>
</tbody>
</table>
What approach would you propose to address the following:

The purpose of this review was to critically examine the construct of compassion fatigue and to determine if it is an accurate descriptor of work-related stress in healthcare providers and a valid target variable for intervention.
REVIEW METHODS: Seminal articles and theoretical and empirical studies on compassion fatigue in the healthcare literature were identified and appraised for their validity and relevance to our review. Sources were mapped according to the following criteria: 1) definitions; 2) conceptual analyses; 3) signs and symptoms; 4) measures; 5) prevalence and associated risk factors; and 6) interventions. A narrative account of included studies that critically examines the concept of compassion fatigue in healthcare was employed, and recommendations for practice, policy and further research were made.
### Review #3: What kind of review?

<table>
<thead>
<tr>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Realist review</td>
</tr>
<tr>
<td>Meta-analysis</td>
</tr>
<tr>
<td>Rapid review</td>
</tr>
<tr>
<td>Meta-narrative</td>
</tr>
</tbody>
</table>
Review #4

Objective: To evaluate the effect of omega-3 nutritional supplementation on clinical outcomes of adult critically ill patients with sepsis or septic shock
Review #4

We searched the Cochrane Library, MEDLINE, and EMBASE through December 2016 for RCTs on parenteral or enteral omega-3 supplementation in adult critically ill patients diagnosed with sepsis or septic shock. We analysed the included studies for mortality, intensive care unit (ICU) length of stay, and duration of mechanical ventilation, and used the Grading of Recommendations Assessment, Development and Evaluation approach to assess the quality of the evidence for each outcome.
<table>
<thead>
<tr>
<th>Review #4: What kind of review?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic review</td>
</tr>
<tr>
<td>Critical review</td>
</tr>
<tr>
<td>Scoping review</td>
</tr>
<tr>
<td>Rapid review</td>
</tr>
</tbody>
</table>
Review #5

The objective of this review was to identify, synthesize, and report the findings of evaluated breech birth training strategies.
Review #5

METHODS: A systematic search of the following on-line databases: Medline, CINAHL Plus, PsychINFO, EBM Reviews/Cochrane Library, EMBASE, Maternity and Infant Care, and Pubmed, using a structured search strategy. Studies were included in the review if they evaluated the efficacy of a breech birth training program or particular strategies, including obstetric emergency training evaluations that reported differentiated outcomes for breech. Out of 1040 original citings, 303 full-text articles were assessed for eligibility, and 17 methodologically diverse studies met the inclusion criteria. A data collection form was used to extract relevant information. Data were synthesized, using an evaluation levels framework, including reaction, learning (subjective and objective assessment), and behavioral change.
Review #5: What kind of review?

- Realist review
- Systematic review
- Integrative review
- Scoping review

Synthesis
Are some methods better than others?

• Greenhalgh T, Thorne S, Malterud K. **Time to challenge the spurious hierarchy of systematic over narrative reviews?.** European journal of clinical investigation. 2018 Mar 26:e12931.

How familiar are you with systematic reviews?
Systematic Reviews

Pre-defined, explicit methods:

– Clearly formulated research question
– Comprehensive search to identify studies
– Selection criteria for inclusion
– Data collection & critical appraisal
– Synthesis & reporting

Minimize potential biases at each step
Advantages of Systematic Reviews

- Reduced likelihood of being misled
- Increased confidence about expected outcomes
- Decision-makers can focus on local applicability
- Allows stakeholders to constructively contest research evidence
Most Research Reviews

Pre-defined, explicit methods:

– Clearly formulated research question
– Comprehensive search to identify studies
– Selection criteria for *inclusion*
– Data collection & *critical appraisal*
– Synthesis & reporting

Minimize potential biases at each step – or discuss limitations and context in which conclusions apply
Where to find systematic reviews

Who has read a systematic review?
– Where was it published?
Where to find systematic reviews, cont’d
### PubMed Clinical Queries

Results of searches on this page are limited to specific clinical research areas. For comprehensive searches, use PubMed directly.

<table>
<thead>
<tr>
<th>Search Term</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>atherosclerosis</td>
<td>5 of 24006</td>
</tr>
</tbody>
</table>

#### Clinical Study Categories

- **Category:** Therapy
- **Scope:** Broad

#### Systematic Reviews

**Results: 5 of 1175**


- Internet based vascular risk factor management for patients with clinically manifest vascular disease: randomised controlled trial.  
  BMJ. 2012 Jun 12; 344:e3750.  

- Helicobacter pylori infection contributes to high risk of ischemic stroke: evidence from a meta-analysis.  

#### Medical Genetics

**Results: 5 of 15097**

- Mice, men and the relatives: canine immunity.  
  Bryant CE, Monie TP.  
  PubMed Epub 2012 Apr 20.

- Impaired LDL Receptor-Related Protein 1 Correlates with Improved Dyslipidemia in apoE-Deficient Mice.  
  Gordts PL, Bartelt A, Nilsson SK, AnnaChristine Heeren J, Roebroeck AJ.  

- A Genome-Wide Association Study Identifies a Genetic Determinant of Plasma Partial Thromboplastin Time.  
Quality Appraisal of Systematic Reviews

PRISMA 2009 Checklist

SYSTEMATIC REVIEW: Are the results of the review valid?

CHOOSING EVIDENCE WORKSHEET
1E. Summarizing the Evidence

Are the results valid?

- Did the review explicitly address a sensible clinical question?
- Were the results from relevant studies detailed and exhaustive?
- Was the methodology adequate for the logic quality?
### Quality Appraisal of Systematic Reviews

- CEBM Systematic Review Appraisal Sheet
- CASP Systematic Review Checklist
- AMSTAR 2: A MeaSurement Tool to Assess systematic Reviews
Reporting Guidelines

- PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist
- Equator Network (Reporting and transparency)
Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation (selection bias)</th>
<th>Allocation concealment (selection bias)</th>
<th>Blinding of participants and personnel (performance bias)</th>
<th>Blinding of outcome assessment (detection bias)</th>
<th>Incomplete outcome data (attrition bias)</th>
<th>Selective reporting (reporting bias)</th>
<th>Other bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman 2006</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Ramsook 2002</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Roslund 2008</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Stork 2006</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Uhlig 2009</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Yilmaz 2010</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Cochrane Database of Systematic Reviews
7 SEP 2011 DOI: 10.1002/14651858.CD005506.pub5
1.8.1 Required IV rehydration

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemtic Events</th>
<th>Placebo Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman_2006</td>
<td>15</td>
<td>33</td>
<td>0.45 [0.26, 0.79]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>7</td>
<td>107</td>
<td>0.74 [0.29, 1.87]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>0</td>
<td>83</td>
<td>0.05 [0.00, 0.78]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>7</td>
<td>62</td>
<td>0.25 [0.12, 0.54]</td>
</tr>
<tr>
<td>Roslund_2008</td>
<td>11</td>
<td>51</td>
<td>0.40 [0.22, 0.70]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>377</strong></td>
<td><strong>356</strong></td>
<td><strong>0.40 [0.26, 0.60]</strong></td>
</tr>
</tbody>
</table>

Total events 40, 104

Heterogeneity: Tau² = 0.07; Chi² = 5.69, df = 4 (P = 0.22); I² = 30%

Test for overall effect: Z = 4.36 (P < 0.0001)

1.8.2 Required admission

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemtic Events</th>
<th>Placebo Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman_2006</td>
<td>4</td>
<td>107</td>
<td>0.80 [0.22, 2.90]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>1</td>
<td>74</td>
<td>0.95 [0.06, 14.83]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>1</td>
<td>82</td>
<td>3.04 [0.13, 73.46]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>3</td>
<td>62</td>
<td>0.15 [0.05, 0.50]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>2</td>
<td>46</td>
<td>0.21 [0.05, 0.93]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>2</td>
<td>46</td>
<td>0.29 [0.06, 1.33]</td>
</tr>
<tr>
<td>Uhlig_2009</td>
<td>10</td>
<td>117</td>
<td>0.70 [0.32, 1.54]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>534</strong></td>
<td><strong>509</strong></td>
<td><strong>0.44 [0.23, 0.82]</strong></td>
</tr>
</tbody>
</table>

Total events 23, 51

Heterogeneity: Tau² = 0.19; Chi² = 8.26, df = 6 (P = 0.22); I² = 27%

Test for overall effect: Z = 2.57 (P = 0.01)

1.8.3 Return to ED

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Antiemtic Events</th>
<th>Placebo Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freedman_2006</td>
<td>20</td>
<td>105</td>
<td>0.87 [0.51, 1.50]</td>
</tr>
<tr>
<td>Gouin_2012</td>
<td>11</td>
<td>74</td>
<td>0.58 [0.29, 1.14]</td>
</tr>
<tr>
<td>Qazi_2014</td>
<td>14</td>
<td>58</td>
<td>3.09 [1.19, 8.05]</td>
</tr>
<tr>
<td>Ramsook_2002</td>
<td>4</td>
<td>74</td>
<td>8.64 [0.47, 157.62]</td>
</tr>
<tr>
<td>Reeves_2002</td>
<td>4</td>
<td>54</td>
<td>1.31 [0.31, 5.57]</td>
</tr>
<tr>
<td>Roslund_2008</td>
<td>3</td>
<td>48</td>
<td>1.72 [0.30, 9.86]</td>
</tr>
<tr>
<td>Stork_2006</td>
<td>8</td>
<td>27</td>
<td>6.22 [0.84, 45.94]</td>
</tr>
<tr>
<td>Uhlig_2009</td>
<td>4</td>
<td>102</td>
<td>0.76 [0.21, 2.75]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>542</strong></td>
<td><strong>532</strong></td>
<td><strong>1.31 [0.73, 2.35]</strong></td>
</tr>
</tbody>
</table>

Total events 68, 56

Heterogeneity: Tau² = 0.31; Chi² = 14.44, df = 7 (P = 0.04); I² = 52%

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Chi² = 11.50, df = 2 (P = 0.003), I² = 82.6%
Exploring heterogeneity

From CEBM Systematic Review Appraisal Sheet

Heterogeneity can be assessed using the “eyeball” test or more formally with statistical tests, such as the Cochran Q test. With the “eyeball” test one looks for overlap of the confidence intervals of the trials with the summary estimate. In the example above note that the dotted line running vertically through the combined odds ratio crosses the horizontal lines of all the individual studies indicating that the studies are homogenous. Heterogeneity can also be assessed using the Cochran chi-square (Cochran Q). If Cochran Q is statistically significant there is definite heterogeneity. If Cochran Q is not statistically significant but the ratio of Cochran Q and the degrees of freedom (Q/df) is > 1 there is possible heterogeneity. If Cochran Q is not statistically significant and Q/df is < 1 then heterogeneity is very unlikely. In the example above Q/df is <1 (0.92/4= 0.23) and the p-value is not significant (0.92) indicating no heterogeneity.

Note: The level of significance for Cochran Q is often set at 0.1 due to the low power of the test to detect heterogeneity.
Steps to a systematic review:

a) Developing the protocol
b) Defining the review question
c) Literature searching
d) Study selection
e) Risk of bias assessment
f) Data collection
g) Analysis & Reporting
Why would YOU conduct a systematic review?

Justification for research project (often prerequisite to grant proposal)

Project for a research block or thesis
  – Good chance of publication

Your supervisor tells you to do a systematic review!
Publication

Where do systematic reviews get published?

General medical/health profession journals: *BMJ*, *CMAJ*, *Annals of Internal Medicine*, *Nursing Research*, etc.

Specialty topic journals: *Cancer*, *Circulation*, etc.

Cochrane Database of Systematic Reviews
Conducting a systematic review will also...

Give you an excellent grasp of the state of research on a topic of interest to you
  – Helps identify gaps in the existing research
  – Highlights best practices

Increases your understanding of how research is conducted and reported
  – The critical appraisal and assessment of bias used in conducting a systematic review will increase your ability to conduct rigorous, well-reported research
Many meta-analysis studies include the phrase "we searched Medline, Embase, and Cochrane for studies..."

This has led to meta-meta-analyses comparing meta-analysis methods.


We performed a meta-meta-meta-analysis of these meta-meta-analyses.

Methods: We searched Medline, Embase, and Cochrane for the phrase "we searched Medline, Embase, and Cochrane for the phrase "we searched Medline, Embase, and Cochrane for the phrase "we searched Medline, Embase, and Cochrane for the phrase "...

Life goal #28: Get a paper rejected with the comment "too meta"
Important resource for conducting a SR

http://dal.ca.libguides.com/systematicreviews
Instructional resources for conducting systematic reviews:

**Cochrane Training** Learn how to conduct, edit, and read systematic reviews from various training resources. Some restricted to Cochrane Authors.

**Joanna Briggs Institute** Includes information on short courses, online courses. Fees apply.

**John Hopkins MOOC** Free MOOC offered several times per year. Next session starts June 11, 2018.
Steps to a systematic review:

a) **Developing the protocol**
   b) Defining the review question
   c) Literature searching
   d) Study selection
   e) Risk of bias assessment
   f) Data collection
   g) Analysis & Reporting

Done

Planned
Prospective Register of Systematic Reviews: PROSPERO

http://www.crd.york.ac.uk/PROSPERO/
Example Timeline - Systematic Review

- **Protocol**: 3-6 months
- **Search**: 1-2 months
- **Study Selection**: 2-3 Months
- **Risk of bias assessment**: 3-4 months
- **Data extraction**: 1-2 months
- **Analysis and reporting**: 2-3 months

Total duration: 1-2 years
Importance of the Review Question

- Transparency
- Minimizes bias
- Facilitates subsequent steps:
  - Search strategy
  - Selection of studies
  - Planning the analysis
  - Reporting of results
More examples of review questions – beware!

Example – What antibiotic is best for treating UTIs?

Challenges – not specific regarding intervention, comparison, and key outcomes

Solutions – compare two specific drugs, or one compared to several (or no treatment); specify severity of condition and outcomes of interest (e.g., presence of bacteria in culture, reduced duration of symptoms, recurrence)
Do prophylactic antibiotics help prevent recurrent UTIs in healthy, non-pregnant women?

Topics to be Introduced

1. Importance of literature syntheses
2. What are systematic reviews?
3. Steps to a systematic review:
   a) Developing the protocol
   b) Defining the review question
   c) Literature searching
      d) Study selection
      e) Risk of bias assessment
      f) Data collection
      g) Analysis & Reporting
Phases of the Comprehensive Literature Search

Identify existing systematic reviews
  – E.g. the Cochrane Library; Experts

Scoping search
  – Initial search on small range of databases

Comprehensive, systematic search
  – Full search; multiple sources

Update the search during the review process

Watch Yale video tutorials:
http://library.medicine.yale.edu/tutorials/subjects/systematic-reviews
Sources for Locating Studies

Electronic bibliographic databases (e.g. Medline, EMBASE, CINAHL, Cochrane Library)

Specialized registers of trials (CENTRAL, Cochrane review group registries)

Hand-searching relevant journals

Reference lists
  – Other reviews
  – Included studies

Grey literature
  – Pharmaceutical companies
  – Internet

Personal communication
  – suggestions from experts
  – contacting study authors
Isn't it all in PubMed?

Q: Why do I have to use more than one database? Isn't it all in PubMed/Medline?

A: No, it is not all in PubMed/Medline.


From: http://beckerguides.wustl.edu/c.php?g=299565&p=2000712
Developing the Database Search Strategy

- Get help from a librarian
- Review question components: PICO
- Subject headings and free text:
  - Exemplar articles & reviews
  - Cochrane Review Groups
- Boolean operators (AND, OR, NOT)
- Study design filters
Meet with a librarian to help develop and refine your search strategies!

The librarian can also serve as a peer-reviewer to confirm that there are no errors or oversights in your final search strategies.
Search strategy translated to multiple databases

<table>
<thead>
<tr>
<th>Table 1. Search strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MEDLINE (OVID) and Central (OVID)</strong></td>
</tr>
<tr>
<td>1. Acupuncture/ or acupuncture.mp.</td>
</tr>
<tr>
<td>4. electroacupuncture/ or electroacupuncture.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>5. moxibustion.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>6. medicine, oriental traditional/ or medicine, chinese traditional/</td>
</tr>
<tr>
<td>7. Oriental Traditional Medicine.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>8. Chinese traditional medicine.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>9. or/1-8</td>
</tr>
<tr>
<td>10. arthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>11. arthritis/ or exp osteoarthritis/</td>
</tr>
<tr>
<td>12. osteoarthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word]</td>
</tr>
<tr>
<td>13. exp clinical trial/</td>
</tr>
<tr>
<td>14. exp randomized controlled trial/</td>
</tr>
<tr>
<td>15. randomized.ab.</td>
</tr>
<tr>
<td>16. placebo.ab.</td>
</tr>
</tbody>
</table>

| **EMBASE (OVID)** |
| 1. exp ACUPUNCTURE/ or acupuncture.mp. |
| 5. moxibustion.mp. |
| 6. traditional medicine.mp. or exp Traditional Medicine/ |
| 7. 1 or 2 or 3 or 4 or 5 or 6 |
| 8. arthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word] |
| 9. arthritis/ or exp osteoarthritis/ |
| 10. osteoarthritis.mp. [mp=title, original title, abstract, name of substance word, subject heading word] |
| 11. (joint diseases or arthralgia or joint pain or chronic joint symptoms or gonarthritis or osteoarthritis or ostearthritis or degenerative arthritis).mp. [mp=title, original title, abstract, name of substance word, subject heading word] |
| 12. or/8-11 |
| 13. exp clinical trial/|
| 14. exp randomized controlled trial/ |
| 15. randomized.ab. |
| 16. placebo.ab. |
Final Search Strategy

Complete & finalized at the protocol stage

Describe in detail:
- Allow replication
- Facilitate update -> save searches and set alerts!

Document throughout the search process:
- Sources
- Strategies
- Time periods
- Any restrictions
Searches done in all databases?
Next steps…

- Export to citation management software (RefWorks, EndNote, Mendeley, etc.) AND/OR systematic review management software (Covidence, DistillerSR, Rayyan, etc.)
- Identify and Remove duplicate citations
- If using RefWorks etc., need to export for screening to Excel, Covidence, etc.
Study Selection Criteria

Decisions about study inclusion/exclusion:
  – Based on design
  – NOT results

Standardized process (decision rules)
  – Transparent
  – Guide decisions
  – Produce consistent results

Operationalize PICO \textit{a priori}

Studies (not reports) are unit of interest
Study Selection Process

Separate step from collecting data

Pilot test selection criteria

Phases of selection:
– Initial screen (Title & Abstract)
– Detailed screen (Full text)

Two reviewers with consensus
– Each reviewer: Yes, No, Unclear
– Include notes & comments

Track excluded articles & reasons

Consider using Systematic Review Management Software such as Covidence!!
Study Selection: Additional issues

Uncertain inclusion (after full review)
  Information from other publications of the same study
  Contact the study author

Non-English language publications
  Risk of bias if excluded (some topic areas)
  Capture in the search
  Translation assistance
If you don’t have a Covidence account…
log in with:
kellogg@dal.ca
kellogg

https://www.covidence.org/reviews/33703
Topics to be Introduced

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   g) Analysis & Reporting
Risk of Bias Assessment

Component of ‘Quality Assessment’
Internal validity of included studies
Assessment of key potential biases

Validity of included studies will influence:
- Analysis & results
- Interpretation
What is bias?

• Systematic error or deviation from the truth in results or inferences

• Can operate in either direction:
  – Underestimation
  – Overestimation of true treatment effect

• Results of the review could be misleading if risk of bias is not considered

• Empirical evidence:
  – Flaws in design, conduct, analysis lead to bias
Incorporating Risk of Bias Assessments

- Not appropriate to ignore potential biases
- Explore the impact of individual bias domains
- Include in analyses
  - Primary analysis restricted to studies with low Risk of Bias
    - Sensitivity analyses may include higher risk studies
Data collection

*A priori* determine:
- ‘Who’ (two people, independent), and
- ‘How’ (process) to minimize bias

Data extraction form:
- Paper or electronic
- Develop information and instructions
- Pilot test

Study characteristics:
- PICO information
- Potential sources of heterogeneity
Overview of Analysis

• Different analytical methods:
  – Qualitative synthesis
  – Meta-analysis
  – Meta-regression
• Strengths & limitations with each
• Methods should be pre-specified and justified
Quantitative Synthesis
Systematic Review ≠ Meta-analysis

Systematic reviews: use well-defined protocol and methodological principles to attempt to reduce bias
  – Can be qualitative or quantitative

Meta-analysis: statistical analysis of a collection of independent studies
  – Quantitative part of SOME systematic reviews
Why perform a Meta-analysis?

Synthesis: Estimate overall measure of treatment effect
- Combine data from primary studies
- Improve precision of estimate of treatment effect
- Improve statistical power

Exploratory: Assess between-study differences
- Exploring heterogeneity
- Assess sensitivity to study characteristics
- Generate new hypotheses
When is Meta-analysis NOT appropriate?

• If studies are clinically diverse
  – Results may be meaningless
  – Genuine differences may be obscured

• Not appropriate to pool if important differences:
  – Population
  – Intervention
  – Comparisons
  – Outcomes

• Presence of serious publication or reporting biases
Reporting Results

Tables and figures
Forest plots to illustrate results of individual studies and meta-analyses ([Review Manager software – free download](http://www.prisma-statement.org/))

Discussion in context
- Benefits & harms
- Completeness and applicability of evidence
- Quality of the evidence

Implications for practice & for research

Use PRISMA checklist to guide in reporting:
Where to go for more assistance

Systematic literature searching and overview of evidence synthesis process and tools:
– Health Librarians at Dalhousie’s W. K. Kellogg Health Sciences Library (students and faculty)
– http://dal.ca.libguides.com/systematicreviews
More assistance, cont’d
Statistics/meta-analyses:

– RMU/Faculty of Medicine Biostatistics
  Consultants: [http://www.cdha.nshealth.ca/discovery-innovation/research-centres-and-facilities/research-methods-unit](http://www.cdha.nshealth.ca/discovery-innovation/research-centres-and-facilities/research-methods-unit)

– Statistics experts in your faculty

– RevMan software

– **Statistics software through Dalhousie: SPSS**
References


Questions?

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OR
kellogg@dal.ca

Thank you!