Evidence synthesis: Integrative & mixed methods systematic reviews

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Integrative reviews or evidence synthesis of mixed methods studies

- Include quantitative and qualitative studies
- Can be used for empirical research and health policy
- See Joanna Briggs Institute, Adelaide
- Reputable journals publish systematic reviews and integrative reviews
Overview

• Briefly look at approaches for evidence synthesis of quantitative and qualitative studies

• Provide some examples of published systematic and integrative reviews

• Methodological issues and developments
Quantitative approaches to evidence synthesis

- Content analysis

- Bayesian approaches - cross design synthesis
  - meta-analysis
  - decision analysis

- Qualitative comparative analysis using Boolean logic

Interpretive approaches to evidence synthesis

Used mainly for qualitative studies

• Meta-synthesis
• Meta-study
• Qualitative meta-analysis

• Comparative approaches - grounded theory
  - case study

• Translation based approaches – meta-ethnography

See Pope et al (2007), p72
Mixed approaches to synthesis of quantitative and qualitative studies/evidence

• Integrative reviews

• Thematic analysis - reflect directly main ideas/conclusions

• Realist synthesis – testing causal/theories of change, what works?

• Narrative synthesis

• Combining separate syntheses: the EPPI approach

• Meta narrative review


<table>
<thead>
<tr>
<th>Quantitative</th>
<th>Qualitative</th>
<th>Integrative (Quan and Qual)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrative review</td>
<td>Case survey method (Yin &amp; Heald 1975)</td>
<td>Integrative review (Kirkevold, 1997)</td>
</tr>
<tr>
<td>Cochrane review (1993)</td>
<td>- reciprocal translational synthesis</td>
<td>Narrative synthesis</td>
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<tr>
<td><a href="http://www.cochrane.org/">http://www.cochrane.org/</a></td>
<td>- refutational synthesis</td>
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<td></td>
<td>- lines-of- argument synthesis (Noblit &amp; Hare 1988)</td>
<td>* Combining separate synthesis – EPPI approach</td>
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<td></td>
<td></td>
<td>* Combining separate synthesis – EPPI approach</td>
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<td>Meta narrative review</td>
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</tbody>
</table>
Systematic reviews of quantitative and qualitative studies/evidence

• Provide the broadest category of systematic review and can include empirical evidence from quantitative and qualitative studies as well as theoretical or ‘grey’ policy literature.

• They incorporate the findings from a variety of research designs

• As they involve multiple methodological perspectives, they are more complex to undertake

• There is no widely accepted standard but developments in the methods of systematic reviews have contributed to their development
Systematic reviews of quantitative and qualitative studies/evidence

• These reviews aim to include quantitative and qualitative studies and may also incorporate other levels of evidence on a topic.

• They are systematic and rigorous and have the potential to present a comprehensive context and evidence on a health or social care topic or concern. They do not just relate to evidence on effectiveness.

• Due to their complexity the challenges relate to resources, expertise, rigour, transparency and interpretation.

See Evans (2007); Whittemore (2007); Whittemore & Knafl (2005)
Systematic reviews of quantitative and qualitative studies/evidence

• Important to follow international standards for methods and reporting

PRISMA Statement [http://www.prisma-statement.org](http://www.prisma-statement.org)
(See Moher et al 2009; Liberati et al 2009)

PICOS –
- Population/participants
- Intervention
- Comparator groups
- Outcomes or endpoints
- Study design/setting
(See Higgins & Green 2010; Liberati et al 2009)
Welcome to the PRISMA Statement website

PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. It is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.

The aim of the PRISMA Statement is to help authors improve the reporting of systematic reviews and meta-analyses. We have focused on randomized trials, but PRISMA can also be used as a basis for reporting systematic reviews of other types of research, particularly evaluations of interventions. PRISMA may also be useful for critical appraisal of published systematic reviews, although it is not a quality assessment instrument to gauge the quality of a systematic review.

The PRISMA Statement consists of a 27-item checklist and a four-phase flow diagram. It is an evolving document that is subject to change periodically as new evidence emerges. In fact, the PRISMA Statement is an update and expansion of the now-outdated QUOROM Statement. This website contains the current definitive version of the PRISMA Statement.

We invite readers to comment on the PRISMA Statement by contacting us.

The PRISMA Explanation and Elaboration document explains and illustrates the principles underlying the PRISMA Statement. It is strongly recommended that it be used in conjunction with the PRISMA Statement.

PRISMA is part of a broader effort to improve the reporting of different types of health research, and in turn to improve the quality of research used in decision-making in healthcare.
PRISMA 2009 Flow Diagram

1. Identification
   - # of records identified through database searching
   - # of additional records identified through other sources
   - # of records after duplicates removed

2. Screening
   - # of records screened
   - # of records excluded

3. Eligibility
   - # of full-text articles assessed for eligibility
   - # of full-text articles excluded, with reasons

4. Included
   - # of studies included in qualitative synthesis
   - # of studies included in quantitative synthesis (meta-analysis)

For more information, visit www.prisma-statement.org.
Systematic reviews of quantitative and qualitative studies/evidence

Systematic steps, considerations and procedures

• Purpose
• Protocol development, registration and publication
• Problem identification
• Inclusion and exclusion criteria
• Locating studies and searching the literature
• Evaluating studies - classification of studies and evidence
  - inclusion or exclusion of reference
  - quality appraisal
• Data extraction
• Data analysis
Systematic reviews of quantitative and qualitative studies/evidence

Data analysis
- descriptive data synthesis
- statistical data synthesis and meta-analysis
- qualitative data synthesis
  - narrative summary/ synopsis
  - thematic analysis
  - meta-ethnography
  - grounded theory techniques e.g.
    - constant comparison
  - meta-study
- content analysis – qualitative but can convert qualitative data to quantitative data (QUAL/quan)

See Evans (2007)
Methodological procedures to reduce sources of error in integrative reviews

1. Literature search and sample selection
   Use multiple search strategies
   Evaluate quality of primary sources and effort in analysis

2. Data analysis
   Define coding procedures
   Use piloted data extraction form
   Have two independent reviewers extract data from primary sources
   Develop inclusion and exclusion criteria to avoid double counting
   Critique primary sources and include quality assessment of analysis
   Include all evidence from primary sources in data analysis
   Explore variability of findings, conflicts and rival hypotheses
Methodological procedures to reduce sources of error in integrative reviews

3. Conclusion drawing

Use systematic and objective methods
Use well-specified data extraction and analysis procedures

Systematic Review of Respite Care in the Frail Elderly (Shaw et al 2009)

Objectives: To assess effectiveness and cost effectiveness of breaks in care in improving well-being in informal carers of frail and disabled older people living in the community and to identify carer needs and barriers to uptake of respite services

Data sources: Major electronic databases were searched from the earliest possible date to April 2008

MEDLINE, EMBASE, PsychoInfo, AMED, ASSIA, IBSS CINAHL, Econolit, Social Care Online, Sociological Abstracts, Web of Science, Cochrane's databases of reviews and trials (CDSR, CMR, CENTRAL, DARE). PubMed Cancer Citations, Scopus and databases of ongoing research (NRR, CRISP)
Review methods:

• Selected studies were assessed and subjected to:

  • Extraction of numerical data for meta-analysis of quantitative studies (104 papers)

  • Extraction of text for thematic analysis of qualitative studies (70 papers)

• Independent data extraction and quality appraisal by two reviewers was undertaken with cross check for consensus

• Separate specifically designed data extraction and quality appraisal forms for quantitative or qualitative studies were used
Results: Quantitative synthesis

104 papers identified, 16 appropriate for meta-analysis

• Carer burden was reduced at 2-6 months’ follow up in single sample studies but not in RCTs and quasi-experimental studies

• Depression was reduced in RCTs in the short term and for home care but not for day care

These effects were not significant in random-effects models

There was a trend for longer interventions to have more positive effects than shorter interventions
Results: Quantitative synthesis

- There was no effect of respite on anxiety, but it had positive effects on morale and anger and hostility. Single group studies suggested that quality of life was worse after respite use.

- There were increased rates of institutionalisation after respite use; however, this does not establish a causal relationship as it may be a result of respite being provided late in the care giving career.
Results: Qualitative synthesis

70 papers identified for inclusion

Uptake of respite care was influenced by:

• carer attitudes to caring and respite provision
• the care giving relationship
• knowledge of, and availability of, services
• the acceptability to, and impact of respite care
• quality of respite care
• the appropriateness and flexibility of service provision

Respite should provide a mental break and not just a physical break
Carers expressed needs for active information provision about Services and support early in the care giving experience
Conclusions:

• There was some evidence to support respite having a positive effect on carers but the evidence was limited and weak

• There was a lack of good-quality larger trials and respite interventions were varied, often with poor descriptions of the characteristics of interventions and limited provision and uptake

• There was also a lack of economic analysis

Implications for health care
Recommendations for research

See Shaw et al (2009) for report of integrative/ systematic review
Integrative reviews incorporating quan & qual studies using narrative synthesis


Used an adapted quality appraisal checklist by Bowling (2002)

- Clarity of aims
- Objectives
- Methods
- Data analysis

Compared studies checklist scores available in supporting table S1
Table S1. Comparison of studies utilizing Bowling’s checklist for critical appraisal of scientific literature (Bowling 2002)

✓ Reported, x Not reported

<table>
<thead>
<tr>
<th>Checklist</th>
<th>Observational Studies</th>
<th>Interviews</th>
<th>Audit of Clinical Software</th>
<th>Questionnaires</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearly stated aims &amp; objectives</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Study design adequately described</td>
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<td>✓</td>
<td>x</td>
<td>✓</td>
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<tr>
<td>Appropriate research methods</td>
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<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Appropriate use of instruments (reliability and validity)</td>
<td>✓</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Adequate description of source sample, inclusion/exclusion criteria, response rates</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Statistical power discussed</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ethical considerations discussed</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Study piloted</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Appropriate analyses (statistical or qualitative)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Results clear and adequately reported</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Discussion of results reported in light of study question &amp; relevant literature</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Limitations of research &amp; design discussed</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Implications of research discussed</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Integrative reviews incorporating quan & qual studies using narrative synthesis


• Also used the adapted Bowling (2002) quality appraisal checklist by Desborough et al.

• The checklist did not address possible threats to validity for experimental studies so they also used Quality Assessment Informatics Instrument QUASII (Weir et al 2009)
Quality appraisal tools

- Checklists
- Scales
- Domain based
Cochrane Collaboration Quality appraisal

GRADE Assessing the risk of bias using the GRADE methodology framework – The Grading of Recommendations, Assessment, Development and Evaluation

Intervention studies – RCTs
Observational studies

Cochrane qualitative research methods group
http://cqrmg.cochrane.org/
Core Library of Qualitative Synthesis
Resources for Conducting Qualitative Synthesis
Quality appraisal of qualitative studies CERQUAL
GRADE

“A systematic and explicit approach to making judgements about the quality of evidence, and the strength of recommendations can help to prevent errors, facilitate critical appraisal of these judgements, and can help to improve communication of this information.”

Courtesy of Toni Tan, NICE
Organisations that have adopted GRADE methodology

<table>
<thead>
<tr>
<th>Agency for Healthcare Research and Quality (USA)</th>
<th>Joint (Japan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agenzia Sanitaria Regionale (Italy)</td>
<td>Journal of Infection in Developing Countries (International)</td>
</tr>
<tr>
<td>American College of Chest Physicians (USA)</td>
<td>Kidney Disease: Improving Global Outcome (International)</td>
</tr>
<tr>
<td>American College of Physicians (USA)</td>
<td>Ministry for Health and Long-Term Care, Ontario (Canada)</td>
</tr>
<tr>
<td>American Thoracic Society (USA)</td>
<td>National Board of Health and Welfare (Sweden)</td>
</tr>
<tr>
<td>Arztliches Zentrum fur Qualitat in der Medizin (Germany)</td>
<td><em>National Institute for Health and Care Excellence (United Kingdom)</em></td>
</tr>
<tr>
<td>British Medical Journal (United Kingdom)</td>
<td>Norwegian Knowledge Centre for the Health Services (Norway)</td>
</tr>
<tr>
<td>BMJ Clinical Evidence (United Kingdom)</td>
<td>Polish Institute for EBM (Poland)</td>
</tr>
<tr>
<td>COMPUS at The Canadian Agency for Drugs and Technologies in Health (Canada)</td>
<td><em>SIGN (UK, Scotland)</em></td>
</tr>
<tr>
<td>The Cochrane Collaboration (International)</td>
<td>Society for Critical Care Medicine (USA)</td>
</tr>
<tr>
<td>EMB Guidelines (Finland/International)</td>
<td>Society for Vascular Surgery (USA)</td>
</tr>
<tr>
<td>The Endocrine Society (USA)</td>
<td>Spanish Society for Family and Community Medicine (Spain)</td>
</tr>
<tr>
<td>European Respiratory Society (Europe)</td>
<td>Surviving Sepsis Campaign (International)</td>
</tr>
<tr>
<td>European Society of Thoracic Surgeons (International)</td>
<td>University of Pennsylvania Health System Center for Evidence-Based Practice (USA)</td>
</tr>
<tr>
<td>Evidence-based Nursing Südtirol (Italy)</td>
<td>UpToDate (USA)</td>
</tr>
<tr>
<td>German Center for Evidence-based Nursing “sapere aude” (Germany)</td>
<td><em>World Health Organization (International)</em></td>
</tr>
<tr>
<td>Infectious Diseases Society of America (USA)</td>
<td></td>
</tr>
<tr>
<td>Japanese Society for Temporomandibular</td>
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</tbody>
</table>
‘Traditional’ approach
Checklist system

- **Selection bias**: randomisation, concealment of allocation, comparable at baseline
- **Performance bias**: blinding (patients & care providers), the comparison groups received the same care apart from the intervention studied.
- **Attrition bias**: systematic differences between the comparison groups with respect to participants lost
- **Detection bias**: appropriate length of follow-up, definition of outcome, blinding (investigators)

<table>
<thead>
<tr>
<th>++</th>
<th>All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought <strong>very unlikely</strong> to alter.</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought <strong>unlikely</strong> to alter the conclusions.</td>
</tr>
<tr>
<td>-</td>
<td>Few or no criteria fulfilled. The conclusions of the study are thought <strong>likely or very likely</strong> to alter.</td>
</tr>
</tbody>
</table>
GRADE

- Interventional studies of effectiveness
- Currently in development for diagnostic accuracy studies, prognostic and qualitative studies
- Makes sequential appraisal about:
  - The quality of evidence across studies for each critical/important outcome (instead of individual study)
  - Which outcomes are critical to a decision
  - The overall quality of evidence across these critical outcomes
  - The balance between benefits and harms
- Result is an assessment of:
  - Quality of the evidence for an outcome
  - Strength of the recommendations
- Perspective of guideline developers

Courtesy of Toni Tan, NICE
How is this achieved?

• Transparent framework to consider confidence (certainty) of an effect estimate through assessing
  o Systematic errors (bias)
  o Chance errors (random errors)

• Using criteria
  o Systematic errors (bias)
  o Limitations, Indirectness, Inconsistency
  – Chance errors (random error)
    o Imprecision
    o Other considerations (any other factors)

Courtesy of Toni Tan, NICE
## GRADE Definitions

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>
Worked example


Review

‘Informed and uninformed decision making’—Women’s reasoning, experiences and perceptions with regard to advanced maternal age and delayed childbearing: A meta-synthesis

Alison Cooke\textsuperscript{a,*}, Tracey A. Mills\textsuperscript{b}, Tina Lavender\textsuperscript{c}

- Quality assessment tool developed by Walsh & Downe; 2005
- Grading tool developed by Downe et al. 2009, based on work by Lincoln & Guba, 1985.

Courtesy of Alison Cooke
<table>
<thead>
<tr>
<th>Stages</th>
<th>Essential Criteria</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scope and Purpose</td>
<td>Clear statement of, and rationale for, research questions/aims/purposes</td>
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<tr>
<td></td>
<td>Study thoroughly contextualised by existing literature</td>
<td></td>
</tr>
<tr>
<td>Design</td>
<td>Method/design apparent, and consistent with research intent</td>
<td></td>
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<tr>
<td></td>
<td>Data collection strategy apparent and appropriate</td>
<td></td>
</tr>
<tr>
<td>Sampling Strategy</td>
<td>Sample and sampling method appropriate</td>
<td></td>
</tr>
<tr>
<td>Analysis</td>
<td>Analytic approach appropriate</td>
<td></td>
</tr>
<tr>
<td>Interpretation</td>
<td>Context described and taken account of in interpretation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clear audit trail given</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Data used to support interpretation</td>
<td></td>
</tr>
<tr>
<td>Reflexivity</td>
<td>Researcher reflexivity demonstrated</td>
<td></td>
</tr>
<tr>
<td>Ethical Dimensions</td>
<td>Demonstration of sensitivity to ethical concerns</td>
<td></td>
</tr>
<tr>
<td>Relevance and Transferability</td>
<td>Relevance and transferability evident</td>
<td></td>
</tr>
</tbody>
</table>
## Grading System

created by Downe et al based on the work by Lincoln & Guba

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>No, or few flaws. The study credibility, transferability, dependability and confirmability is high.</td>
</tr>
<tr>
<td>B</td>
<td>Some flaws, unlikely to affect the credibility, transferability, dependability and/or confirmability of the study.</td>
</tr>
<tr>
<td>C</td>
<td>Some flaws that may affect the credibility, transferability, dependability and/or confirmability of the study.</td>
</tr>
<tr>
<td>D</td>
<td>Significant flaws that are very likely to affect the credibility, transferability, dependability and/or confirmability of the study.</td>
</tr>
</tbody>
</table>
Quality appraisal tools

• Compare and contrast the checklists, scales and domain based appraisal tools
  – Look at types of ‘quality’ assessed
  – Look at how items are assessed
  – Identify at least one strength and one weakness for each of the tools

Courtesy of Michelle Maden
What are you appraising conduct or reporting?

Quality of reporting compared with actual methodological quality of 56 RCTs conducted by Radiation Oncology Group

Things to consider

• Role of the reviewer (Booth, 2007)
  – Knowledge
  – Novice vs. expert

• Purpose of tool

• How does it assess ‘quality’?

• Weighting – is equal weighting fair?

• How will you use judgements of quality?

• Valid/reliable?

Courtesy of Michelle Maden
Margarete Sandelowski et al USA - NIH funded review

Mixed methods synthesis of research on childhood chronic conditions and family. Text in context (JAN 2012, 69,6, 1428-1437)

• New method for data extraction from mixed-methods mixed research synthesis studies

• Aimed to preserve text-in-context of findings

• Data extraction and integration to preserve methodological context of findings when statements read individually and in comparison to each other

• Concurrently used Bayesian meta-analysis and realist synthesis
Lucas et al 2007. Worked examples of alternative methods for synthesis of qualitative and quantitative research in systematic reviews. http://www.biomedcentral.com/1471-2288/7/4

- Systematic review of lay perspectives of infant size and growth 19 studies (quan & qual)
- Data extraction and synthesis using textual and thematic synthesis
- Found both have strengths and weaknesses in relation to research questions
- Thematic synthesis most potential for hypothesis generation, but may obscure heterogeneity and quality appraisal
- Textual narrative synthesis able to describe scope of existing research, account for strength of evidence but less good at identifying homogeneity
Literature searching and locating studies

• Higgins & Green – Cochrane Handbook for highly sensitive search strategy for RCTs

Five search strategies with term pressure ulcers, searched seven electronic databases and looked at sensitivity, specificity, precision and accuracy of each strategy
  Subject specific strategies identified all studies while research methodology strategies did not identify qualitative data in mixed methods studies
MEDLINE, CINHAL, EMBASE produced most yields

Some suggested references


Thank you

Any Questions?

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Barbara Hepworth – The Hepworth in Wakefield Exhibition – 2012/013
Studies of Orthopaedic Surgeons at Work in NHS Hospitals