Use of Non-Randomized Study Designs in Evidence-based Practice Center Reports

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RCT evidence limited for many questions

- New devices and surgical therapies, public health and system interventions, etc.

Controversy over use of non-randomized studies (NRS) to assess effectiveness

- Deeks et al., HTA Review 2003

Other possible reasons to include NRS

- Explore generalizability of RCTs
- Long-term outcomes not examined in RCTs
- Estimate expected outcomes for consumers
13 AHRQ-funded research centers

“User-driven” agenda
- Reviews support guidelines, quality measures, coverage decisions, research agenda

Scope and questions shaped by AHRQ, partner, experts and EPC
- “Best-evidence” approach encouraged

Methodology follows general principles but exact approach varies
Objectives

Examine use of non-randomized study designs in EPC reports, to review:

- Inclusion criteria
- Variation by topic area
- Quality assessment
  - Methods used
  - How quality incorporated
- Influence of NRS on conclusions
• Inclusion criteria
• Contribution to total body evidence
• Quality assessment
• Use of quality assessment
Evidence Practice Center reports completed 1998-2004

107

Report included ≥1 clinical effectiveness question

78

Included NRS in search

51

Included NRS in review

49

No clinical effectiveness question

29

Included RCTs only

27

No studies found

2
Rationale for Including Non-Randomized Study Designs

49 Reports

- Rationale not reported - 30
- Insufficient RCTs - 18
- Generalizability - 1

Best evidence:
- Explicit
- Implicit
Study Designs of Included NRS

- Reports containing NRS: 49
  - RCTs: 44
    - Non-randomized trials: 24
  - Prospective Cohort: 28
  - Retrospective Cohort: 16
  - Case control: 9
  - Cross-Sectional: 5
  - Time series, before-after, case series: 25
Figure 2. Study design and type of intervention

Study design by topic area

Type of intervention:
- Pharmacotherapy
- Surgery
- Complementary and alternative medicine
- Behavioral interventions

Frequency (number of reports):
- Randomized controlled trial
- Nonrandomized trials
- Prospective cohort
- Retrospective cohort
- Before-after, case series
- Inclusion
- Contribution to total body evidence
- Quality assessment
- Influence on conclusions
Contributions of Study Designs to Total Body of Evidence

49 Reports

- RCTs >75% total # studies: 19
- RCTs 25-75% total # studies: 18
- RCTs <25% total # studies: 12
- No RCTs: 5
• Inclusion
• Contribution to total body evidence
• Quality assessment
• Influence on conclusions
Quality Assessment Used in Reports

Percent (n=49)

- No QA
- Previously published checklist/score
- Adapted from previously published checklist/score
- In-house, ≤3 attributes
- In-house, >3 attributes
Was Quality of NRS Discussed in Results?

49 Reports

- Performed QA: 36
- No QA: 13

Narrative results: 29
Conclusions: 30
Future research: 35
Not presented: 1
Inclusion
Contribution to total body evidence
Quality assessment
Influence on conclusions
Influence on Conclusions

- A small number of reports based conclusions (qualified) primarily on NRS
  - Islet cell transplantation for DM
  - Total knee replacement (vs. medical mgt.)
  - Surgery for obesity (vs. medical care)
  - Vaginal birth after Cesarean
  - Management of clinically inapparent adrenal mass

- Often NRS had little apparent effect on conclusions
  - May reflect availability of RCT evidence
  - Limitations in NRS designs
Total Knee Arthroplasty and Revisions

- Both TKA and TKAR are associated with improved function … over a follow-up period of up to two years.
- The mean effect size … is considered large in magnitude and varies from 1.6 to 3.9 …
- There is reason to suspect selection effects in both the type of patients referred for TKA and those being reported in the literature as well as the attrition on follow-up.
- These conclusions are tempered by the limitations of the designs of many studies included in the analysis.
Study Limitations

- Single series of reports by one program
- Methods influenced by stakeholders
- Single reviewer extraction
- Retrospective extraction of information
Results in Context

- Similar issues identified in Deeks review
- Of 1162 systematic reviews:
  - 50% included NRS
  - 5% had *only* uncontrolled studies
- Of these 35% used some quality assessment
  - About 40% develop own tool
  - 40% used existing tool
  - 20% modified existing tool
Conclusions

- Variability in terminology, inclusion criteria, quality assessment and synthesis
- Rationale for including NRS not transparent
- Small number of reports base conclusions primarily on NRS
- Influence of NRS (if any) on conclusions not explicit
Recommendations for the Use of Nonrandomized Studies

Reviewers

- Assess availability of RCTs prior to deciding to include NRS
- Consider specific purpose of including NRS and limitations of specific study designs
  - Provide explicit rationale for inclusion in review
- Clarify terminology for included study designs
  - Describe key design features
- Assess important domains of quality
- Make explicit the contribution of NRS results to conclusions
Recommendations for Research on Use of NRS

Researchers

- Explore direction and extent of bias in specific NRS designs
  - For specific outcomes and interventions
  - Additional studies comparing estimates of effectiveness in RCT vs. NRS

- Examine efficient search strategies

- Test/adapt recommended quality assessment tools

“A strong presentation is designed to close down debate, not open it up”

Sherry Turkle, MIT