



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

Susan L. Norris, MD, MSc, MPH
David Atkins, MD, MPH (presenter)

Context

- 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



AHRQ's Evidence-Based Practice Center Program

- 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

No clinical effectiveness
question

29

Included NRS in search

51

Included RCTs only

27

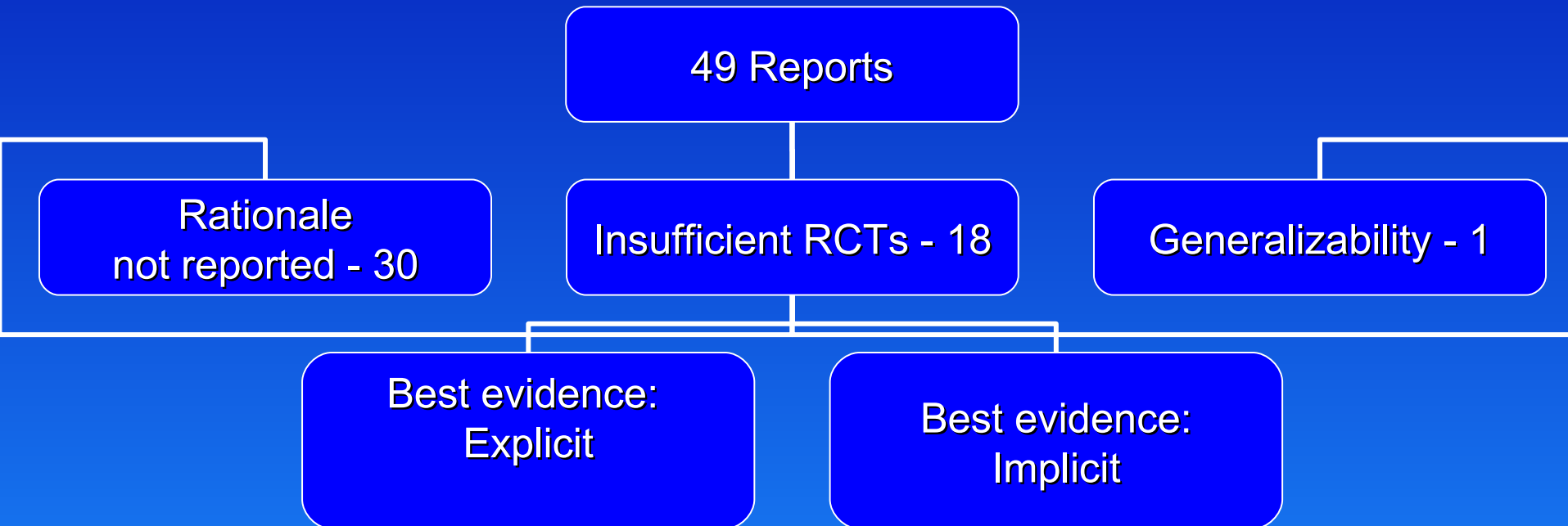
Included NRS in review

49

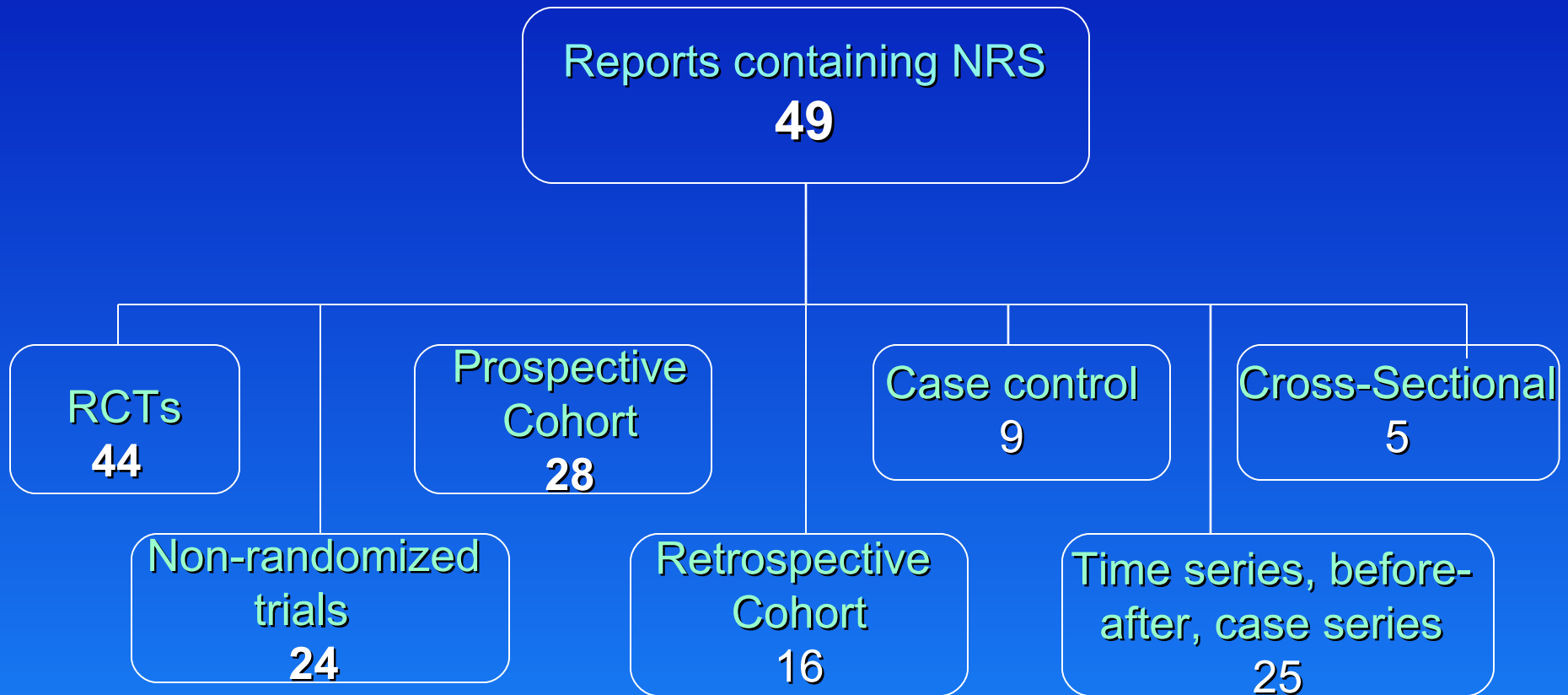
No studies found

2

Rationale for Including Non-Randomized Study Designs

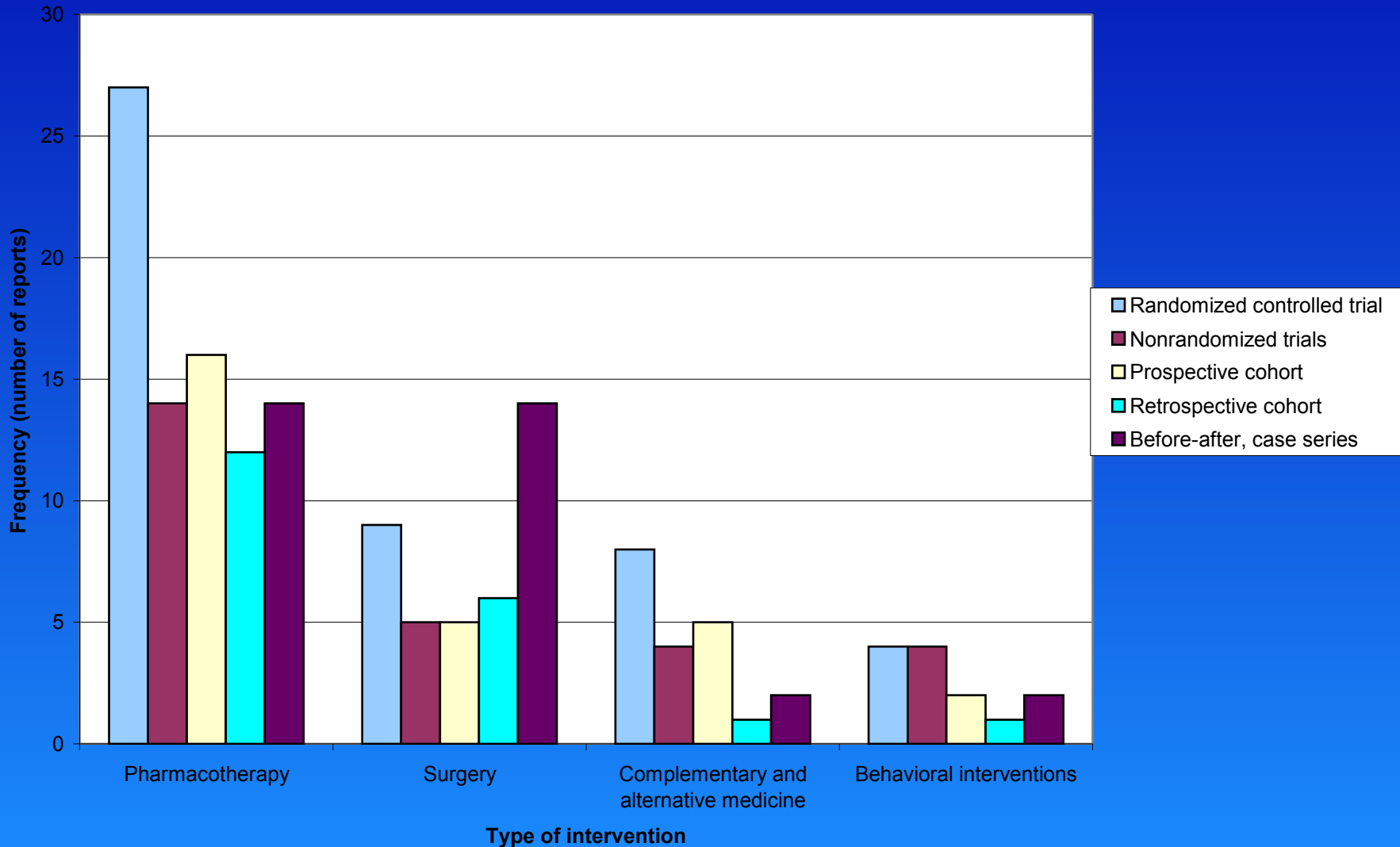


Study Designs of Included NRS



Study design by topic area

Figure 2. Study design and type of intervention





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- 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

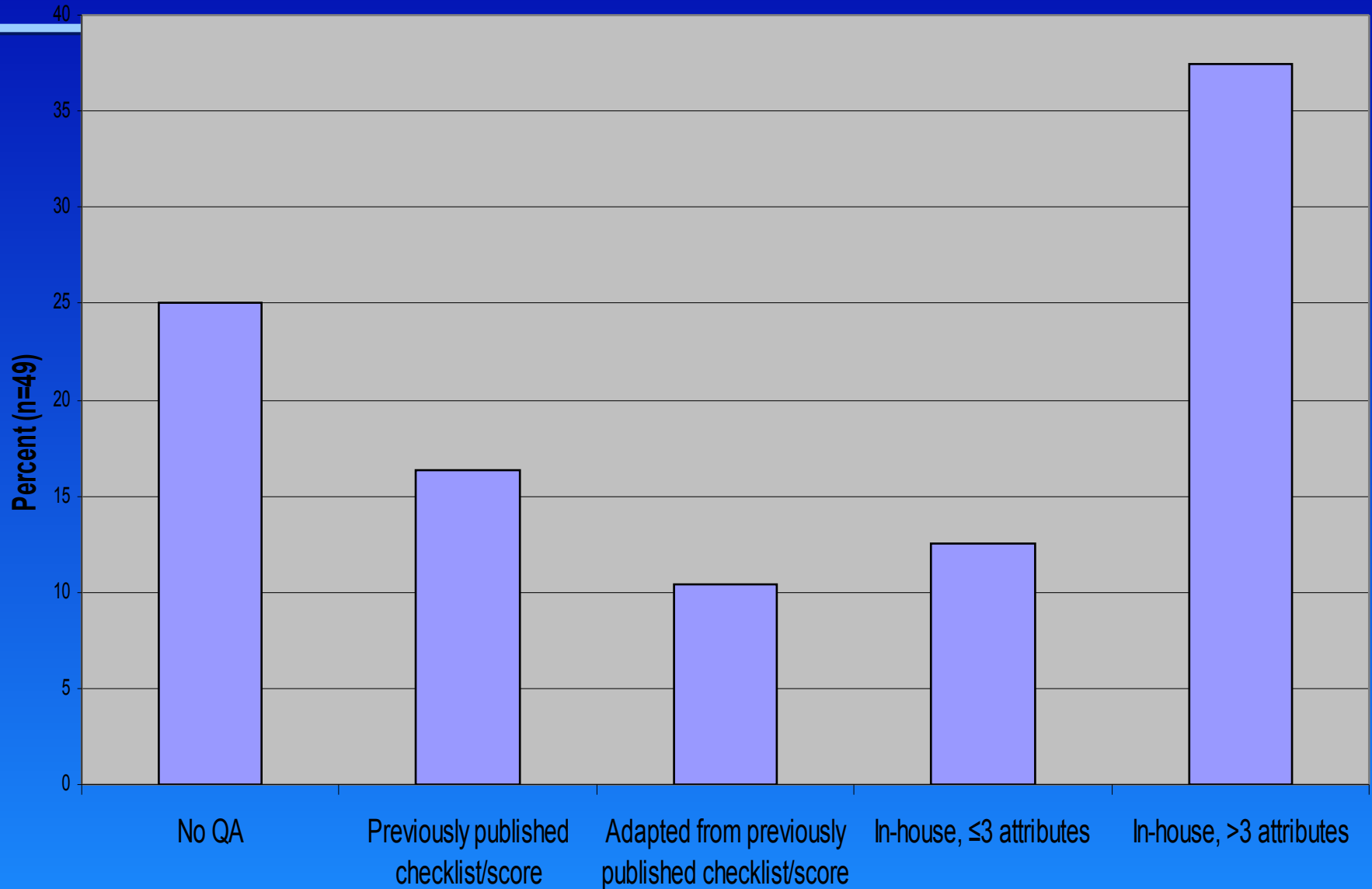
RCTs 25-75%
total
studies:
18

RCTs <25% total
studies:
12

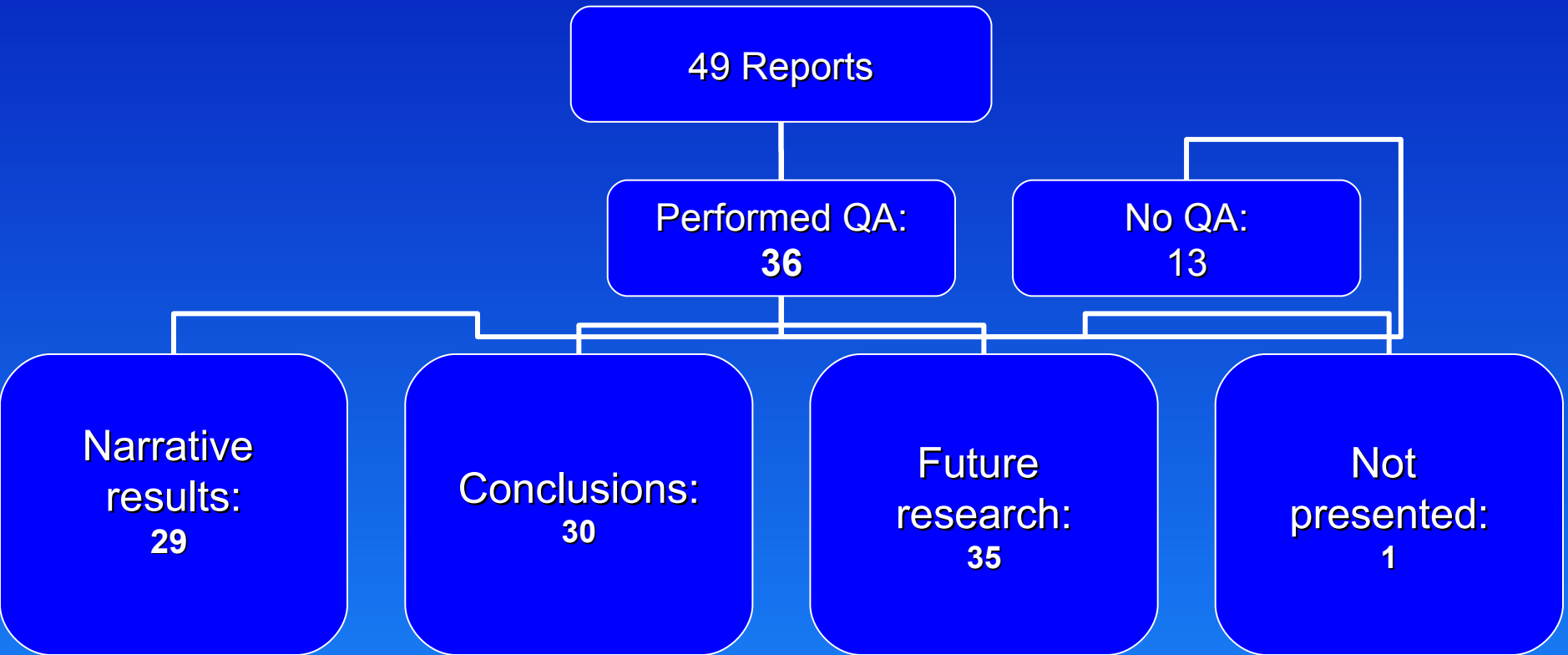
No RCTs:
5

- Inclusion
- Contribution to total body evidence
- **Quality assessment**
- Influence on conclusions

Quality Assessment Used in Reports



Was Quality of NRS Discussed in Results?





-
- **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



Example of conclusions based on NRS

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



Closing

- Norris SL, Atkins D. *Challenges in Using Nonrandomized Studies in Systematic Reviews of Treatment Interventions*. *Ann Intern Med*. 2005;142:1112-1119.
- “A strong presentation is designed to close down debate, not open it up”
Sherry Turkle, MIT