

What's the harm in harms?

New AHRQ EPC Program guidance for
selection of harms

Karen A. Robinson

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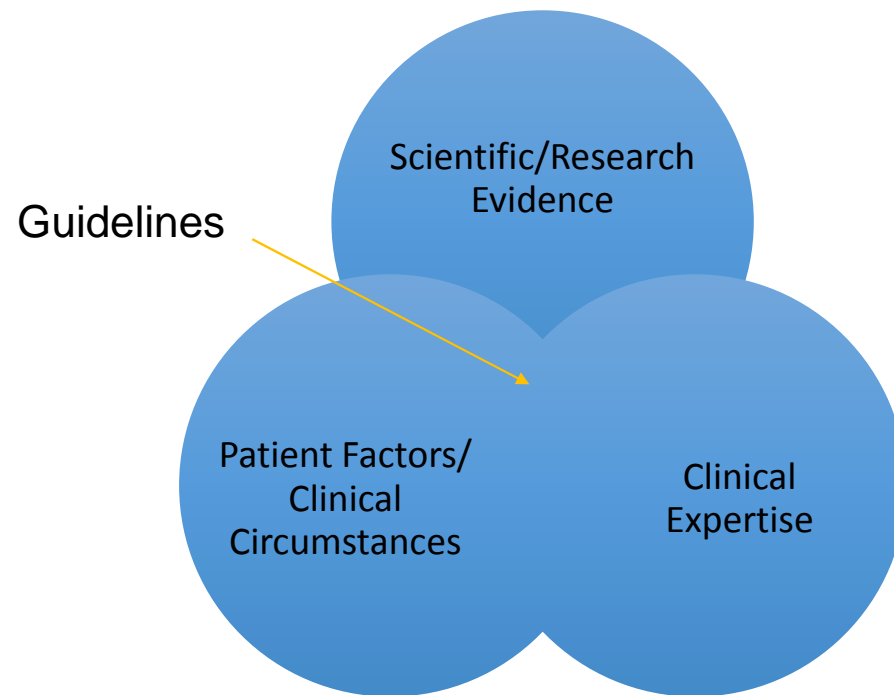


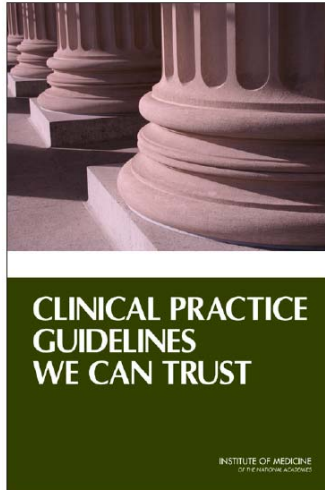
Evidence-based Medicine

“The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”

- Sackett et al., 1996

Evidence-based Decision-making





“Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of the evidence and an assessment of the benefits and harms of alternative care options.”

IOM (Institute of Medicine). 2011. *Clinical Practice Guidelines We Can Trust*. Washington, DC: The National Academies Press

Challenges

- Systematic reviews (SRs) methods guidance focus on efficacy
- AEs are the primary outcome in less than 10% of systematic reviews
- Data on harms are often pooled without consideration of heterogeneity
- Few SRs assess specific quality of studies for harms
- Lack of details on how harms defined

EPC Program Guidance (2010)

- Assess all important harms, whenever possible.
- Use multiple sources of information, including clinical experts and stakeholders, to identify important harms.
- Use consistent and precise terminology when reporting data on harms, and avoid terms implying causality unless causality is reasonably certain.
- Gather evidence on harms from a broad range of sources, including observational studies, particularly when clinical trials are lacking; when generalizability is uncertain; or when investigating rare, long-term, or unexpected harms.
- Do not assume studies adequately assess harms because methods used to assess and report benefits are appropriate; rather, evaluate how well studies identify and analyze harms.
- Be cautious about drawing conclusions on harms when events are rare and estimates of risk are imprecise.
- Include placebo-controlled trials, particularly for assessing uncommon or rare harms, but be cautious about relying on indirect comparisons to judge comparative risks, and evaluate whether studies being considered for indirect comparisons meet assumptions for consistency of treatment effects.
- Avoid inappropriate combining of data on harms, and thoroughly investigate inconsistent results.

EPC Program Guidance (2018)

"Assess all important harms, whenever possible." (EPC Guidance, 2010)

Focus: Prioritization and selection of harms

- 12 people from EPCs, AHRQ, SRC
- Methods:
 - Literature review
 - Review of EPC reports
 - Interviews with experts

Literature Search

- SRC Methods Library from 2007
- 257 citations identified. No empiric research on prioritization or selection
 - Prior EPC methods guidance:
 - “important to decision makers”
 - High priority are serious harms or most common events
 - To select harms use prior reviews, FDA reports, postmarketing surveillance, TEP
 - Cochrane:
 - General guidance regarding narrow or broad focus
 - GRADE
 - Rec: Guideline panels prioritize all outcomes using 1-9 rating system

Review of EPC reports

- 18 reports from 2014
- No report described:
 - How harms selected
 - Formal prioritization methods
 - Sources used to inform selection

Interview with experts

- 14 experts: conduct of reviews, assessment of harms, users of reviews
- Interviews guided by 12 questions around:
 - Use of guidance for prioritization or selection of harms
 - Criteria for prioritizing
 - Use of input from stakeholders
 - Use of other sources of information
 - Thresholds for maximum number of harms to include
 - Inclusion of composite harms
 - Methods for addressing harms not included in protocol
 - Reporting of methods for prioritizing and selecting harms

Question	Result
Use of guidance for prioritization or selection of harms	No.
Criteria for prioritizing	No. “importance to decision makers”; regardless of evidence
Use of input from stakeholders	Clinicians; patients
Use of other sources of information	FDA MedWatch; case reports
Thresholds for maximum number of harms to include	No. Limiting outcomes to 7 could exclude important harms
Inclusion of composite harms	Facilitate comparisons; more serious composite
Methods for addressing harms not included in protocol	Hypothesis generating
Reporting of methods for prioritizing and selecting harms	Helpful to include

Recommendations

1. Include harms that are of greatest importance to decision-makers.
2. Use a prioritization process to help narrow the number of harms included in a review.
3. The specific prioritization process used can vary. The prioritization may be informal (e.g., input or informal interviews with experts in the field, patients, and other stakeholders; literature search; review of information from regulatory agencies) or more formal (e.g., Delphi or GRADE-like scoring process).
4. The method used to prioritize harms should be concordant with methods used to select outcomes related to benefit.
5. Routinely include serious harms or less serious but frequent or bothersome harms, or describe why they are not included.

Recommendations

6. Composite adverse events may help facilitate comparisons across interventions; routinely consider including “serious adverse events” or “withdrawal due to adverse events,” particularly when evaluating head-to-head comparisons.
7. For reviews that involve effects of diagnostic tests, consider inclusion of overdiagnosis and overtreatment, as well as other harms related to diagnostic testing (e.g., false positives and false negatives and effects thereof, labeling, and others).
8. A reasonable rule of thumb is to limit to 5-10 prioritized harms for each comparison involving two interventions, though there is no preset threshold for the number of harms selected for a review.
9. Be prepared to add harms to the review that were not specified in the original protocol or identified in the prioritization process; in some cases, findings for such harms will be considered hypothesis generating.
10. Report the methods used to prioritize harms, differentiate serious from frequent but less serious harms, and indicate interventions for which serious harms are not believed to be an issue and why.

Next Steps?

- Future research:
 - Which study types should be considered?
 - How best to report? (PRISMA harms checklist)

- Our EPC?

References

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