Module 9: Putting it All Together: Appraising a Systematic Review

Category 11: Systematic Reviews

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**Abstract:** Multiple glucose-lowering drugs are available for patients with type 2 diabetes mellitus, but uncertainty exists about their effects on long-term cardiovascular outcomes. In this review, we examine the evidence on the effects of oral glucose-lowering drugs on cardiovascular risk factors and outcomes ...
Appraising a Review: Is It Really a Systematic Review?


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What should you look for to be convinced it is a systematic review?

- Focused question specifying population, interventions, comparisons, and outcomes
- Documented comprehensive search of evidence sources
- Explicit criteria for including studies
- Assessment of study quality
- Systematic approach to qualitative or quantitative synthesis
“PURPOSE: To summarize English-language literature on benefits and harms of oral agents (sulfonylureas, biguanides, thiazolidinediones, meglitinides and α-glucosidase inhibitors) in treatment of adults with type 2 diabetes.

DATA SOURCES: MEDLINE, EMBASE, and Cochrane Central Register databases were searched from inception thru Jan 2006 for original articles. FDA and industry data were also searched.

STUDY SELECTION: 216 controlled trials and cohort studies, and 2 systematic reviews that addressed benefits and harms of oral diabetes drug classes available in U.S.

DATA EXTRACTION: Using standardized protocols, 2 reviewers serially abstracted data.”
DATA SYNTHESIS:

“Most oral agents ... improved glycemic control to the same degree as sulfonylureas (absolute decrease in hemoglobin A1c level of about 1 percentage point). Nateglinide and alpha-glucosidase inhibitors may have slightly weaker effects, on the basis of indirect comparisons of placebo-controlled trials. Thiazolidinediones were the only class that had a beneficial effect on high-density lipoprotein cholesterol levels (mean relative increase, 0.08 to 0.13 mmol/L) but a harmful effect on low-density lipoprotein (LDL) cholesterol levels (mean relative increase, 0.26 mmol/L) compared with other oral agents. Metformin decreased LDL cholesterol levels by about 0.26 mmol/L, whereas other oral agents had no obvious effects on LDL cholesterol levels. Most agents other than metformin increased body weight by 1 to 5 kg. Sulfonylureas and repaglinide were associated with greater risk for hypoglycemia, thiazolidinediones with greater risk for heart failure, and metformin with greater risk for gastrointestinal problems compared with other oral agents.”

Did the Review Follow the IOM Standards?

- **Standard 2.1: Establish a team with appropriate expertise and experience to conduct review**
  - Team included experts in diabetes and systematic review methods

- **Standards 2.2 and 2.4: Manage bias and conflict of interest**
  - Funding agency required disclosure, and excluded anyone with significant conflict from the team, but that information was not reported in the article

- **Standard 2.3: Ensure user and stakeholder input as review is designed and conducted**
  - Full report indicates “we recruited a panel of internal and external technical experts to give input on key steps including selection and refinement of the questions ...”
Did the Review Follow the IOM Standards?

- **Standard 2.5: Formulate the topic**
  - Team used PICOTS and analytic framework

- **Standards 2.6, 2.7, and 2.8: Systematic review protocol**
  - Funding agency had a standard protocol that was followed, but the protocol was not submitted for peer review or public posting
Standards 3.1 through 3.6: Finding and assessing studies

- MEDLINE, EMBASE, and Cochrane Central Register databases were searched from inception through January 2006 for original articles
- FDA and industry data were also searched
- Did not contact original researchers or do a web search
- Included observational studies as well as randomized trials
- Used independent dual review to identify eligible studies and assess study quality
- Documented the search strategy and results, with list of excluded studies
- Used sequential dual review to extract data
Standards 4.1 through 4.4: Synthesizing the body of evidence

- Used Jadad scale to assess the quality of trials and GRADE approach to grade strength of evidence in terms of risk of bias, consistency, precision, and directness
- Used tables and text to qualitatively synthesize findings about study characteristics, study quality, and results
- Performed meta-analysis when two or more relatively homogeneous studies were available on an outcome and comparison of interest
Standards 5.1 through 5.3: Reporting a systematic review

- Prepared a full report and journal article, each using a structured format
- Submitted full report and journal article for peer review
- Full report published on publicly available website