

## Continuous Quality Improvement for Cost-Effective Research (QICER): Assessing Health Outcome Analyses and Global Policy

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## Sections Of The Current Draft Report

### Section 1 -- Introduction and Overview of Issues.

### Section 2 -- Guidelines around the Globe.

How do various country guidelines differ? How well are they working?

### Section 3 -- Statistics and Science.

What are the statistical challenges in cost effectiveness models and research? How can we enhance the science?

### Section 4 -- Journals and Publication Quality.

Which journals have guidelines for publication? How can we improve the quality of publications?

### Section 5 -- Evidence Based Practice, Decision Makers, Patients.

How can we overcome barriers to use and application?

### Section 6 -- Overall Recommendations.

## SECTION 1

## Introduction and Background

## Issue Description

Continuous quality improvement is an integral component of ISPOR's regional and global endeavors to improve the economics and quality of life in all health care sectors and patient populations.

There is a crucial responsibility for ISPOR to regularly perform a macro review and examination of overall quality and trends in pharmacoconomics, health care economics research, and the potential relationships to health delivery and global policies.

## Issue Description (continued)

Recommendations and reports from ISPOR are intended to advance international health care efficiency and quality and provide a foundation for our global mission to improve the economics and patient outcomes in all health care sectors.

### Mission of the Task Force

The mission of the ISPOR Task Force on Quality Improvement in Cost Effectiveness Research (QICER) is to generate periodic quality reviews and formulate recommendations for needed improvements to facilitate the betterment of pharmacoeconomics and health outcomes research and their use in stimulating more efficient and effective health care, patient care and policy.

### Methods

- The Task Force goals are being accomplished through periodic systematic reviews and surveys.
- The periodic results and findings will be made available on the ISPOR website for membership comment and,
- After revision, published as white papers and reports that include recommendations for future ISPOR projects, educational programs, and services, both internal and external to the Society.

### ISPOR Initiatives

#### Research Practices

- ISPOR Health Science Policy Initiatives
- ISPOR Quality of Life Initiatives
- Pharmacoeconomic Guidelines

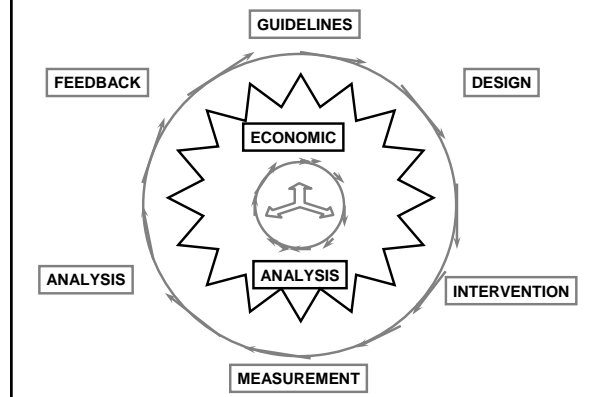
#### ISPOR Good Research Practices

- ISPOR Code of Ethics
- Modeling Studies
- Retrospective Databases
- CEA with Clinical Trials
- Real World Data Task Force
- Budget Impact Analysis Task Force

#### Research & Communication Issues

- General Pharmacoeconomics Research and Use Issues
- Quality of Life / PRO Regulatory Issues
- Use of Research by Decision Makers

### Quality Improvement Model



## SECTION 2

### HEOR Guidelines and Quality Improvement

### The Role of Guidelines in Quality and Improvement of HEOR

- *It is assumed* that the presence of guidelines leads to improvement in the quality of HEOR.
- Established guidelines are expected to increase the credibility and usefulness of HEOR. They define:
  - generally accepted standards
  - the requirements of specific audiences

### The Role of Guidelines in Quality and Improvement of HEOR (continued)

- There is not a lot of evidence to support or disprove this assumption for HEOR
- A number of studies have evaluated the quality of various studies
- However, few have examined the relationship between *the presence or quality of guidelines and the quality of studies*

### The Role of Guidelines in Quality and Improvement of HEOR (continued)

Two areas thus need to be examined

1. The quality of guidelines
2. The impact of guidelines on the quality of HE studies

### The Quality of Guidelines

- A few authors have reviewed available guidelines and compared and contrasted (*Hjelmgren et al, Jefferson et al, Chiou et al*) and there are some other resources available as well ([www.ispor.org](http://www.ispor.org), Interface database)
- Guidances tend to have numerous similarities across the board, and significant differences, due to
  - Ultimate purpose
  - Audience addressed
  - Regional, cultural, political variation
  - Author or Sponsor preferences

### The Impact of Guidelines on HEOR Quality

- How to measure guideline impact
  - Most journals don't have specific guidelines or requirements for HEOR (see section 4) so even though published articles are easily accessible, their quality and improvement of quality are not easily linked to guidelines
  - Several formulary submission bodies (e.g., NICE, CADTH, PBS) have developed specific guidances/requirements for HEOR studies submitted, but these studies are generally not publicly available for evaluation

### The Impact of Guidelines on HEOR Quality (continued)

- How to measure guideline impact
  - Some bodies have performed, or allowed, evaluation of the studies submitted to them and these have been published, but these are often small sample size, qualitative and not comparable across jurisdictions

### The Evolution of HE Guidelines

- Guideline development began in Australia in 1992, followed closely by Canada (CCOHTA, now CADTH and Ontario) and a few academic groups (such as *Siegel et al*)
- Many developed countries have produced their own guidances in the last decade
- There are 29 HE guidances from 25 countries (multiples from US, Canada). Of these:
  - 12 were produced by government bodies
  - 6 were developed by academic groups
  - 1 was produced by a healthcare insurer
  - 10 were collaborations between government agencies, academics, & insurers
- 14 of these have been prepared specifically to be part of formulary submission guidances/requirements

## HE Guidelines Currently in Existence

- > Australia
- > Baltics (Latvia, Estonia, Lithuania)
- > Austria
- > Belgium
- > Canada (CADTH, Ontario)
- > China
- > Finland
- > France
- > Germany
- > Hungary
- > Ireland
- > Israel
- > Italy
- > Netherlands
- > New Zealand
- > Norway
- > Poland
- > Portugal
- > Russia
- > Scotland
- > Spain
- > Sweden
- > Switzerland
- > UK (England & Wales)
- > USA (Task Force, Gold Panel, AMCP, WellPoint)

## Measuring & Improving Quality of Guidelines

- No instrument currently available to compare or measure guideline quality
- Early on it was found that guidelines were very practical from a logistics perspective, improving the relevance and timeliness of information available for decisionmakers (*Mather et al*)

## Measuring Impact of Guidelines on Quality of Studies

- A number of studies have been published looking at the quality of studies submitted to guideline-producing bodies, e.g.,
  - *Hill et al* evaluated 326 Australian submissions and found significant issues in interpretation and conduct of studies
  - *Colmenero et al* analyzed 53 economic submissions in the US (AMCP) and found low levels of compliance with standards
- None have measured the relationship between the guidelines and the studies
- All vary on measures of quality

## Measuring Impact of Guidelines on Quality of Studies

- To assess the impact of guidelines on the quality, and improvement of quality, of HE studies, a tool is required that is
  - Quantifiable
  - Anchored to the guidelines of interest, as well as generally accepted practices
  - Comparable across guidelines, studies and time
    - » E.g., *Goetghebeur et al* quantifiably assessed the quality of studies submitted to the Canadian CDR directly linking CADTH requirements and the studies submitted, using a composite of all HE guidelines and MCDA methodology

## Measuring Impact of Guidelines on Quality of Studies

- There may be an instrument already available that will suit this purpose, or a new one might be developed that incorporates the most relevant aspects of existing tools, e.g.,
  - *Neumann et al* measured the quality of economic analyses in several studies over the last decade
  - *Chiou et al* developed a grading system to measure the value and quality of HE analyses using the QHES instrument

## Future Work

- Evaluate available instruments or promote development of one to quantify and compare quality of guidelines
- Approach harmonization of guidelines
- Evaluate available instruments or promote development of one to quantify impact of guidelines on quality of studies
  - Comparable across guidelines
  - Comparable over time

## **SECTION 3**

### Statistics and Science

#### **Section Objectives**

- What are the statistical problems in cost effectiveness research?
  - Randomized clinical trial (RCT) based economic evaluations
  - Decision model based cost-effectiveness studies
- How can we make the science better?

#### **Current State of the Science**

- In the past decade, cost-effectiveness research methods have matured substantially, including the advancement of appropriate statistical methods
  - Yet adoption in the applied literature is low
- There still remain areas where there is a lack of evidence or consensus on the most appropriate method

#### **RCT-based Economic Evaluations: Key Issues**

- Analysis of cost data
- Handling of censored or missing cost data
- Joint comparison of costs and effects and estimation of sampling uncertainty
- Sample size and power
- Transferability (generalizability) of economic data across regions

#### **Decision Modeling-based Studies: Key Issues**

- Starting point: ISPOR Task Force Modeling Studies (2003)
- Transparency
- Probabilistic sensitivity analysis
- Methods for evidence synthesis
- Value-of-information analysis

#### **Strategies for Quality Improvement**

- Joint Effort by all Key Stakeholders
- Thought leaders/researchers
  - Study sponsors and funding agencies
  - Peer-reviewed journals
  - Regulatory and reimbursement authorities
  - ISPOR and other scientific societies

## SECTION 4

### Journals and Publication Quality

#### The Types of Publications We Would Like to Consider

- Peer reviewed publications
- Abstracts, posters and podiums
- Newsletters and other non-peer reviewed publications (educational texts, patient or marketing materials) *Rosen et al 2003, 2006*
- Our initial focus has been on peer-reviewed publications because these are the most accessible, the easiest to track, and can be used to establish a process for other types of evaluation

#### Role That Journals and Other Publications Play in Quality and Improvement of HEOR Research

- Establishing requirements and guidelines
- Peer review process
- Dissemination of studies
- Peer feedback
- Ongoing learning process for researchers

#### What Journals Have HEOR Guidelines

- A few thousand journals globally
- Many peer-reviewed biomedical journals have representatives in WAME (World Association of Medical Editors)
  - Over 965 journals represented
  - Over 91 countries
  - From all geographic regions of the world
  - International, national and regional constituencies
  - special interest and generalist audiences
  - Varying levels of impact factor
- As such, WAME was an ideal captive audience for a survey to capture some qualitative & quantitative info

#### WAME Survey Developed

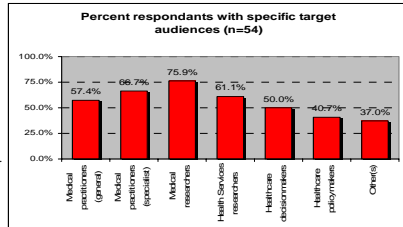
- We asked about:
  - Journal type, location, scope, circulation
  - Whether they accepted HEOR
  - Which types of HEOR
  - Finding reviewers for HEOR
  - Guidelines recommended/required
    - For authors
    - For reviewers
  - Their willingness to require guidelines for HEOR studies

#### Results of WAME Survey

- 6% response rate (55 of 965 WAME journals)
- 29 countries
- All continents (45% from developed western countries)
- 83% of respondents were high level staff (editor-in-chief, editor, managing editor)
- 72% of journals had international scope
- 98% peer reviewed
- Broad range of circulation size (difficult to compare because of issues with online and free access)

## Target Audiences

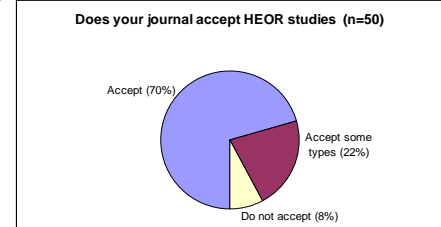
- Clinical/academic healthcare researchers: 76%
- Healthcare decisionmakers, health service researchers, and generalists and specialists: 50% - 67%
- Healthcare policymakers: 40%
- Other types of readers\* : 37%



\*students, patients or the general public, the paramedical professions, other areas of academia

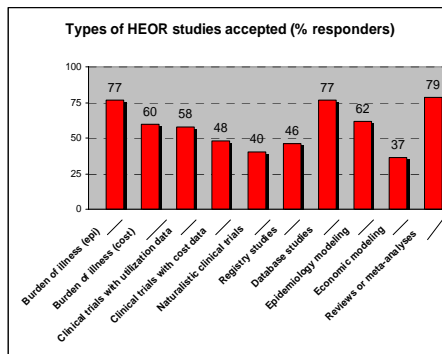
## Which Journals Accept All or Some Types of HEOR Work

- The vast majority (92%)
- 8% do not because scope of their journal narrowly focused on other topics (e.g., nursing ethics, clinical fertility).



## Types of HEOR Research Accepted

We broke HEOR down into 10 specific categories:



## Guidelines for Authors

- None of the journals who said they provided their own guidelines covered HEOR
- Most journals recommended either ICJME requirements\* or specific guidances\*\* directly in their Author Instructions.
- Only 4 journals recommended the BMJ health economic study guidelines
- Two journals provided checklists but nothing specifically for HEOR
- The Cochrane website had links to guidelines, including some PRO and HEOR guidances

\* which promote certain relevant guidances (MOOSE [meta-analysis of observational studies in epidemiology], CONSORT [RCTs], STARD [studies of diagnostic accuracy], QUORUM [systematic reviews and meta-analyses] and STROBE [observational epi studies]), but no economic guidelines.  
 \*\* (QUORUM, STROBE, CONSORT, REMARK [tumor marker prognostic studies], STARD) and a two references for basic statistics

## Would Journals Consider Using a Standard Set of HEOR Guidances From a Recognized Professional Body to Enhance the Quality of Published HEOR Research in Their Journal

- 91% would consider recommending or requiring a standard set of guidelines
- 9% said they would not
  - not relevant to the journal's scope
  - the editorial board felt that potential contributors were unable to use them

## Reviewing and Reviewers

### Difficulty finding reviewers:

- ~27% of journals had great difficulty finding HEOR reviewers
- ~60% said it was sometimes difficult depending on type of paper
- 6% had no problem

### Guidelines for reviewers:

- About 58% of journals did not provide their reviewers with any guidelines for evaluating the HEOR studies
- For the 42% who said they did, in all cases these were the same as author guidelines (e.g., instructions to authors, ICJME) and only rarely specific to HEOR

### Reviewing and Reviewers

- ~90% of respondents said it would be useful if they had a pool of expertise available to perform reviews of HEOR for their journal.
- Areas of expertise specifically mentioned were
  - policy analysis
  - economic outcomes
  - resource utilization
  - clinical epidemiology
  - public health
  - preventive medicine
  - mental health (or other specialties)
  - statistics, ethics and methodologies

### WAME Survey Conclusions

- Clear message that many journals accept and publish HEOR research
- Almost all do so without clear guidance to either authors or reviewers about quality standards
- Many journals have difficulty finding HEOR reviewers
- Almost all journals expressed interest in having a larger pool of reviewers for HEOR

### WAME Survey Conclusions (continued)

- To improve the overall quality of HEOR research in journals we need to
  - a) Develop standard guidances for journals
  - b) Lobby to establish them within the ICJME Uniform Requirements and have journals use them
  - c) Support those journals that do not have sufficient reviewer expertise

### Future Plans: Ongoing Evaluation of the Quality of HEOR Research in the Published Literature

- Already ongoing evaluation of the quality of HEOR studies by some groups (*Bell et al, Neumann et al, Drummond et al, etc.*)
- We would like to follow evolution of quality over time
- Looking at possible quantitative measures already established, e.g.,
  - QHES (quality of health economic studies) instrument (*Ofman et al 2003; Chiou et al*)
  - MCDA (multicriteria decision analysis)(*Neissen et al, Goetghbeur et al 2008*)
  - Others

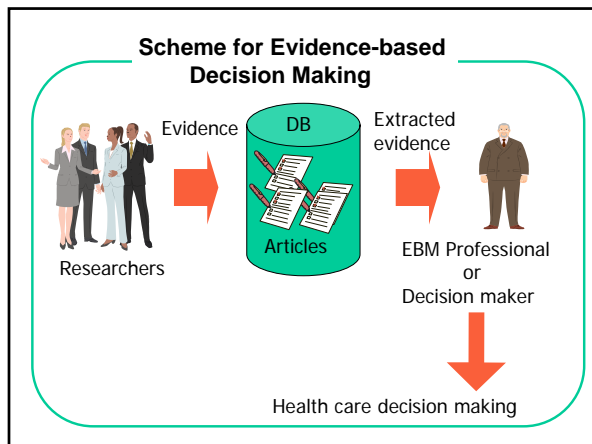
### Future Plans: Further Evaluation of the Quality of HEOR From Other Published Sources

Once standard quantitative quality measures can be agreed, possibility of ongoing assessment and reporting through longitudinal sampling of

- journals
- abstracts
- other materials

## SECTION 5

### Keys for Recommendation on EBM Professionals and Decision Makers



- ### Evidence Gap
- Full range of evidence
  - The gap between evidence stored in DB and the extracted one by EBM professionals, decision makers:
    - Partial evidence
    - Abstract
    - Conclusions
    - Summary for executives
    - Commentary
    - Translation

- ### Physicians/Decision Makers Common Claims
- *Duthie et al, 1999*: Health-economics outcomes (ex. ICER, QALYs) were either not understood or considered irrelevant.
  - *Drummond, Hutton, 2002*: Decision makers
    - want to read only commentary rather than whole abstract
    - prefer studies to be scored for quality

- ### Conditions Causing Claims - Drummond 2002
- Insufficient knowledge/skills on CEA
  - Lack of good-quality data.
  - Without good clinical data, CEA does not come to be good.
  - CEA makes the shortcomings of the clinical data much more apparent.
  - Poor connection between the clinical research and the strategy for generating economic evidence.
  - A long and inexplicable lag between the publication of the first clinical data, and the subsequent publication of the first CEA.

- ### Conditions Causing Claims (continued)
- Poor generalizability
  - Narrowness of research questions
  - *Drummond et al, 2007*: Lack of methodological rigor at the local level was not extensive
    - inflexibility of budgets
    - large number of assumptions
    - credibility of industry-funded studies

- ### Expert Opinions
- *Hutton and Brown, 2002*:
    - If economic decision framework is not satisfactory for decision makers, then it must be assumed that they have a different and superior model of decision makings.
    - If decision makers do not find economic evaluations useful, the way the evaluations are conducted or presented must be changed.
    - The constraints can be changed and the method of measuring the outcomes can be varied, but the basic approach remains the same.

### Expert Opinions (continued)

- *Grump et al, 2000:*
  - Factors encouraging decision makers to make more use of economic evaluations
    - appraisal of studies by a trusted source
    - need for more flexibility in healthcare budgets
    - more detailed explanations of the practical relevance of study results

### Expert Opinions (continued)

- *Drummond 2002:*
  - As for generalizability,
    - Greater understanding at the local level, in order to adapt study findings
    - A stronger commitment to fund local studies
    - It is important, through databases like NHS EED, to continue to explore making economic studies more accessible, without losing the key elements of critical appraisal.

### Expert Opinions (continued)

- *Drummond et al, 2002:*
  - Reorganization provides opportunities to rectify some of the problems of using economic evidence in decision making, but it may merely shuffle the pack rather than bring about real change.
  - Requests for quality scores:
    - which might lead decision makers to undertake even less critical assessment of findings than they currently perform

### Challenges for EBM Professionals

- Understanding of CEA methods
- CEA alongside RCT
- Transferability of evidence
- Evidence and Bias
  - Efficacy-Efficiency gap: RCT vs. Real world
  - An individual patient vs. population
- Selection of a comparator
- Priority for a patient: clinical benefit vs. cost-effectiveness

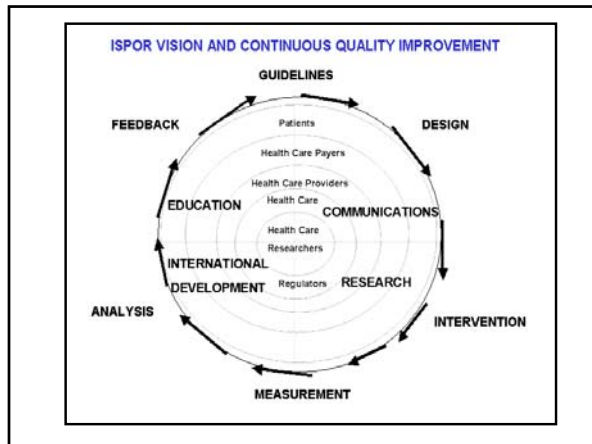
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### Challenges for Decision Makers

- Understanding complexity of socioeconomic evaluations
- Improving decision processes:
  - subjective vs. objective
- Measuring WTP for a different disease
- Applying ICERs for budget impact analyses
- Capturing the multi-dimensional values
- Recognizing the era of value-based health care
- Developing social equity of patients

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## SECTION 6 Conclusions and Recommendations



**PRELIMINARY SAMPLE OF TASK FORCE RECOMMENDATIONS FOR REVIEW**  
(other sections of the QICER report may have additional recommendations)

The QICER Task Force recommends that ISPOR expeditiously implement the following:

1. Periodic reports on range of journals publishing CEA and outcomes research.
2. Periodic reports on quality of CEA publications.
3. Periodic review of internal and external use of all ISPOR guidelines.
4. ISPOR guidelines and reports must have a periodic update schedule.
5. Periodic reports on statistical and methodological challenges in CEA.
6. Periodic reports on number of countries (and how well) using CEA guidelines.
7. Frequent publication of case studies (posters) of successful/practical use of CEA concepts/guidelines.
8. ISPOR annual recognition of countries (agencies) for exemplary CEA use.
9. ISPOR annual recognition of practitioner/groups for exemplary CEA use.
10. ISPOR annual recognition of clinical research/pharma firms for exemplary CEA use and development.
11. ISPOR annual recognition of practitioners/researchers helping patients to consider CEA in decision making.

**Resources - Sample**

- *Stirling B.* Seeing The Nice Side Of Cost-effectiveness Analysis. Health Economics, 2007.
- *Hoffman C. et al.* Do Health-Care Decision Makers Find Economic Evaluations Useful? *ViH* 2002.
- *Dhalla I. and Laupacis A.* Moving from opacity to transparency in pharmaceutical policy. *CMAJ* Feb 2008.
- NHS Economic Evaluation Database Handbook. CRD. Univ. of York. April 2007
- *Neumann P. et al.* Cost-Effectiveness Analysis Registry (CEA). <https://research.tufts-nemc.org/cear>.
- Inst. Of Medicine. Crossing the Quality Chasm: A New Health System for the 21st Century, 2001.
- *Brown MM et al.* Evidenced Based to Value Based Medicine, AMA Press, 2005.
- *Cox P. et al.* Financing Sustainable Healthcare In Europe, Feb 2007. [www.SustainHealthCare.org](http://www.SustainHealthCare.org).