The importance of quality in HEOR information development and dissemination

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Introduction

The fundamental role of health economics and outcomes research (HEOR) is to produce scientific evidence that informs decisions on the economic and humanistic value of pharmaceutical products and medical devices; thus, the quality of those data are critically important. To be considered high-quality research in any form, be it clinical outcomes or bench discovery, science has to be reliable and valid. In the still new and emerging area of science of HEOR, quality has to be at the forefront in both methodology and communication. Quality in pharmaceutical HEOR can only be achieved when the data are gathered under the premises of strict scientific methods and are communicated clearly, simply, and without bias to inform policy decisions related to coverage and reimbursement or to inform clinical practice guidelines.[1] The fundamental sources of data for HEOR studies include secondary data sets (eg, paid claims, electronic medical records, or real-world data [RWD]) for retrospective studies to reflect product utilization and economic outcomes, as well as primary data from patients for patient-reported outcomes, including health-related quality of life, to reflect humanistic or patient-centered outcomes. We present some of the challenges to quality in HEOR information development and dissemination, the consequences resulting from the lack of quality, lessons to be learned from other sectors in healthcare, and potential solutions to assure quality in HEOR.

Fragmentation in HEOR

The fragmented nature of HEOR information creation and dissemination is not always conducive to optimize the desired outcome (**Figure 1**). HEOR departments often receive input from a variety of stakeholders including (but not limited to) medical affairs, access and reimbursement, regulatory, and legal. This presents challenges in ensuring quality outputs are developed and delivered to meet multiple needs. HEOR publications development may not always adhere to Good Publication Practices, especially when written by less-experienced HEOR scientists, creating the risk of publication withdrawal and damaged reputation for the sponsoring company. Lack of organization and communication in the manuscript development process can lead to missed timelines and/or publication rejections from journals, contributing to the risk of ineffective publication production. Writing quality is one of the first checks journal editors make before sending manuscripts out to peer reviewers. Further, HEOR data and communication tools that are of poor quality and/or do not address the information needs of the customer not only reflect badly on the reputation of the sponsor but can also foster payers' distrust of the data and lead to unfavorable reimbursement and utilization decisions (ie, ineffective HEOR outcomes, poor quality).

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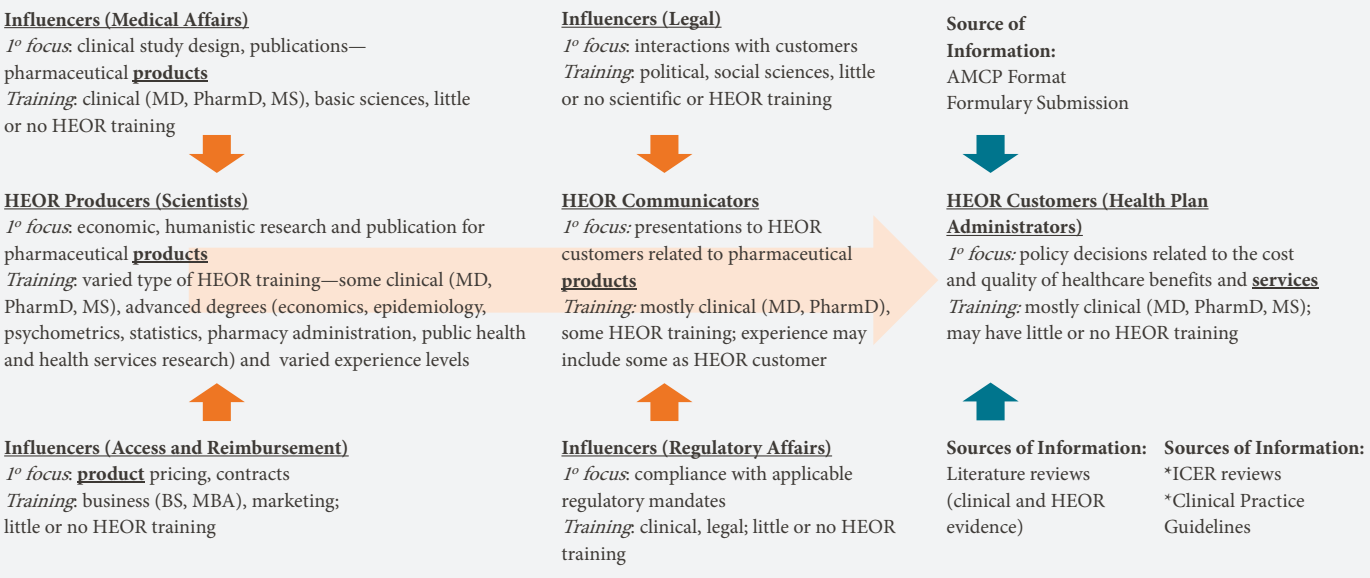
ISPOR has established a set of competencies for HEOR professionals that includes 41 competencies organized into 13 topic domains that collectively comprise the ISPOR HEOR Competencies Framework.[2] This diversity and multitude of skills needed in HEOR poses a challenge to those who manage HEOR scientists and the work they produce. A lack of health plan experience combined with a primary focus on pharmaceutical products rather than services can produce studies that do not address the needs of health plan customers. For example, the use of registration trials using placebo comparators as evidence gives rise to health plan customers saying, "When we have a situation where our therapeutic alternative is a placebo, we'll use your data."

Another issue is the process of HEOR evidence development. Often, this is done by HEOR-specific vendors who focus solely on HEOR work and often perform this work on a project-by-project basis. This puts the manufacturer in a bind, trying to find a HEOR vendor that works seamlessly with their scientific communications vendor. It also poses a risk to the on-time delivery of results, submissions for congresses and publications, as well as message continuity and integration into the product's overall publication plan. Continuity of HEOR data production can also threaten quality due to personnel turnover in these positions.

HEOR scientists can face challenges within their organizational structure. While Medical Affairs managers may have expertise in clinical trial design, they may not have the experience to critically evaluate and understand HEOR work. For example, they may be tempted to apply their experience in developing substantial evidence from clinical trials to HEOR situations where competent and reliable scientific evidence is the basis of such work. HEOR scientists may also be subject to the influence of those involved in access and reimbursement, where the primary focus is to create contracts with customers based on price and rebates. Another source of pressure may be the legal department. Conflict can arise when someone with legal training asserts their judgement on the suitability of customer communication tools based on their opinion of the science, which may be at odds with HEOR scientists. Field-based HEOR communicators with direct contact with customers can serve to bridge the gap between HEOR scientists and the information needs of the customer. However, the development of HEOR communication tools without the benefit of integrated customer needs may not yield quality in terms of informing customer decisions. Thus, depending on the structure of the HEOR department within an organization, many challenges can arise when delivering quality, meaningful, and useful outputs.

Figure 1. Fragmentation in HEOR: Stakeholders, Primary Focus, Training and Sources of Information

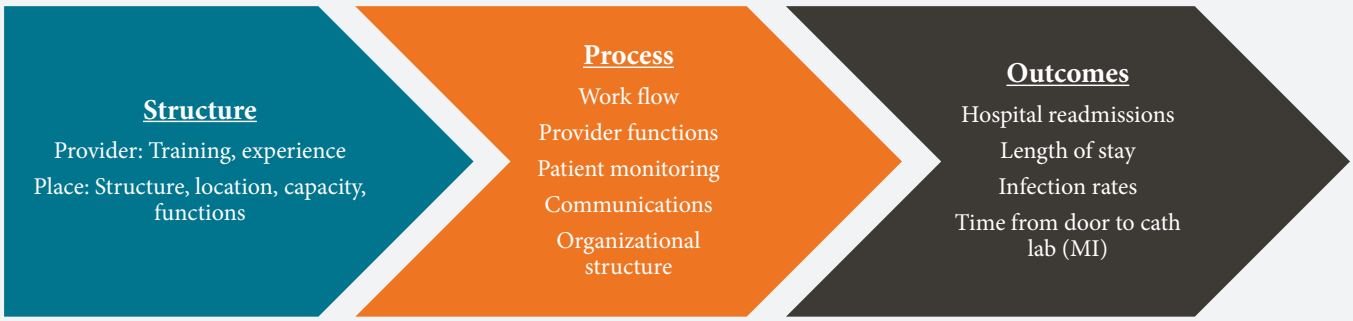


"Since healthcare resource allocation decisions by payers, clinicians, and other stakeholders are made under conditions of uncertainty, they may turn out to be suboptimal if not fully informed with the best available HEOR information. "

A Model of Quality from Health Services Delivery

An understanding of HEOR quality, as well as its measurement and management, can be gleaned from that used in healthcare services quality. Within this context, quality is defined as the optimal utilization of an organization's structure and processes to effectively achieve desired outcomes.[3] The Donabedian model is used as a framework for understanding the components of quality, interactions, and measurement to assess quality (**Figure 2**). For decades, hospitals and managed care organizations involved in both the financing and delivery of healthcare services have used this approach to measure and improve quality. Here, structural measures include the number and qualifications of staff, as well as their geographic proximity to patients. Process measures reflect the way in which the systems and healthcare providers interact to deliver the desired outcome. Patient outcomes is a construct of the model since the ultimate outcomes in healthcare services delivery, such as patients' longevity and long-term quality of life, are difficult to measure. As a result, most quality measurement and management focuses on the structure and processes employed to deliver services. Hence, the highest quality can be expected to result from organizations and systems that have the most trained and experienced people working in the best possible processes to deliver healthcare services to patients.

Figure 2. Example of the Donabedian Model in Healthcare Quality



In pharmaceutical HEOR, a key desired outcome is to effectively create and communicate HEOR information regarding the value of pharmaceutical products to inform payers' policy decisions regarding coverage and utilization of medical devices and pharmaceutical products, as well as population-based decisions for clinical practice guidelines. Since healthcare resource allocation decisions by payers, clinicians, and other stakeholders are made under conditions of uncertainty, they may turn out to be suboptimal if not fully informed with the best available HEOR information.[4] And as with healthcare delivery, HEOR data outcomes can be difficult to measure. So the optimization of the HEOR provider organizations' structure and processes can be used as a proxy to manage the delivery of optimal outcomes.

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Quality Efforts in the Conduct of HEOR Studies and Dissemination

An example of work in the area of HEOR quality improvement is Mike Drummond's checklist for assessing economic evaluations.[5] Due to the nascent nature of the HEOR field composed of scientists from a variety of disciplines, ISPOR in 1999 began the development of Practices for Outcomes Research Reports to provide expert consensus guidance recommendations to set international standards for outcomes research and its use in healthcare decision making.[6] These best practices espoused by ISPOR (and other scientific organizations) have been incorporated into FDA guidance as the basis for their judgement as to whether HEOR evidence has been developed using generally accepted scientific standards, appropriate for the information being conveyed, that yield accurate and reliable results.[7]

Economic data is not usually available in the product label, so FDA allows "off-label" health economic discussions with payers as the learned intermediaries. Such discussions are subject to FDA guidance. Section 114 of the 1997 Food and Drug Administration Modernization Act[8] codified rules about the evidence that drug manufacturers need to support economic claims about their products. In 2009, the FDA published its "Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims."[9] And in 2018, the FDA published "Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities,"[10] which clarified some of key areas of uncertainty arising from the 1997 Guidance. Importantly, this latest guidance document clarified the definition of the evidentiary basis of economic discussions with customers. In HEOR communications, the evidentiary standard is Competent and Reliable Scientific Evidence (CARSE) for approved indications, in contrast to the substantial scientific evidence required for clinical studies. The FDA considers existing current good research practices for substantiation developed by authoritative bodies such as ISPOR, International Society for Pharmacoepidemiology (ISPE), Patient-Centered Outcomes Research Institute (PCORI), and the Agency for Healthcare Research and Quality (AHRQ). Failure to comply with these guidances regarding the communication of HEOR data with health plan customers creates the risk of FDA rebuke and/or penalties.

The CARSE standard, as the evidentiary basis of HEOR, is based on its use to inform administrative (ie, pharmaceutical policy decisions), not clinical decisions. Administrative decisions are expected to be made under a blanket of uncertainty, and the consequences of wrong decisions are not expected to have the potential life-or-death impact of a clinical decision. Nonetheless, the need for high-quality HEOR data remains crucial. A recent example of problems that can arise with the publication of questionable data was the "Retraction: Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19."[11] In this case, the article was retracted because all the authors were not granted access to the raw data and the raw data could not be made available to a third-party auditor, so there was no way to validate the primary data sources underlying the article. In HEOR, the large (usually paid claims) data set should be archived as an analytic file, along with the SAS code used to manipulate and analyze the data, subject to inspection by reviewers to assess validity and reproducibility.[12] HEOR scientists and the quality of their work benefit from the curation of good data, aligning with regulatory agencies, health technology authorities, clinicians, patients, and healthcare payers around the world who expect high-quality, real-world evidence to make good decisions. To foster the optimal uptake of HEOR studies using real world evidence (RWE), an ISPOR task force recently called for transparency of the research process to enable decision makers to evaluate the quality of the methods used and the applicability of the evidence that results from the studies.[13] Their plan includes registering retrospective HEOR studies using RWD, as is currently the case for clinical studies. The recommendations address which studies should be registered, where and when these studies should be registered, how and when analytic deviations from protocols should be reported, how and when to publish results, and incentives to encourage registration.

Structure and Processes to Assure Quality in HEOR Publication Development and Dissemination

Thus, the creation of HEOR information and communication with payers is complex, dependent on and influenced by multiple stakeholders, and subject to much fragmentation in the field. A comprehensive and systematic approach to manuscript development, publication, and communication tool creation is necessary to provide high-quality economic information and the best outcomes in HEOR data generation and communication.

When HEOR information is not effectively communicated with payer decision makers, there exists the risk of lost revenue for the manufacturer, as the product is not used in appropriate patients due to delayed or adverse coverage or utilization policies, and its value is not realized by patients or health plans. Additionally, failure to comply with FDA guidances in the conduct of HEOR work can lead to rebuke and/or penalties.

Alternatively, high quality in HEOR can be attained by a structure that employs best-in-class scientific personnel with advanced training and experience in their fields (Figure 3), as the personnel's ability to adapt to new therapeutic modalities and the capacity to take on new assignments is key to ensuring quality. The integrity and passion brought to the work is crucial to the quality of the product.

Bringing that expertise together to create best-in-class processes is key to ensuring the highest HEOR quality. Systematic project management processes that permit optimization of manuscript development provides the greatest opportunity to maintain production timelines, thereby increasing effectiveness in producing accurate and effective publications. Further, integrating HEOR publication plans with clinical publication plans permits more continuity of the manufacturer's overall messaging and better ability to comply with submission deadlines at targeted meetings and congresses. The use of a systematized publication process ensures compliance with a firm's internal publication processes and facilitates better integration with product messaging. Another important component of the HEOR quality process is consistent compliance with FDA guidances, including best practices promulgated by HEOR scientific organizations. Also important is that this includes a process that ensures adherence to publication standards, such as those promoted by the Good Publication Practices (GPP3) and the International Committee of Medical Journal Editors (ICMJE) to ensure publication success. In addition, the availability of a quality control (QC) staff and consistent application of QC checks during the publication development process contributes to information integrity by checking annotations to ensure that the paragraphs, tables, and figures are cited and formatted correctly and that references reflect the totality of data published in the area. All these processes combine to ensure the precision of scientific communications. The coordinated, consistent, and systematic approach to these processes provides the greatest likelihood of optimal HEOR outcomes: effectively informing pharmaceutical policy decisions about product value using HEOR data.

Figure 3. HEOR Quality

QC Process

STEP ONE

- [ ] Verify main body of text by matching all annotations to their source document
- [ ] a. Annotations, provided by the writer, denote where in each reference document to find the information necessary to verify each claim or data discussed in the main text
  - [ ] i. Verify that that each statement in our writing is supported by the referenced document
  - [ ] ii. Ensure the correct document is being referenced
  - [ ] iii. For data or results, verify numbers against source data provided by client
- [ ] b. Check annotations are followed throughout the entire document

STEP TWO

- [ ] Tables verified
- [ ] a. Check the reference data for accuracy
- [ ] b. After all data is verified, title rows and columns are checked to make sure they are formatted properly
  - [ ] i. Check that all titles and corresponding units are correct per the source data
  - [ ] ii. Check that each title is formatted to house style, with units ordered the same way throughout and for correct font/size for each title
- [ ] c. Check the footnotes
  - [ ] i. Verify footnotes in the source document are included in our tables
  - [ ] ii. Verify each footnote corresponds to the correct part of the table
  - [ ] iii. Verify all footnote symbols that appear in the table have corresponding text in the footnote
- [ ] d. Check the abbreviations list
  - [ ] i. Verify each abbreviation listed in the table is included in the abbreviations list
  - [ ] ii. Verify every abbreviation listed is used in the table
- [ ] e. Once all tables are completed, review in order to verify that all tables are consistent with each other

STEP THREE

- [ ] Figures verified
- [ ] a. Process is similar to QC for tables
- [ ] b. Verify that data in each figure/graph matches the data in the source document
- [ ] c. Verify figure formatting presents data as clearly as possible
  - [ ] i. Includes correct graph type, category grouping, corresponding colors, etc
  - [ ] ii. Also includes alignments, distributions, and aesthetics
- [ ] d. Check that axes, titles, and data labels are formatted to house style
- [ ] e. Once figures are checked, review in order to verify that all graphs are consistent with each other

References

1) Jeffrey L. Anderson, Paul A. Heidenreich, et al. ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. Journal of the American College of Cardiology, Vol. 63, No. 21, 2014 (ISSN 0735-1097/$36.00); 2) Pizzi LT, Onukwugha E, Corey R, et al. Competencies for Professionals in Health Economics and Outcomes Research: The ISPOR Health Economics and Outcomes Research Competencies Framework. Value in Health VOLUME 23, ISSUE 9, P1120-1127, SEPTEMBER 01, 2020; 3) Donabedian, A (2005) Evaluating the Quality of Medical Care, The Milbank Quarterly,83(4):691-729; 4) Fenwick E, Steuten L, Knies S, et al. Value of information analysis for research decisions—an introduction: report 1 of the ISPOR Value of Information Analysis Emerging Good Practices Task Force. Value Health. 2020;23(2):139 – 150; 5) Drummond M et al. Methods for the economic evaluation of health care programmes. 2nd ed. Oxford. Oxford University Press. 1997; 6) https://www.ispor.org/heor-resources/good-practices-for-outcomes-research; 7) Communications With Payors, Formulary Committees and Similar Entities — Questions and Answers Guidance for Industry and Review Staff. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Office of the Commissioner (OC). June 2018. OMB Control No. 0910-0857; 8) FDAMA, P.L. 105-115; 9) Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), December 2009, Clinical/Medical; 10) U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Office of the Commissioner (OC). June 2018, Procedural . OMB Control No. 0910-0857, Expiration Date: 08/31/2021; 11) June 25, 2020, N Engl J Med 2020; 382:2582, DOI: 10.1056/NEJMc2021225; 12) Wang SV, Schneeweiss S, Berger ML, et al. Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0. Value in Health. 2017;20(8):1009-1022; 13) Orsini LS, Berger M, Crown W, et al. Improving Transparency to Build Trust in Real-World Secondary Data Studies for Hypothesis Testing—Why, What, and How: Recommendations and a Road Map from the Real-World Evidence Transparency Initiative. VALUE HEALTH. 2020; 23(9):1128–1136.

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