Bridging the credibility gap: Establishing competent and reliable scientific evidence to support productive health care economic information discussions with US payer audiences

Workshop Presenters

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Workshop objectives

- Define “competent and reliable scientific evidence” (CARSE) in the context of supporting dissemination of health care economic information (HCEI)
- Compare various approaches to CARSE designation and identify relevant resources to support CARSE assessment
- Describe the challenges with establishing CARSE from manufacturer and payer perspectives
- Identify best practices to facilitate more productive discussions of HCEI with payer decision-makers

Health Care Economic Information (HCEI) and CARSE: Setting the Stage

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Defining the Key Elements

FDA Guidance Document, June 2018, OMB Control No. 0910-0686

What is HCEI?

Who is the appropriate audience?

What is the CARSE standard?

What Is HCEI?

HCEI is defined in section 502(a) of the FD&C Act as:

"Any analysis (including the clinical data, inputs, clinical or other assumptions, methods, results, and other components underlying or comprising the analysis) that identifies, measures, or describes the economic consequences, which may be based on the separate or aggregated clinical consequences of the represented health outcomes, of the use of a drug. Such analysis may be comparative to the use of another drug, to another health care intervention, or to no intervention."

FDA Guidance Document, June 2018, OMB Control No. 0910-0686

Who Is the Appropriate Audience?

"HCEI can be provided to a payor, formulary committee, or similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement."

- This guidance does not apply to dissemination of HCEI to other audiences, such as healthcare providers making individual patient prescribing decisions

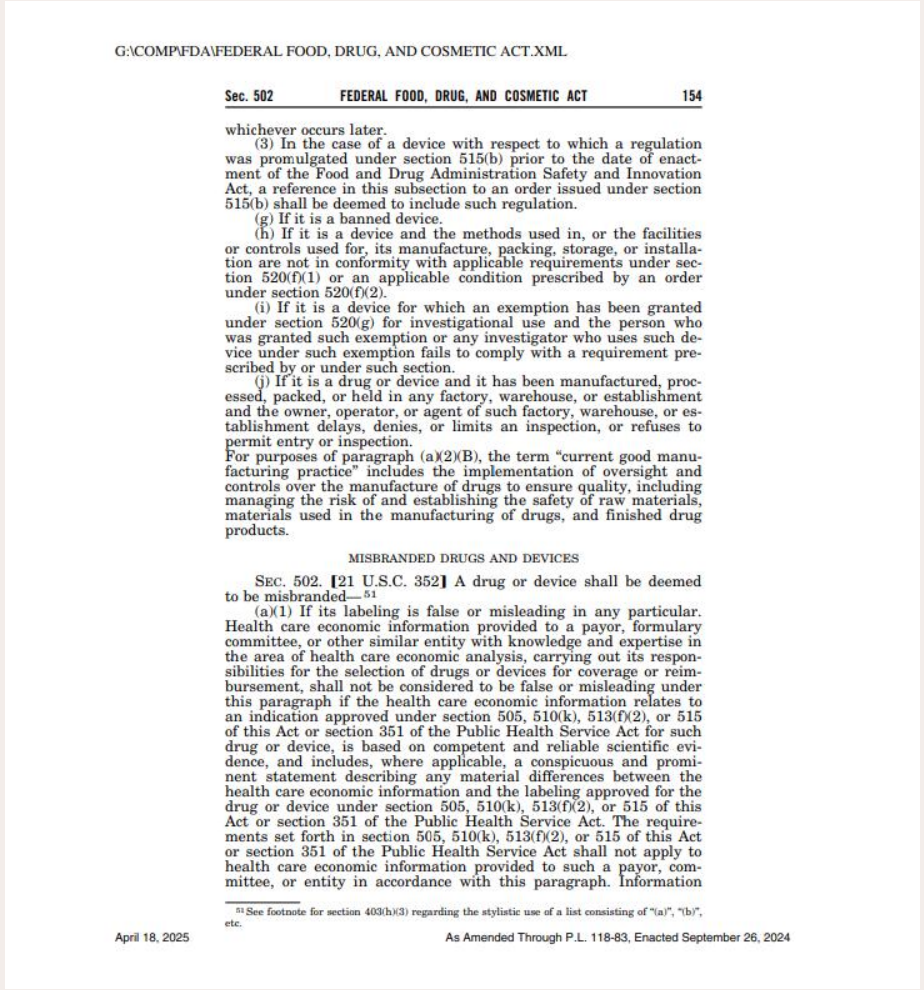
FDA Guidance Document, June 2018, OMB Control No. 0910-0686

What Is the Standard for HCEI?

- "…HCEI shall not be considered false or misleading if, among other things, it is based on competent and reliable scientific evidence (CARSE)"
- HCEI is based on CARSE if it has been developed using generally accepted scientific standards, appropriate for the information being conveyed, that yield accurate and reliable results
- This standard includes clinical data and inputs underlying the drug's economic consequences, including indirect treatment comparisons

FDA Guidance Document, June 2018, OMB Control No. 0910-0686

What guidance do we have to support appropriate HCEI communication?



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Sec. 502 FEDERAL FOOD, DRUG, AND COSMETIC ACT 154

whichever occurs later.

(3) In the case of a device with respect to which a regulation was promulgated under section 515(b) prior to the date of enactment of the Food and Drug Administration Safety and Innovation Act, a reference in this subsection to an order issued under section 515(b) shall be deemed to include such regulation.

(g) If it is a banned device.

(h) If it is a device and the methods used in, or the facilities or controls used for, its manufacture, packing, storage, or installation are not in conformity with applicable requirements under section 520(f)(1) or an applicable condition prescribed by an order under section 520(f)(2).

(i) If it is a device for which an exemption has been granted under section 520(g) for investigational use and the person who was granted such exemption or any investigator who uses such device under such exemption fails to comply with a requirement prescribed by or under such section.

(j) If it is a drug or device and it has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection.

For purposes of paragraph (a)(2)(B), the term "current good manufacturing practice" includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products.

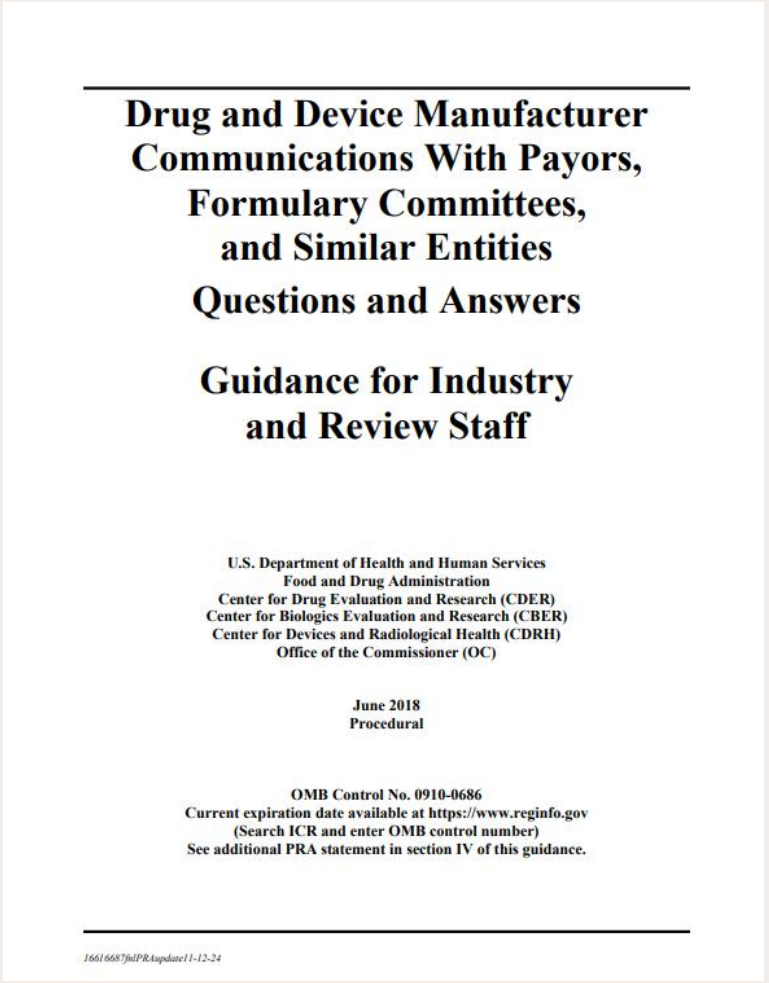
MISBRANDED DRUGS AND DEVICES

SEC. 502. [21 U.S.C. 352] A drug or device shall be deemed to be misbranded—[51]

(a)(1) If its labeling is false or misleading in any particular. Health care economic information provided to a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs or devices for coverage or reimbursement, shall not be considered to be false or misleading under this paragraph if the health care economic information relates to an indication approved under section 505, 510(k), 513(f)(2), or 515 of this Act or section 351 of the Public Health Service Act for such drug or device, is based on competent and reliable scientific evidence, and includes, where applicable, a conspicuous and prominent statement describing any material differences between the health care economic information and the labeling approved for the drug or device under section 505, 510(k), 513(f)(2), or 515 of this Act or section 351 of the Public Health Service Act. The requirements set forth in section 505, 510(k), 513(f)(2), or 515 of this Act or section 351 of the Public Health Service Act shall not apply to health care economic information provided to such a payor, committee, or entity in accordance with this paragraph. Information

[51] See footnote for section 403(h)(3) regarding the stylistic use of a list consisting of "(a)", "(b)", etc.

April 18, 2025 As Amended Through P.L. 118-83, Enacted September 26, 2024



Drug and Device Manufacturer 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
Procedural

OMB Control No. 0910-0686
Current expiration date available at https://www.reginfo.gov
(Search ICR and enter OMB control number)
See additional PRA statement in section IV of this guidance.

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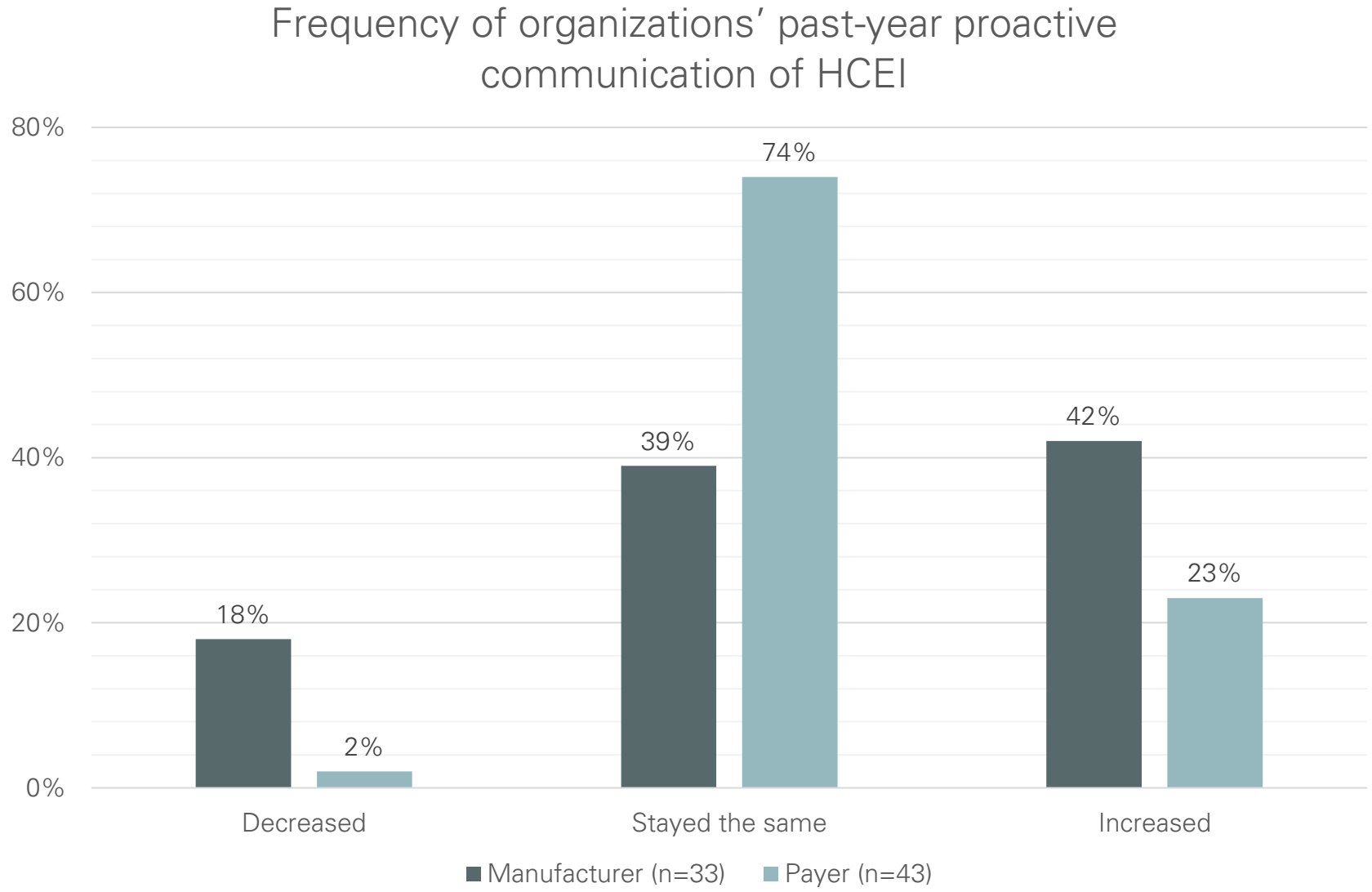
How frequently is HCEI being communicated?



Maliqi M, Mody L, Hughes J, et al. Comparing payer and manufacturer experiences with communication of healthcare economic information (HCEI). 2022 AMCP Annual Meeting; Chicago, IL.

Building credible economic evidence can strengthen value evidence and access strategy and assuage payer skepticism

To effectively convey the value of a product to payers, it's important to ensure that economic evidence is not only robust but also trustworthy.

Manufacturer Narrative

THE BRIDGE

- Ensuring the clinical plausibility of the model framework
- Appropriate, conservative assumptions
- Rigorous assumption testing via sensitivity analysis
- Third-party or internal CARSE assessment and certification using appropriate external resources*
- Thorough field team training on model resources

Payer Perception of Manufacturer Credibility

Lumanity

Note: *e.g. ISPOR Good Research Practices, AMCP RWE Initiative

Key: CARSE, competent and reliable scientific evidence; RWE, real world evidence

Approaches to CARSE and Identifying Relevant Resources

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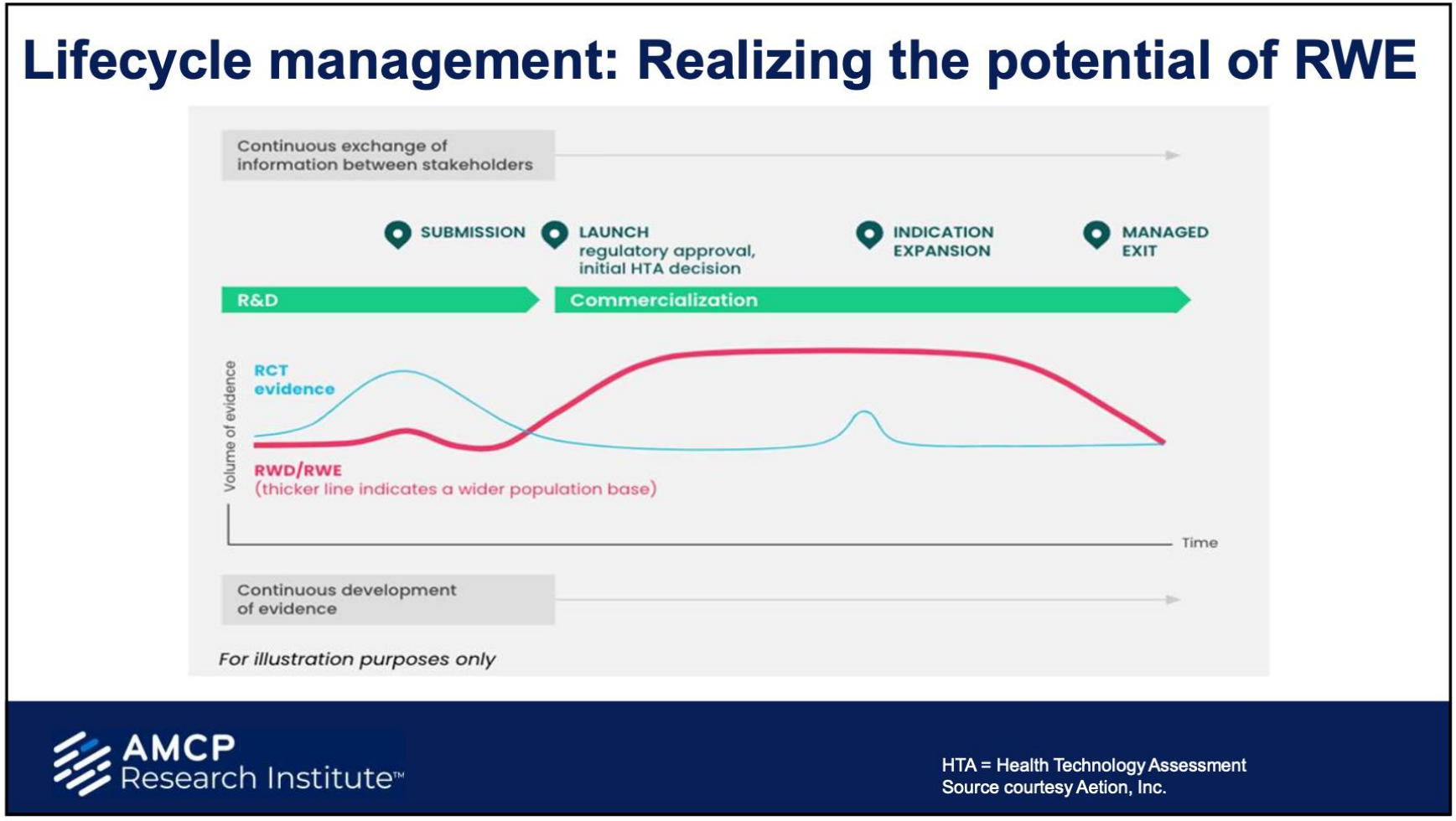
Executive Board; Access Forum

Lifecycle management of RWE



Triad of Question, Design, and Data for HCEI:

1. The *research question* aligns with the decision-maker's needs.
2. The *study design* is methodologically appropriate for the question and the data source.
3. The *data are suitable* and of sufficient quality to address the question. Only when all three are aligned can the RWE be considered fit-for-purpose for healthcare decisions

https://pmc.ncbi.nlm.nih.gov/articles/PMC8771197/

ISPOR Good Practice Reports for HCEI:

- ISPOR Good Practices Reports are highly cited, expert consensus guidance recommendations that set international standards for HEOR and its use in healthcare decision making.
- Key ISPOR Good Practice Areas:
    - Cost-Effectiveness Models (CEM)
    - Budget Impact Models (BIM)
    - Real-World Evidence (RWE)
    - Patient Preferences & Outcomes
    - Reporting Standards (CHEERS)
- Other ISPOR Reports provide guidance on important areas such as HTA, health policy, and AI

https://www.ispor.org/heor-resources/good-practices

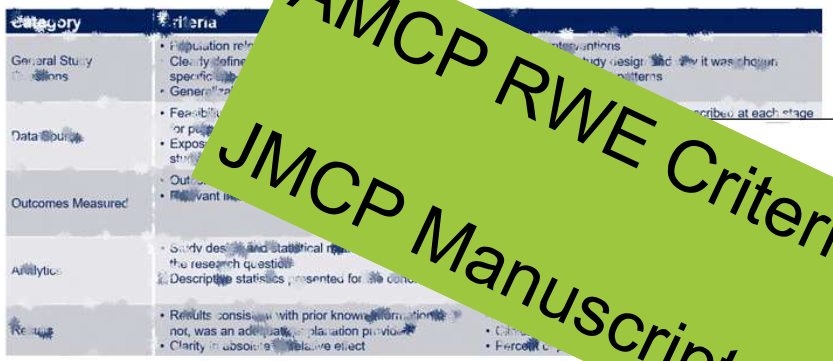
ISPOR-ISPE Joint Guidelines for RWE STUDIES of Treatment and/or Comparative Effectiveness for healthcare decision making

- ISPOR and ISPE created a task force to recommend good procedural practices to enhance decision makers' confidence in evidence derived from RWD studies.
- The recommendations cover seven topics including study registration, replicability, and stakeholder involvement in RWE studies to provide a trustworthy foundation for the expanded use of RWE in health care decision making.
- The focus of these recommendations is good procedural practices for studies that test a specific hypothesis in a specific population.

Berger ML, Sox H, Willke RJ, et al. Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value in Health. 2017;20(8):1003-1008.

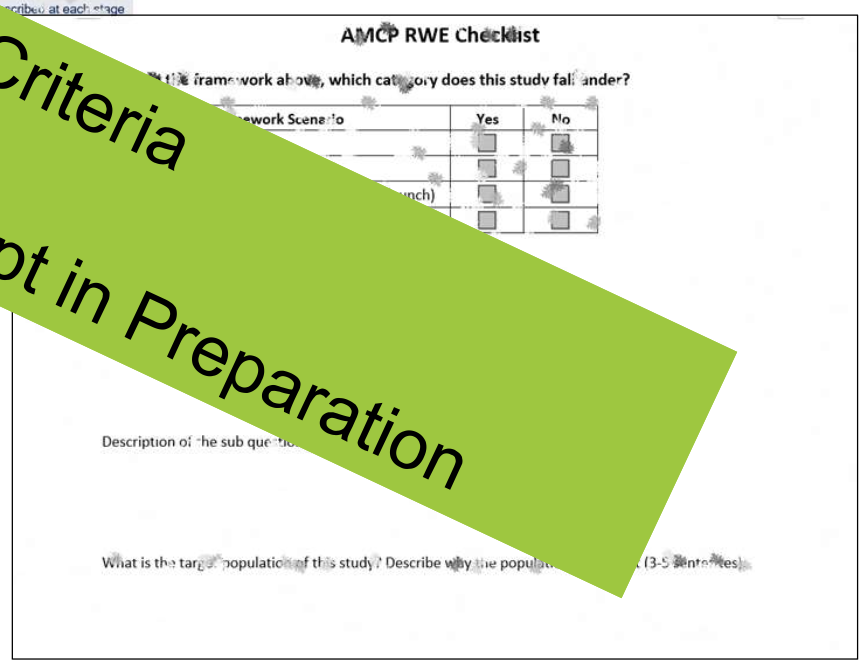
RWE STANDARDS FOR Payers: CRITERIA

The criteria help payers understand RWE studies



AMCP RWE Criteria

JMCP Manuscript in Preparation



Questions include:

- What are the limitations of your study?
- What data source(s) was used? Why was it relevant/appropriate for the research question?

Evaluation of HCEI for CARSE: third parties

Group/Initiative	Role in RWE Review
ICER	Systematic review and appraisal for value assessments
HTA Agencies (NICE, CADTH, etc.)	Review RWE for coverage/ reimbursement decisions
FDA, EMA, Health Canada	Regulatory review of RWE for approvals/label changes
ISPOR/ISPE	Develop guidelines and participate in review panels
Duke-Margolis/Transparency Initiative	Registry and methodological guidance for RWE studies
IMI GetReal, ImpactHTA	Multi-stakeholder collaboration on RWE standards and reviews

Millcreek Outcomes Group, LLC
https://www.millcreekoutcomes.com/

https://icer.org/our-approach/methods-process/considering-clinical-real-world-and-unpublished-evidence/
https://becarispublishing.com/doi/10.2217/cer-2020-0228
https://healthpolicy.duke.edu/topics/real-world-evidence
https://www.sciencedirect.com/science/article/pii/S1098301517333533

Approaching CARSE from A Manufacturer Perspective

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Disclaimer and Acknowledgements

- The views and opinions expressed here are my own and do not reflect the official policy or position of my employer
- I would like to acknowledge my colleagues who provided their perspectives to help enrich today's discussion

Manufacturer Framework for HCEI to Meet CARSE

- All HCEI claims must be presented in a way that is truthful, medically accurate complete, and not misleading
- Adherence to the highest and most rigorous research standards, and with utmost transparency
  - Truthful, non-misleading presentation
  - Appropriate background and contextual information presented clearly and prominently
    - Study design and methods
    - Generalizability
    - Limitations
    - Sensitivity Analysis
- Additional material information for a balanced and complete presentation

Framework serves as foundation for manufacturer interpretation and establishment of appropriate processes for vetting materials

Manufacturer Approaches to Establish CARSE

External (third party) CARSE Review

- Submission of materials to outside organization with relevant research and regulatory guidance expertise for review
  - Academic institution
  - Consulting firm
- Certification issued upon confirmation that research meets CARSE standards
- Good option for smaller organizations with limited in-house expertise

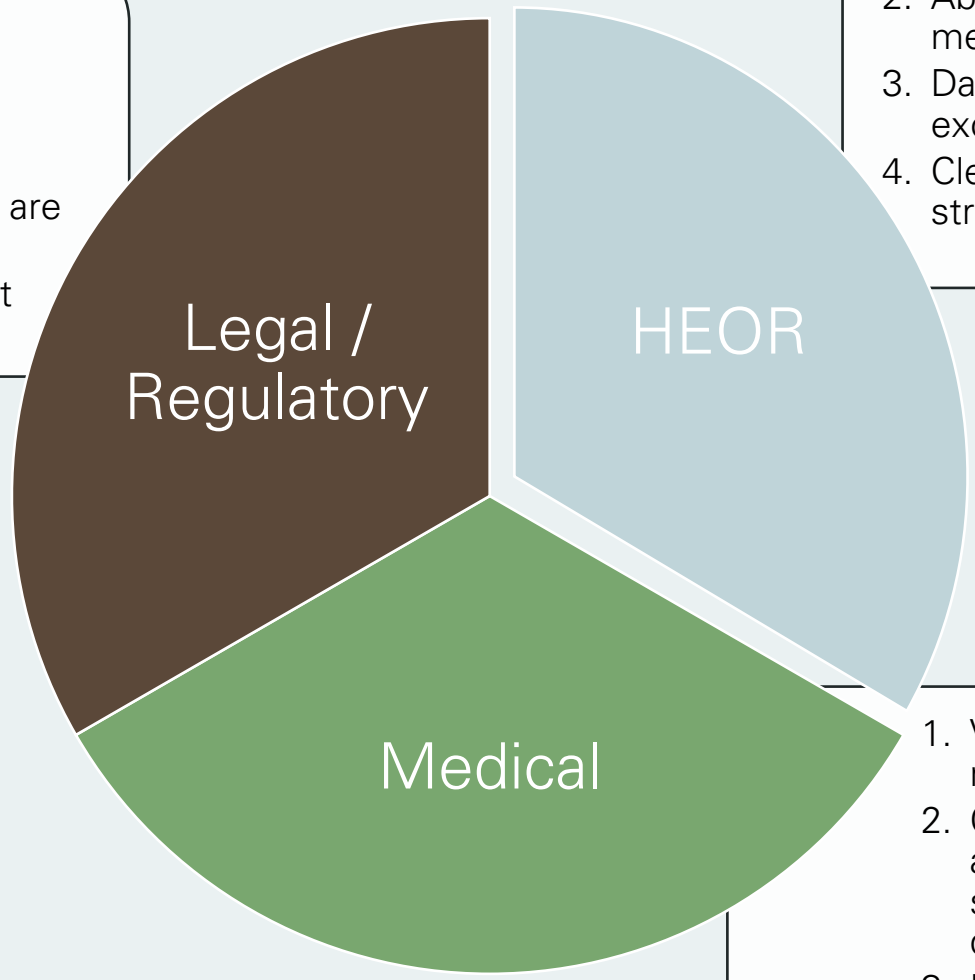
Internal CARSE Review

- Established CARSE certification methods baked into internal processes for approval of materials
- Committee evaluates research to determine whether it meets CARSE standard
  - Study lead provides materials to peers and addresses questions / input
  - Timelines considerations
- CARSE evaluated against rubric of criteria to determine if certification will be issued
  - Accepted methodology, pre-specified outcomes, appropriate data source, accurate and balanced analysis
- Potential option for larger organizations with in-house expertise

- All CARSE certified materials should go through internal promotional review via typical channels
- Promotional review typically contingent upon CARSE certification

Guiding Principles for Key Stakeholders Perspectives HCEI Evaluation

1. Verify material is within scope for HCEI guidance
2. Ensure adherence to legal and regulatory framework
3. Confirm methods, data, and interpretation are clear and non-misleading
4. Data are provided with appropriate context



1. Rigor of research evident
2. Ability to train field teams to deliver message effectively
3. Data facilitates meaningful scientific exchange with health care decision makers
4. Clear messaging aligned with organization's strategy

1. Validate medical accuracy of relevant methods, inputs, and conclusions
2. Confirm sources of data are most appropriate for context of use (type of source, relevance to population, date of data disclosure/publication)
3. Fair and balanced depiction of other therapies and treatment landscape

Finding the Right Balance

- Common barriers result from miscommunication between stakeholders
  - Need for internal alignment as to what guidance will allow so that it may be effectively implemented
  - Alignment on appropriate process for approval of HCEI communication (e.g., CARSE process)
- Stakeholder understanding of the data gap that HCEI communication addresses allows for productive dialog to identify solutions to mitigate risk
  - Best research practices should be balanced with potential legal/regulatory risks
  - Escalation processes may be implemented if consensus cannot be reached
- Important for HEOR colleagues to be aware of business priorities and organization's interpretation of legal and regulatory framework as they plan for pull-through of their work
  - Ensure research initiatives ultimately meet framework for promotion

Approaching CARSE from A US Payer Perspective

Jessica Daw, PharmD, MBA
VP, Pharmacy
Sentara Health Plans

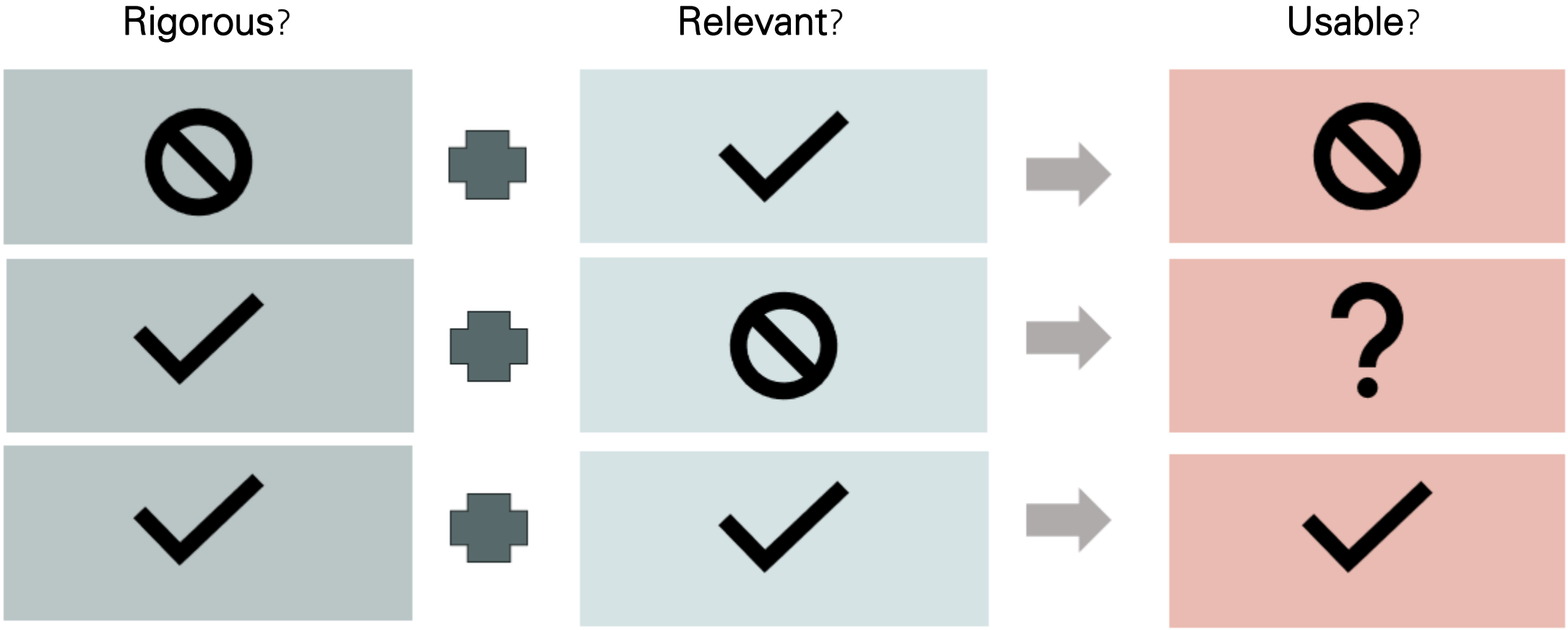
Payer Perspective

- Credible
- Reliable
- Background
- Contextual
- Validity
- Patient-Reported Outcomes
- Real World Evidence

- Transparent
- Relevance
- Interactive
- Interpretability
- Comparators
- Place in Therapy

- Formulary
- Reimbursement
- Pharmacy Trend
- Budget Impact
- Benefit Pricing

Applicability (Payer Perspective)



- Accelerated approvals/ orphan diseases
- Non-published studies (lack of transparency)
- Multiple indications
- Digital health/therapeutics

Closing Considerations

- Communicating HCEI based on CARSE provides opportunities to broaden the typical scientific dialogue between manufacturers and payers
- Guidance exists to help frame these discussions, but may be applied very differently across manufacturers due to risk tolerance and lack of clarity
- Establishing a plan to assess CARSE in a systematic way is a key success factor for manufacturers looking to communicate HCEI in a rigorous and meaningful way
- Rigor is critical, but designing studies to generate HCEI for payer audiences must be relevant and, where possible, tailored to specific audiences

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To effectively convey the value of a product to payers, it's important to ensure that economic evidence is not only robust but also trustworthy.

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Panel discussion