

Real World Evidence: Determining Quality and Application of Data Metastatic Hormone-Sensitive Breast Cancer

Real world evidence is more accessible following the digitization of healthcare. This change has led to the development of new analytics and visualization tools and has prompted more collaborative relationships between providers, stakeholders, and patients. Real world evidence is at the heart of payer-pharma outcomes-based reimbursements, and it will also drive clinic reimbursement as payments shift to value-based over volume-based.¹

Potential impact of real world evidence:²

- Support for regulatory decisions
- Advance disease understanding
- Improve clinical guidelines
- Clarify outcomes-based reimbursement
- Confirm trial findings
- Identify medication use problems
- Hypothesis generation
- Elucidate drug metabolism differences between races

Sources of real world evidence:³

- Observational studies
- Insurer’s claim data
- Patient surveys
- Electronic medical records
- Patient registries

Table 1. Comparison of real world evidence and controlled trials

	Real World Evidence	Randomized Controlled Trials
 Pros	<ul style="list-style-type: none"> • Increases diversity • Includes patients with comorbidities • Large sample size • Uncovers rare toxicities • Demonstrates tolerability • Inexpensive • Flexible timeframe • Known cost of treatment to patient 	<ul style="list-style-type: none"> • Controlled environment to evaluate treatment efficacy • Limits outside influence on results • Easier to prove causality • Confounding by baseline characteristics can be minimized
 Cons	<ul style="list-style-type: none"> • Difficult to prove causality • Missing data points • More patients lost to follow-up • Susceptible to bias • Group allocation not blinded • No structured data collection methods 	<ul style="list-style-type: none"> • Poor reflection of the real world • Lack of diversity in trial population • Time consuming • Costly • Shorter follow-up period • Unknown cost of treatment to patient

Real world evidence is complementary to randomized controlled trials: In oncology, we need both. Long-term real world evidence provides additional information to patients to support shared decision making³



Understand metabolic differences between races:

Not all patients metabolize medications the same way. The use of real world evidence to support prescribing practices will help providers prescribe the right dose of the medication the first time instead of adjusting due to poor tolerance and risking therapy discontinuation.

Determining High-Quality Versus Low-Quality Real World Evidence

How to perform an assessment of real world evidence:

1. Consider the limitations of the data set – What was the source? How was the data collected? What information is missing? What biases could be included? How was the population different from the original studies?
2. Was there a transparent explanation of how the data was handled for purposes of published information?
3. If groups were compared, were statistical methods applied to help balance the data?
4. Apply the appropriate tool from the list below to aid your assessment

Table 2. Statistical methods to reduce bias

Balancing Methodology	When Should It Be Used?
Stabilized Inverse Probability of Treatment Weighting (sIPTW) ⁵	<ul style="list-style-type: none"> • Useful in observational studies to reduce selection bias • Creates a pseudo dataset by weighing subjects with IPTW and conventional regression models • Stabilized weight helps directly estimate the main effect and its variance from conventional regression models
Propensity score matched groups ⁶	<ul style="list-style-type: none"> • Predicted probability of being assigned specific treatment given what is known about the patient's confounding factors • Useful for patients with similar performance status but different treatments • Mimics baseline equivalence in a controlled trial • Balance can only be demonstrated in measured covariates • Examples: Matching, restricting, stratifying, weighting

Data Limitations

- Incomplete
 - New guidelines for data management are in development, as there is currently a lack of defined standards
 - Best practice is a transparent explanation of methodology used to control for differences in patient groups or missing information
- Unbalanced groups are hard to compare

Table 3. Additional tools to help determine the quality of evidence

ISPOR Questionnaire⁷ Assesses relevance and credibility of modeling studies for informing healthcare decisions	ISPOR Checklist⁸ Focuses on issues that are unique to database studies or problematic in database research
GRACE Checklist⁹ Guidelines for noninterventional studies	ROBINS-1¹⁰ Assesses risk of bias in non-randomized studies of different interventions

Discussing real world evidence with your hormone sensitive metastatic breast cancer patients

What do patients want to know?¹

- What is real world evidence?
 - Results from insurance claims, disease registries, electronic medical records, observational studies, and patient surveys¹
 - Cancer care changes quickly and real world evidence gives us a chance to make sure these medicines work for everyone, not just the people studied in the clinical trial
- Is it safe and reliable?
 - This information can help show us how safe a medicine is over a long period of time
 - Real world evidence reinforces information that we have already learned from controlled clinical trials
- What does this tell me about side effects?
 - Each patient is different: Previous treatments and ethnic background may play a role in how they are affected by medications
 - Real-world evidence helps us recommend specific treatments for individual patients, even they weren't represented in the original trials



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This is part of a continuing medical education program titled **RWE Where RCTs Fall Short: Optimizing Frontline Treatment of HR+/HER2- Metastatic Breast Cancer**

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