

# COMPARATIVE EFFECTIVENESS AS A DRUG DEVELOPMENT TOOL



A Q&A with John Doyle, Vice President and Practice Leader of Quintiles Consulting, sheds light on the complex issue of comparative effectiveness research, and its strategic importance in successful and efficient biopharmaceutical development.

Recently, there has been a great deal of media coverage examining comparative effectiveness research (CER). From your perspective, what is comparative effectiveness research, and what is it not?

CER involves the conduct and the synthesis of research that compares the clinical process, treatment outcomes and even the appropriateness of health care interventions. The recently created Federal Coordinating Council for Comparative Effectiveness Research defines CER as “the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in ‘real world’ settings.”

Notably, CER is not simply a focused evaluation of cost or cost-effectiveness. First and foremost, the goal of CER is improving patient outcomes. As the findings of CER are adopted by providers, it should reduce variation in treatment, thereby improving the efficiency of the treatment process. With this improvement in process and outcomes, cost savings can be realized as a byproduct. At its core, the overarching goal of CER should be to inform evidence-based medical decisions between patients and physicians.

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## What major challenges face the industry as they try to implement CER?

The first challenge is practicality. If manufacturers want to compare a new agent to the standard of care in the real world setting – which is what CER currently implies – that’s difficult to do until the product has launched. During the development stage, for example, the challenge is collecting real world information about the product.

However, developers can still cover a lot of ground by evaluating the disease epidemiology, etiology, treatment patterns and technologies that are being used today as the gold standard for the disease. At launch, you might not have the complete picture of how your product

compares versus the gold standard in practice, yet if you've engaged in observational, prospective and retrospective work to evaluate how the current treatment paradigm is being implemented, you'll have a good starting point.

The process begins with answering the questions: "What patient is the burden of disease and unmet medical need that persists across various patient populations?" And, "what are the clinical and humanistic outcomes that can be realized today based on the gold standard?" From there, you can simulate the comparative effectiveness of your new product, and thereby set up a plan to demonstrate the products benefits and risks vis-à-vis the gold standard.

It's important to emphasize that universal adoption of CER will fundamentally change the manner in which drugs are developed and have significant effects on the industry. The end goal of achieving regulatory approval based solely on placebo-controlled RCTs will no longer be sufficient. But rather, companies will need to complement traditional clinical development with additional comparative research in order to establish a new drug's value proposition in the very early phases of development. This comparative need not necessarily be conducted by randomized head-to-head (H2H) trials, but should also encompass observational research on the current standard of care to better understand unmet medical need.

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### How do you substantiate the benefits of CER?

It all comes down to health outcomes. Initially, CER can shed light on how a new drug should be utilized most appropriately for the patient population with greatest unmet medical need. Second, the research can illuminate how treatment patterns vary across patient populations, provider types, treatment settings and geography in the day-to-day, real-world health care setting. It is important to describe that heterogeneity of treatment process and investigate whether it precipitates mixed outcomes.

Ultimately, this research can highlight how a new product can be best used to maximize beneficial outcomes and minimize patient risks. The composite measure of benefits and risks provide a measure of value to various stakeholders, such as patients, physicians and policymakers. Accordingly, all of these stakeholders should provide input into CER metrics.

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### From a patient's perspective, how can CER really help them?

Everybody wants to have access to the best, proven treatment for their condition. That's the first manner in which patients can derive benefit from CER – the promotion of evidence-based medicine. Secondly, because CER focuses on a more holistic outcome metric, which may include humanistic endpoints as well as traditional clinical endpoints, it encompasses patient-reported outcomes. PROs enable researchers to evaluate a treatment's risks and benefits from a patient's perspective by investigating concepts such as quality of life, patient utility and even convenience.

## Globally, are regulatory agencies or government payers getting more interested in CER?

NICE (the U.K. National Institute for Health and Clinical Excellence) employs a form of CER known as a Healthcare Technology Assessments, or HTAs. This form of CER is a structured analysis of existing evidence that provides input to a policy decision. It's emerging globally as a tool to help payers and providers make informed decisions on coverage, payment and patient care. They typically use a blend of retrospective and modeling practices. In addition to the U.K., HTAs have been historically implemented in Canada and Australia and are increasingly being implemented throughout Europe and the U.S.

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## What are some of the best practices or key success factors for integrating CER into clinical development?

The best practice always centers on concern for the patient. Rather than only considering regulatory requirements or the payer's perspective, it's important to consider the patient's view. For example, patient advocacy groups can voice a message about comparators or endpoints in clinical trial planning. In addition, indirect health care stakeholders such as employers and employer coalitions dedicated to quality initiatives may provide insightful recommendations for pragmatic clinical research. Therefore, all of these groups should have a say in some aspects of CER design.

One such group is the Partnership to Improve Patient Care, a group focused on ensuring that potential CER solutions support both providers and patients with the right information to make treatment decisions.

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## On a macro level, what trends do you see occurring in this area in one to three years?

I see consumer-driven health care as being a major, macro trend as patients convert to consumer status in the health care system. They're having a greater say in the choices they make in concert with their physicians about prescriptions and health care interventions. As payers and policymakers shift an increasing share of the economic burden of health care interventions onto patients, consumers are asking for, and rightfully deserve, better access to information.

Consumer-driven health care is a call to manufacturers to package evidence of a product's benefits and risks better suited for patients. Consumers want to be able to evaluate health

care products just as they do with other resources they use in their everyday life. The industry needs to improve the way it evaluates, compares and communicates the comparative effectiveness and safety of health care interventions to patients.

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### Overall, then, how will CER affect pharma?

Ultimately, CER broadens the market and ensures optimal application of health care innovation. Manufacturers are accustomed to serving a very focused, well-informed market – physicians, managed care organizations, government payers and policymakers are savvy and market-intelligent consumers. Patients, on the other hand, often don't have access to the level of information that is necessary to create fair market dynamics. Again, this is a call to the pharmaceutical industry to not only embrace the patient as a consumer, but also think about process and outcome from the consumer's perspective. Universal interest in CER provides manufacturers with an historic opportunity to take the lead in setting new standards for research design to evaluate treatment processes and outcomes from multiple perspectives, and ultimately communicate this information to stakeholders in a way they can understand and apply to their health care decision-making.