Contemporary Issues

Comparative-Effectiveness Research to Aid Population Decision Making by Relating Clinical Outcomes and Quality-Adjusted Life Years

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ABSTRACT

Background: Comparative-effectiveness research (CER) at the population level is missing standardized approaches to quantify and weigh interventions in terms of their clinical risks, benefits, and uncertainty.

Objectives: We proposed an adapted CER framework for population decision making, provided example displays of the outputs, and discussed the implications for population decision makers.

Methods: Building on decision-analytical modeling but excluding cost, we proposed a 2-step approach to CER that explicitly compared interventions in terms of clinical risks and benefits and linked this evidence to the quality-adjusted life year (QALY). The first step was a traditional intervention-specific evidence synthesis of risks and benefits. The second step was a decision-analytical model to simulate intervention-specific progression of disease over an appropriate time. The output was the ability to compare and quantitatively link clinical outcomes with QALYs.

Conclusions: The outputs from these CER models include clinical risks, benefits, and QALYs over flexible and relevant time horizons. This approach yields an explicit, structured, and consistent quantitative framework to weigh all relevant clinical measures. Population decision makers can use this modeling framework and QALYs to aid in their judgment of the individual and collective risks and benefits of the alternatives over time. Future research should study effective communication of these domains for stakeholders. (*Clin Ther*. 2013;35:364–370) © 2013 Elsevier HS Journals, Inc. All rights reserved.

Key words: CER methods, comparative-effectiveness research, decision analysis, framework, quality-adjusted life years.

INTRODUCTION

The US government took another step toward promoting evidence-based health care decision making with the initiative known as comparative-effectiveness research (CER) and through the investment made by the American Recovery and Reinvestment Act.[1] The Institute of Medicine defined CER as "The generation and synthesis of evidence that compares the benefits and risks of alternative methods to prevent, diagnose, treat, and monitor a clinical condition, or to improve the delivery of care," to "assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health-care at both the individual and population levels."[2] The Agency for Healthcare Research and Quality (AHRQ) suggests 2 main methods to generate CER evidence: (1) through synthesizing existing evidence, or (2) through generating new comparative evidence on benefits and risks.[3] Following the AHRQ methods to generate CER evidence, population-based decision makers still face the difficult task of placing weights on unique risks and benefits to prioritize alternative interventions.

A gap exists in an approach for bridging various forms of evidence for the pursuit of population-level

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decisions about the superiority of alternative interventions. The main objective of this article is to present a framework for population-based decision makers to quantitatively weigh and better grasp the collective intervention-specific clinical risks and benefits and their uncertainty. We propose a CER framework that extends decision-analytical modeling, without requiring the inclusion of cost, to incorporate comparative risks and benefits. The approach addresses time horizon, uncertainty, and generalizability. We present the framework, provide example displays of the outputs, and discuss the implications for population decision makers.

FRAMEWORK FOR AIDING COMPARATIVE-EFFFECTIVENESS RESEARCH DECISION MAKING

The US Food and Drug Administration (FDA) has a regulatory process that ensures that new interventions are efficacious and have a favorable risk-benefit profile. Randomized controlled trials (RCTs) are the gold standard for providing evidence of efficacy and answering the question of "can the intervention work in a focused and tightly controlled environment?"[4] Population-based decision makers would like to know if the intervention works and provides good value compared with its alternatives (not placebo) in the real-world population. Decision makers, such as public and private payers, are often forced to use the regulatory-driven evidence and rule of law to make coverage and reimbursement decisions. Efficacy trials have strong internal validity, answering the question "can it work," but low external validity or generalizability as in "does it work" in the real world, for a wide variety of patients. In addition, developers are incentivized to quickly deliver their interventions to the market; often these incentives result in designing RCTs with surrogate outcomes, short observation time, and limited information on risks. CER recognizes this disconnect. We proposed a decision-analytical framework designed to increase external validity for such decisions.

Our approach was a 2-step health outcomes approach to CER that incorporated decision-analytical modeling. Figure 1 depicts the conceptual framework involved with these 2 steps. To begin to conduct pop-

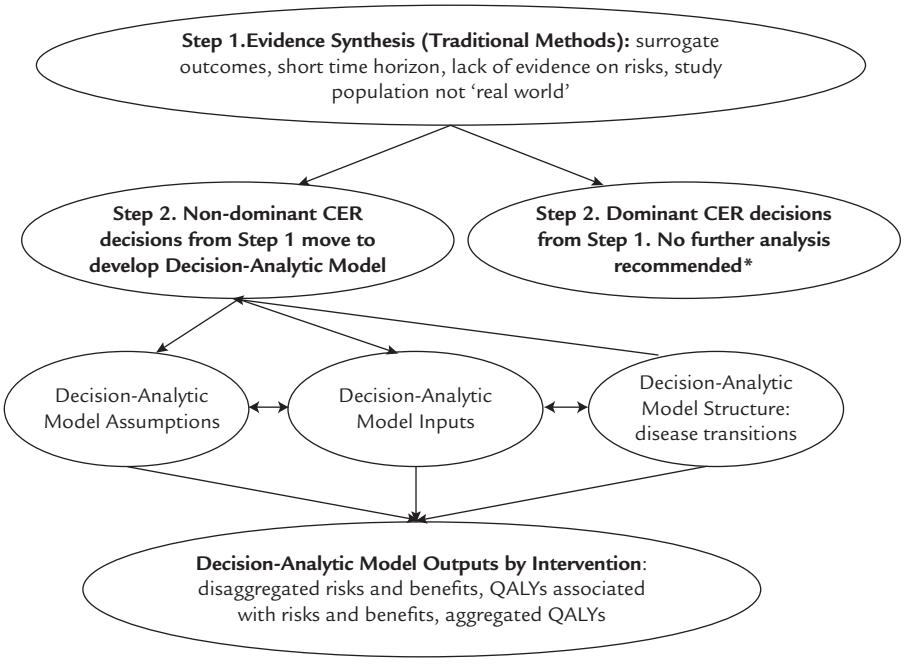

Figure 1. Theoretical framework: 2 steps for improving information for comparative-effectiveness research (CER) decision making. *Reasons to continue to a second step may include: an interest in cost as well as benefits and risks; a concern that the population of interest does not match the evidence base; or a concern that a more appropriate time horizon for the disease may introduce competing risks and other attributes that could sway certain risks or benefits to favor a different alternative. QALYs = quality-adjusted life years.