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POLICY FORUM

Comparative Effectiveness Research Would Contribute More to Ethical Policy Making if Cost Were Considered

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A common framework for ethical considerations in medical decision making includes four principles: (1) respect for autonomy (the patient should be able to make choices), (2) beneficence (medical care professionals should act in the best interest of the patient), (3) nonmaleficence (physicians should not harm), and (4) justice (benefits should be distributed equitably) [1]. Three of the four principles are most easily interpreted at the patient level; the fair distribution of benefits, however, cannot be considered without thinking at the population level. As payers and policymakers demand a more evidence-based approach to ethical medical care, they must ask the following questions: (1) Does the relatively new field of comparative effectiveness research (CER) better serve medical ethics than research designs that provided evidence previously? (2) Is CER still missing elements important for ethical decision making?

Before Comparative Effectiveness Data

Prior to the Affordable Care Act's comparative effectiveness research initiative, constructing evidence-based arguments for policy, guidelines, or best-practice recommendations required ranking the quality of clinical evidence; generally, randomized controlled trials (RCTs) were ranked as [the highest quality form of evidence](#) [2-4]. Since participants in such trials are randomly assigned to trial treatment or control groups, if differences between the groups' average outcomes are statistically significant, they are taken as evidence that the trial treatment had some effect or that one treatment is better than another. Randomization is the only way to ensure that unobservable participant characteristics are initially distributed more or less similarly across treatment groups. The use of the term "unobservable" here means patient information unavailable to the researcher. The patient and clinician may be aware of information that the researcher does not have that could affect the decision about which treatment to assign and the expected effectiveness of alternative treatments in nonrandomized settings. This can cause bias in this type of study.

Despite the potential for high levels of internal validity, randomized trials can lack external validity or generalizability to individuals not included in the study. The clinical centers at which randomized trials are conducted are not generally representative of the sites at which all patients receive care. The inclusion criteria for study subjects are often extensive, may eliminate people who have comorbidities that may be common in the

“real” patient population, and may otherwise limit the subjects in ways that make the conclusions clear but not necessarily applicable to the general population with the condition being studied. Additionally, the results of randomized trials are average results for everyone in the study. Studies that have a large enough sample size to allow clear inferences about subsets of the clinically relevant population tend to be expensive and are therefore less likely to be undertaken.

Comparative Effectiveness Research

As the field of evidence-based medicine has grown, the need was recognized for clinical evidence with greater external validity for the purpose of developing policy, guidelines, and best practices. In this context, the field of CER emerged. While there are numerous definitions of this term, the definition that is found on the White House website [5] is:

Comparative effectiveness research is 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. The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision-makers, responding to their expressed needs, about which interventions are most effective for which patients under specific circumstances.

- To provide this information, CER must access a comprehensive array of health-related outcomes for diverse patient populations and sub-groups.
- Defined interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
- This research necessitates the development, expansion, and use of a variety of data sources and methods to access comparative effectiveness and actively disseminate the results.

CER and Ethics

Given this definition, it is worth contrasting the ethical dimension of decision making using randomized trial results (i.e., findings applicable primarily to patients in academic medical centers) with that of decision making using CER results (i.e., findings based on data reflecting real-world conditions for diverse patients covered by heterogeneous payers in varying clinical settings).

Controlled randomized trials address ethical principles at a population level—recommendations based on RCT results are in the average best interest and avoid overall harm. However, individual patients and medical care professionals acting in the best interest of and doing no harm to those individual patients will be helped by having

information about the effect of care for clearly defined subpopulations in specific, real-world settings. The variation in clinical settings that can be captured in CER—different levels of facility quality, wide variation in professionals' training settings and experiences, and heterogeneous support staff—are crucial and may lead to a range of outcomes applicable within the general patient population. Hence, the type of information that will lead to better-informed decisions will be more readily available from [comparative effectiveness studies](#) in which information for each subgroup is ascertained and then combined with the epidemiological data on the patient population.

Cost

Critically, however, while high-quality CER provides clinical effectiveness information for specific patient populations, it [lacks any reference to cost](#) [6, 7]. This omission was intentional; CER focuses solely on clinical effectiveness in real-world settings with real-world populations while avoiding the sticky political debates that invariably arise when making decisions about allocating limited resources and having to acknowledge explicitly that at least some people will be denied health care resources. Yet cost information is critical because the distribution of benefits is only partially determined by who would benefit more, clinically, from the treatment if they received it in the real world; it is also determined by how many patients *can* receive that treatment in the real world, i.e., the distribution of available resources to varying subpopulations.

In other words, assuming that the average costs apply to everyone does not make any more sense than assuming that everyone would have the average clinical outcome. It is worth considering [adding cost to the data](#) for making ethical medical policy and guidelines recommendations—a concept encapsulated by the term comparative cost effectiveness (CCE), which I first heard used by my colleague Josh Feldstein at the Center for Applied Value Analysis [8]. CCE entails using data from comparative effectiveness studies to inform cost-effectiveness analyses or other economic evaluations, applying the same expectations to cost data that apply to clinical effectiveness data. We would have to find ways to link the cost results to the heterogeneous populations being treated by heterogeneous clinicians in real world settings, taking into account complication rates, failure to receive treatment, and other real-world conditions. An example of the CCE approach is to look at a new device or pharmaceutical product, compare it with existing competitive products, and assess how the adoption of the new product would affect the bottom line of a hospital, insurer, or integrated delivery network.

Adding cost considerations to CER results would allow those setting policy and making treatment recommendations to make decisions that are more in line with the four principles of medical ethics: patients and their clinicians could make decisions with an understanding of the clinical *and financial* consequences, expanding the principles of doing no harm, beneficence, and respect for autonomy into [the financial sphere](#) (assuming that patients are clear about tradeoffs between money and quality and length

of life), and the population distribution of potential benefits and burdens in light of individual and population financial constraints could be projected with greater precision. Finally, on a societal level, cost data could help policymakers understand what else would have to be given up to achieve a given set of benefits, facilitating deliberations about both justice and how to prioritize medicine and other public needs.

In sum, CER may advance ethical medical decision making, but without including cost data, important aspects of the distribution of benefits and burdens will remain unaddressed.

References

1. Gillon R. Medical ethics: four principles plus attention to scope. *BMJ*. 1994;309(6948):184-188.
2. Hadorn DC, Baker D, Hodges JS, Hicks N. Rating the quality of evidence for clinical practice guidelines. *J Clin Epidemiol*. 1996;49(7):749-754.
3. US Preventative Services Task Force. *Guide to Clinical Preventative Services: Report of the US Preventative Services Task Force*. 2nd ed. Baltimore, MD: Williams and Wilkins; 1996.
4. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians task force. *Chest*. 2006;129(1):174-181.
5. Nabel EG. Comparative effectiveness research: National Institutes of Health PCAST session on health reform and CER. August 6, 2009. <https://www.whitehouse.gov/files/documents/ostp/PCAST/Nabel%20Presentation.pdf>. Accessed May 7, 2015.
6. Comparative Effectiveness Act of 2008, S 3408, 110th Cong, 2nd Sess (2008).
7. Children's Health and Medicare Protection Act of 2007, HR 3162, 110th Cong, 1st Sess (2007).
8. Center for Applied Value Analysis website. <http://www.cavalue.com/>. Accessed May 7, 2015.

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