

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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Cost-Effectiveness Analysis in Oncology

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H&O How has cost-effectiveness analysis been utilized in oncology?

DM One can think about cost-effectiveness analysis (CEA) in oncology as having different eras. The earliest era focused on screening and preventive healthcare, which included the cost-effectiveness of Pap smears, colonoscopies, and mammograms. CEA was prominent during this period because physicians made medical decisions based on the belief that these preventive measures would improve health at an acceptable cost. Costs were, and still are, a natural concern in screening, and in the United States, preventive healthcare has been an area where cost-effectiveness has been used as an advocacy tool.

The second era of CEA in oncology was its application in expensive biologics and advanced therapeutics. In this period, studies evaluated bone marrow transplantation as well as expensive therapies for various cancers. Because treatments were very costly, payers began questioning whether the treatments were worth the money they were paying, which in turn prompted pharmaceutical companies to try to prove that the clinical benefit of the drug was worth the price. We are probably still in the midst of this second era.

I think that the third era of CEA will be its application in targeted therapies and biomarkers. This is a new area of research and something that will require much more investigation. It is a natural outgrowth of the second era, because when oncologists have an expensive therapy, they may be less eager to use it in a population that is low risk, and therefore, it may be possible to justify higher prices for specific high-risk patients who are going to benefit from this therapy.

H&O How does CEA apply to drug development?

DM CEA can both drive innovation and hinder drug development. In the case of a high value drug, when it comes off patent, pharmaceutical companies have the incentive to develop a new high quality drug to replace the newly generic drug. However, if a drug offers minimal benefits relative to its costs, companies are going to sell less of it and receive a lower price than they would have otherwise, which in turn would decrease investment in producing such a drug. Hence, CEA appears to have a more negative effect on low value drugs than on high value drugs and the associated pricing policies, and encourages movement away from drugs with minimal benefit.

H&O How do we put a value on life? Is it possible to use CEA as a health policy tool?

DM There are many estimates regarding the worth of a quality-adjusted life year: often \$50,000–200,000. These estimates are generally developed by looking at tradeoffs people make that risk their life or health in return for some sort of financial benefit. It is surprising to see that in the United Kingdom, the choice between these numbers seems to govern treatment and payment decisions. I think we are rarely confident enough about the exact short- and long-term benefits and costs of specific therapies to make very nuanced decisions in general. In my experience, I usually look for results that suggest that a therapy is very cost-effective, or really low benefit and not cost-effective, and I do not put much weight on the finer distinctions. A great example is CEA and Pap smears. We know that there are significant benefits of having a Pap smear every 3 years for most women, but if the frequency of the procedure is shorter, there are smaller benefits. The value of getting an extra Pap smear can fall by 10-fold or more; this is the kind of waste we need to look for and eliminate.

H&O Why do you think there has been more resistance to the use of CEA in the United States?

DM We have resisted any approach to rationing in this country because historically our government has a smaller role in healthcare, although clearly Medicare and Medicaid are immense. However, many of our patients rely on the private system and on co-pays. We have very powerful political forces that attempt to impede efforts to limit care, and Americans who are insured are not accustomed to not receiving healthcare. We also have a very powerful political lobby of people who benefit from this very expensive way of providing coverage, and there is a degree of a lack of realism about the long-term ability to fund healthcare. I think people are beginning to understand the situation we are in, and I hope we start to make these adjustments sooner rather than later because the longer we wait the harder it will be.

H&O Do you think there is resistance from community oncologists in regard to discussing costs and incorporating them into treatment decisions?

DM We have conducted some research on doctor-patient communication on out-of-pocket costs and the research suggests that both doctors and patients agree that these conversations are important to have, but that they rarely occur. I think there will be more discussions as out-of-pocket costs get larger, because with some of the very expensive therapies, it is impossible to avoid the question of cost-effectiveness. It is possible that physicians will lose many patients if they do not address patients' economic needs at the same time as addressing their medical needs.

H&O What are future costs?

DM When an individual invests in a medical intervention that extends life, he or she creates cost from the future years that come not just from future medical expenditures (because he or she is living longer), but also from non-medical expenditures that accompany the benefit of living a longer life, such as the cost of having a house, paying for food, etc. There are also savings that come when a patient lives longer; for example, he or she could work longer or provide better care to family members. These benefits, referred to as future costs, should be measured. We have shown that in order to conduct CEA correctly, it is necessary to measure all future benefits and costs, including medical and nonmedical expenditures and any effects on earnings. Excluding these costs from CEA results in too

much time spent on interventions that extend life and not enough time spent on things that improve quality of life. This is very applicable in oncology because there are chemotherapeutic regimens that have very negative effects on quality of life, yet extend survival. These types of calculations can suggest that, from a cost-effectiveness perspective, appropriately including future costs and benefits can create a shift toward things that are less damaging to quality of life. Future costs also suggest that new therapeutic approaches for cancer, which may not necessarily improve survival but improve quality of life, might be highly cost-effective, and correctly analyzing these things from the theoretical perspective is important to illustrate in CEA.

H&O What is CEA alongside clinical trials?

DM There are many studies that collect cost and utilization data concurrently with collecting data on effectiveness and safety; this is called CEA alongside clinical trials. Many clinicians are considering this analysis because of the demand for timely economic data, but it is unclear how early in the process these data should be collected since the cost data become irrelevant when a drug is not found to have therapeutic advantages.

H&O What do you foresee as the future for CEA in oncology?

DM I think that we will see CEA being used more frequently in the United States; we have already seen it increasingly utilized worldwide. I do not think we will use CEA as the only factor in making decisions. I hope that over time, people will get more used to seeing these results, understanding what they mean, putting them into context, and making reasonable decisions with cost-effectiveness being one factor. I do not think that a naïve decision based only on the results of a cost-effectiveness study is the right approach for making a judgment about a therapy, but I think these can be useful statistics that help oncologists in making these decisions.

In addition to incorporating CEA in our decision-making, researchers have also begun looking at value of information analysis to help set priorities for research. This is currently a very important area in oncology, as it enables prioritization of clinical trials based on numerous factors. Value of information analysis allows researchers to prospectively identify the expected gain in life expectancy, quality-adjusted life expectancy, or other measures of population health in various studies in order to decide where to best invest research money.