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The right amount of chemotherapy in non-curable disease: Insights from health economics

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ABSTRACT

This article applies concepts from health economics to address what is the "right" amount of chemotherapy in non-curable disease. A health economics perspective is beneficial because it forces a focus on objectives and constraints. We review and apply the concepts of "Choice of Comparator", "Use of QALYs" and "Equating Marginal Benefit to Marginal Cost", demonstrating their fit for purpose when considering the optimal amount of chemotherapy for non-curable disease. Many efforts underway to improve healthcare can be viewed as applications of these key economic principles. The true value is in the concepts themselves and not in the associated calculations. Given the difference between a population and a patient perspective, different "optimal" amounts of chemotherapy may exist. For many, however, best may not be most. Optimal decisions may vary depending on whether the goal of treatment is to maximize hope or health.

1. Introduction

In a recent *Forbes* post entitled, "The FDA Is Basically Approving Everything", Matthew Herper argues that the Food and Drug Administration's approval rate for new drugs is over 95% [1] in sharp contrast to when it "once approved as few as 40% of new drugs"[2]. This trend produces pressure around the world for healthcare providers to prescribe and healthcare payers to fund these new products. There is agreement throughout medicine and especially in oncology that the current rate of growth in healthcare expenditures is unsustainable [3,4]. Recently published warnings have appeared in both general and specialty medical journals [5,6]. Experts note that the direct medical costs of cancer in the USA have increased from nearly $27 billion in 1990 [7] to more than $90 billion in 2008 [8] more than two-fold increase even after adjusting for inflation [9]. Smith and Hillner [4] report that annual direct costs in the USA for cancer care are projected to increase by over 66% from $104 billion in 2006 to over $173 billion in 2020 [4,10].

In cancer, there has been a pronounced focus on the cost of drugs in relation to their clinical benefits. Bach [11] observed that spending from 1997 to 2004 on Medicare's Part B drugs, "a category dominated by drugs used to treat cancer", increased by 267% compared with overall Medicare spending which increased by 47% during the same period. The problem of skyrocketing drug costs is compounded by evidence suggesting that increased expenditures are producing only minimal gains in terms of decreases in mortality and increases in quality of life [11]. In other words, healthcare payers are paying more and getting less [12]. In her editorial, "Why do drug companies charge so much? Because they can", Marcia Angell observes that "Unlike every other advanced country, the United States permits drug companies to charge patients whatever they choose" [13].

Although the USA has taken steps to prevent the simultaneous examination of both drug costs and patient outcomes [11,14], other countries have embraced methods from health economics to address the challenge of introducing controls in an attempt to curb healthcare spending [15–17]. First and foremost, cost-effectiveness analysis (CEA) has been implemented in a variety of settings to help with "smart shopping" for cancer drugs. However, there are other health economics concepts that can help, especially with address-

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ing the question of chemotherapy. This paper describes and then applies three principles from health economics to consider the "right" amount of chemotherapy for non-curable disease.

2. Principles

In this section we describe the economic principles we will demonstrate later in the Application section. The three key principles are

1) To compare treatment options, a comparator is needed;
2) Quality Adjusted Life Years (QALYs) are useful when considering both quality and length of life;
3) Optimal care occurs when the marginal benefit equals the marginal cost of care.

We now describe and explain each principle in more detail.

2.1. To compare treatment options, a comparator is needed

An essential part of any evaluation is the choice of a comparator. In economic evaluations of healthcare interventions and treatments, "something new" is often compared to "usual care". In CEA, the extra costs (ΔC) are compared to the extra effects (ΔE) with ΔC computed as the difference between the expected costs of the new treatment (C_{NT}) and the expected costs of usual care (C_{UC}); ΔE is computed in a similar fashion using a patient outcome chosen to be the *Effect* variable. The term "expected" is used in the statistical sense, where outcomes are weighted by their respective probabilities of occurrence. For example, with a new drug there might be a 50% chance of living 9 more months and a 50% chance of living 1 more month. The expected effect of the new treatment (E_{NT}) is

$$E_{NT} = \tfrac{1}{2}(9\text{months}) + \tfrac{1}{2}(1\text{month}) = 5\,\text{months}.$$

If patients receiving usual care are expected to live 4 months, then $\Delta E = E_{NT} - E_{UC} = 5-4 = 1$ more month.

Simply knowing the new treatment's expected effect (E_{NT})—or expected cost (C_{NT})—is not enough to do comparative analysis, such as economic evaluation. This is because the calculation of ΔE involves two components (i.e., E_{NT} and E_{UC}) as does the calculation of ΔC. In addition, the choice of a different comparator frequently yields different estimates of ΔC and ΔE. For example, if usual care instead were associated with an expected patient outcome of 7 months of life, then $\Delta E = E_{NT} - E_{UC} = 5-7 = -2$ (i.e. 2 less months). Thus, CEA relies on four expected values for the estimation of ΔC and ΔE to inform policy and practice decisions. This is impossible to do without a choice of comparator.

An appropriate comparator has a large impact on the finding of effectiveness and 'value for money' of a treatment. Traditionally, palliative care interventions as 'usual care' have not been compared against chemotherapy for best care in end of life. However, where they have, there is evidence for the potential of improved quality of life (and sometimes even improved life expectancy [18]).

2.2. Quality adjusted life years (QALYs) consider both quality and length of life

Health economists often study the efficiency of different ways to accomplish an objective. When considering toxic treatments for incurable disease, a reasonable objective could be to maximize an outcome with quality of life (*qol*) and length of life (*lol*) dimensions. In these circumstances, health economists use the quality adjusted life year (QALY) which is equal to the product of *qol* and *lol*. The *qol* variable is called a "utility weight" and generally ranges between 0 (death) and 1 (perfect health) [19]. When QALYs are taken as the outcome of interest, the resulting economic evaluation is often described as a cost-utility analysis [20].

In these cases, the extra effects are calculated as extra QALYs (ΔQALYs). For example, a complete course of highly toxic chemotherapy may allow patients to live 6 months on average with a quality of life utility score of 0.60. Perhaps with good palliative management patients can be expected to live 4.5 months with a quality of life utility score of 0.80. The additional QALYs from the new chemo are calculated as

$$\Delta\text{QALYs} = \text{QALYs}_{\text{newchemo}} - \text{QALYs}_{\text{palliativecare}}.$$

$$\begin{aligned}\text{TheQALYs}_{\text{newchemo}} &= \text{qol}_{\text{newchemo}} \times \text{lol}_{\text{newchemo}} \\ &= 0.60(\tfrac{1}{2}\text{year}) = 0.30\text{QALYs}.\end{aligned}$$

This is the same as the result from the calculation of

$$\begin{aligned}\text{QALYs}_{\text{palliativecare}} &= \text{qol}_{\text{palliativecare}} \times \text{lol}_{\text{palliativecare}} \\ &= 0.80(0.375\,\text{year}) = 0.30\text{QALYs}.\end{aligned}$$

Thus, ΔQALYs = 0. QALYs are a relevant way to consider different amounts of chemotherapy, especially with non-curable disease. However, some critics argue that the QALY may not capture adequately quality of life at the end of life, which is relevant for the majority of high-cost cancer drugs that provide limited gains in life extension in the last year of life [21]. To reach a decision about the optimal amount of chemo, marginal benefits and marginal costs must be considered.

2.3. Optimal is where marginal benefit equals marginal cost

To maximize Net Benefit (NB), which is the difference between Total Benefits (TB) and Total Costs (TC), it is necessary to consider marginal benefit (MB) and marginal cost (MC). The term "marginal" describes the resulting "extra" for very small changes in consumption or use. Technically, NB = TB − TC and the quantity that maximizes NB is one such that MB = MC. Intuitively, if more chemo would add benefit greater than its additional costs (i.e., MB > MC) then one should consume more chemo. Alternatively, if the additional cost of more chemo is greater than the additional benefit (i.e., MB < MC), it does not makes sense to consume more (it makes sense to consume less). An optimal amount occurs when MB = MC, as the gain in benefit from doing a bit more or a bit less equals the increase in costs (so the gain in NB is zero). Although traditionally benefits and costs are thought of in monetary units, it is only necessary that they be in the *same* units. For example, benefits and costs could be considered in terms of usefulness, satisfaction, energy or effort. Regardless of the units employed, the optimal quantity of chemo is the level at which MB = MC. This simple rule can lead to counter-intuitive recommendations when applied; for example, the best amount of treatment may not be most amount of treatment.

3. Application

Next, we apply the principles described in the previous section to analyze what is the right amount of chemotherapy in non-curable disease. We assume a patient can receive an amount of chemo (*chemo*) for a non-curable disease ranging from 0% and 100% of the patient's remaining time. The optimal level of *chemo* can differ by perspective. While applying the economic principles, we illustrate contrasts between a population and an individual perspective.

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