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The Bottom Line

Assessing Costs, Benefits, and Risks in Chronic Disease: Taking the Long View

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The cost of medical interventions raises legitimate concerns at both individual and societal levels. Patients and their families must bear some or all of these costs, which their budgets often cannot accommodate. Additionally, health care systems operate within budgets and, thus, strive to maximize the outcomes within that budget. It is, thus, not only reasonable but also ethically responsible to be concerned with the cost of delivery of health care. Medical interventions involving a high upfront cost, such as allogeneic hematopoietic cell transplantation (alloHCT), are particularly troublesome and deserving of scrutiny. Paying for them might be impossible or come at the expense of painful tradeoffs [1]. However, it is not always true that high upfront costs involve high overall costs. Indeed, in this issue of *Biology of Blood and Marrow Transplantation*, Arnold et al. [2] show that in the case of alloHCT for children with sickle cell disease (SCD), what seems to be the higher cost alternative constitutes a more economic path over a period of 3 years.

Though the higher cost alternative was deemed superior on economic grounds when viewed over 3 years, it constitutes a relatively short period of time, potentially underestimating the positive economic impact of this high cost intervention. Importantly, there is evidence that the cost of treating SCD increases significantly during adult years. Furthermore, when costs are instead calculated from charges that include costs, anticipated profits, and adjustments in charges to cover for uncollected charges, annual charges for an adult with SCD reach $231,050 [3]. Most importantly, these annual charges were estimated to increase progressively in the following way: $35,488 for ages 0 to 5; $56,576 for ages 6 to 10; $111,749 for ages 11 to 18; and $231,050 for ages 19 to 50. As such, 3 years of pediatric costs do not show the significance of the savings that result from transplantations for SCD patients, not just because of the accumulation of costs but also because of the increase of yearly costs over time. The latter results from the facts that SCD is a chronic debilitating condition and organ damage becomes more severe over time, and, thus, its management becomes more and more costly.

This analysis also points to ways to make alloHCT for SCD patients even more economically attractive. Indeed, significant contributors to the cost of the intervention included the poor results obtained using cord blood grafts, the care required for the treatment of graft-versus-host disease, and treatment required for cytomegalovirus reactivation. Improvements in these 3 areas could substantially reduce the cost of the intervention. Indeed, in our own experience with adult patients undergoing nonmyeloablative peripheral blood stem cell transplantations for severe SCD, in which engraftment rates are high without graft-versus-host disease and only rare cytomegalovirus reactivation [4], the median cost is $147,595, which is 49% of the cost of a myeloablative transplantation performed at our institution (personal communication, Theresa Jerrusi). Moreover, the reduction in the yearly hospitalization rate in adults observed in our experience was from 3.23 in the year before transplantation, to .63, .19, and .11 in the first, second, and third years and beyond after transplantation, respectively, which represent a more drastic reduction than that presented for pediatric patients. A similar analysis of costs for adults undergoing nonmyeloablative transplantation would, therefore, likely require only 1 year of follow-up to demonstrate its favorability on economic grounds, superior to what currently constitutes the standard of care in the pediatric setting. However, on economic grounds alone, the earlier the transplantation, the greater the savings, as the total lifetime charges to someone with SCD living to age 50 was estimated at over $8 million [3].

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It should, however, be pointed out that claiming that 1 course of action is less costly than the alternative is not synonymous with claiming that it is cost effective. Cost effectiveness presupposes a comparison not only of costs but also of the resulting effects (ie, benefits) of the courses of actions that are compared. For that sake, the authors analyze the quality of life (QOL) that results from alloHCT. The authors demonstrate an improvement in this measure by comparing to published data, although their data on pediatric alloHCT patients does not yield a statistically significant increase in QOL. Oddly, the QOL measures do not differ significantly between the control subjects with SCD and the unaffected siblings, which suggests that the instrument is either not robust or that the QOL of pediatric patients is not as bad as the QOL of adult SCD patients [5]. It is also not clear whether the authors consider in their calculations the decline in QOL that occurs in SCD over time [5]. Certainly, one need only visit the clinic to see the profound debilitating effects that this disorder produces and the equally profound mitigating effects that a successful transplantation allows.

When comparing different courses of actions in terms of costs and effects, it is crucial to take the long view. Yet, in the case of chronic diseases, the same applies to risks. Prospective health-related burdens behave in the same way as prospective economic burdens and prospective health-related benefits. Indeed, just as comparing the costs of an intervention such as alloHCT to its alternative over a short duration of time can lead to the erroneous conclusion that it is too costly, comparing the risks of that same intervention viewed over a similarly short duration can lead to the erroneous conclusion that it is too risky. This mistake can be made when assessing the risks of an intervention, experimental or otherwise. The problem is that the upfront risks of an intervention along with its alternative are often applied to the time frame of the intervention only, not to the timeframe over which the intervention is designed to potentially protect from the harms of the underlying condition. And in the case of chronic diseases, that is a long period of time. In a somewhat extreme example, the shorter view has led to widespread rejection of the use of high-dose cyclophosphamide and autologous hematopoietic cell transplantation for type 1 diabetes because of its high upfront risks, despite evidence for efficacy over the long term [6]. If the risks of this intervention were compared to the long-term risk of type 1 diabetes, its risk profile might be considered acceptable.

In summary, chronic diseases exert their deleterious effects over the long term and interventions that seek to change the inevitable course of chronic disease must be viewed in that long term.

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