WHAT IS THE APPROPRIATE DISCOUNT RATE IN ECONOMIC EVALUATIONS OF GENE THERAPIES (GT)?

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Introduction

Discounting healthcare therapies adjusts future costs and health benefits to present values. Correct discounting values are of particular importance for estimating the cost-effectiveness of therapies that have a temporal distribution of costs and benefits, such as vaccines or curative gene therapies. This conceptual research discusses the issues surrounding discounting curative GT, which are widely debated when assessing the therapy's cost-effectiveness. The authors hypothesize if discount rates for GT should differ from a country's common practice, the methodologies to calculate discount rates, and the consequences per methodology. In addition, this research hypothesizes if discount rates for GT—once altered from common practice—should be uniform or differential, and higher or lower than current practice, as well as other issues that might arise.

Within this paper, gene therapies were defined as 'any therapy that alters genes and has a sustained, long-term, mostly curative effect on patients'.

Conclusion

Decision makers should reconsider their existing discounting methodology to ensure that it is compatible with the high up-front investments and long-term healthcare effects that GT faces, while taking ethical judgments into account.

Results

Comparing therapies

There are currently no guidelines for discounting in economic evaluations addressed at gene therapies. Recommended rates for other interventions vary across health technology assessment agencies and are often assigned with little or no justification [1]. It is common practice to use the same discounting rates across different therapies, ranging from preventive medicines (vaccines, mental health) to end-of-life treatments (oncology); however, this varies between countries. This practice is defendable because the evaluation of most therapies demand ongoing costs versus ongoing benefits. The essence of health economics is to use a standardized approach to compare the investment in various noncomparable therapies, ranging from diabetes to oncology. As all therapies within a country currently undergo the same discount rates, changing discount rates for GT would challenge the comparability between therapies and thus complicate investment/reimbursement priorities for decision makers. However, **NICE has issued special discounting guidance for cases in which treatment restores people health, who would otherwise die or have a very severely impaired life to full or near full health and is sustained over a very long period (>30 years) [2].**

Despite these complications, one area where the need for a different discount rate is often debated is within the field of vaccines. Like GT, vaccines demand upfront costs versus benefits that could either be spread over time (e.g., rotavirus) or manifest decades later (e.g., HPV). Recently, the Joint Committee on Vaccination and Immunization (JCVI) was advised to reduce the benefits discount rate for vaccines to 1.5%, based on CEMIPP recommendations because of high initial investment costs and long term benefits [3]. However, the government declined these recommendations; they believe that changes will impose a deviation from the approach currently taken for medicines [4]. The WHO also suggest, that when it comes to diseases with benefits in the future, the discount rate for benefits should be 50% lower than what is used for costs. [2]

What could discount rates specifically for gene therapies look like?

1. Uniform vs differential rates

Uniform discounting—meaning the same % for costs and benefits—is the dominant practice in all countries except the Netherlands, Belgium, Poland, and Russia [1]. There are various arguments for and against both methodologies; however, to illustrate the key difference, imagine a decision maker prioritizing two similar therapies that only differ in their time of introduction. When using equal discount rates, the two therapies are comparable, assuming the value of achieving health benefits today versus later does not matter when decision makers prioritize treatments [5] [6]. However, differential discounting challenges this notion, as our willingness-to-pay for health is expected to grow with increases in income over time [7] [8] [9].

→ *<u>For GT, it could be argued that…</u> The use of a lower discount rate for health benefits would increase the weight afforded to health in the future. It will also increase the likelihood of the treatment being cost-effective. Lower discount rates could help pharmaceutical companies justify higher prices because ICERs will also be lower, thus providing incentives for the development of such high benefit therapies. However, this would also result in significant budgetary impact for health care payers, as higher prices could lead to higher restraints on national healthcare budgets.*

Slow discounting

In addition, common practice is the use of a constant discount rate, which is supposed to reflect a constantly decreasing value of health and wealth over time [10]. However, there is evidence that the value of health is different from wealth, and that individual time preferences decrease with time. Therefore, the use of "slow discounting" is sometimes proposed—the intermediate between constant discounting and non discounting future health benefits [11]. In France, for example, the first 30 years of a therapy's benefits and costs are discounted at 4%, but after 30 years the discount rate drops to 2% [12]. The WHO suggests slow discounting for interventions that avert death or chronic disability at very early ages, which is often similar for GT [13].

2. Determining the discount rate

When allocating capital for investments—in our case, allocating funds for new healthcare therapies—discounting can be a key determinant. There are two main methodological bases for calculating the discount rate of publicly funded projects (social discount rate): 1) social rate of time preference (SRTP) and 2) social opportunity cost of capital (SOC). For quantifying the SRTP, we either consider the interest rate of government bonds or other low risk securities, or we derive the SRTP from optimal growth theory by using the Ramsey equation. The SOC can be determined as the marginal pretax rate of return on private investments.

The SRTP approach is the preferred theoretical framework (e.g., [14][15]) and is used in the majority of developed economies (i.e., the UK, France, Germany, Italy, Canada, etc.), especially in fields where long time horizons are used [16] because it is believed that it will spread the risk over time. However, SRTP's estimators can be unavailable or clearly unreliable, in which case the SOC approach is suggested [17]. The SOC is frequently criticized because capital markets do not reflect consumer preferences and there are no bonds with maturities longer than thirty years on sufficiently liquid markets, which makes it impossible to provide a risk-free discount rate for projects with long time horizons [14] [15]. The SOC is higher as it bears the risks of not investing in alternative therapy, while the SRTP is lower because government has the advantage in dealing with risk via taxpayers or spreading diversifiable risk.

→ *<u>For GT, it could be argued that…</u> Gene therapies are long term investments which are capitalized by private funds and closely developed within hospitals and the health care sector (public). Therefore, an SRTP would be the preferred consideration. However, because an SRTP will be a lower bound estimation, sensitivity testing with a number of discount rates should be conducted.*

Ethical aspects

Arguments on discounting rates are a highly technical economic issue in an otherwise healthcare-dominated, ethical discussion. Hence, discount rates for GT could change, but most likely in connection to ethical and social arguments. Social and ethical judgements should be openly discussed, not buried in models as inscrutable parameters. In the end it is a discussion about whether we value the health of patients today over patients in the future [16] [17]. As such, discount rates depend on the social welfare function, which is unique to each individual and should be grounded in actual observed behavior [18].

Recommendations

The discount rate will be a prime determinant of the value and thus attractiveness ascribed to GT. Based on argumentation across economics and healthcare, we propose that an appropriate discount rate for GT should differ from current discount rates to adequately value long-term GT efficiency and to remain comparable to innovative therapies with short-term benefits but lower up-front costs [21]. Therefore, the discount rates for GT should do the following:

1. Be determined based on SRTP, which argues a relatively lower discount rate to account for the long-term riskless governmental investment
2. Be differential or "slow", as they should ascribe more value to future health benefits in order to avoid under-valuing future QALYs gained from GT
3. Include alternative discount approaches in sensitivity analyses

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[1] Attema AE, Brouwer WBF, Claxton K. Discounting in economic evaluations. PharmacoEconomics 2018.
[2] Ultsch B, Damm O, Beutels P, et al. Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community. *Pharmacoeconomics* 2016.
[3] DHSC. Cost-effectiveness methodology for vaccination programmes: Consultation on the Cost-Effectiveness Methodology for Vaccination Programmes and Procurement (CEMIPP) Report: Department of Health and Social Care 2018.
[4] DHSC. Cost-effectiveness methodology for immunization Programmes and Procurements (CEMIPP) : The government's decision and summary of consultation responses 2019.
[5] Weinstein MC, and Stason WB. Foundations of cost-effectiveness analysis for health and medical practices. N Engl J Med. 1977;296; 716-21.
[6] Keeler EB, Cretin S. Discounting of life-saving and other non-monetary effects. Mgmt Sci 1983; 29 (3):300-6.
[7] Gravelle H, Smith D. Discounting for health effects in cost-benefit and cost-effectiveness analysis. Health Econ 2001.
[8] Brouwer WB, Niessen LW, Postma MJ, Ruttten FF. Need for differential discounting of costs and health effects in cost effetiveness analyses. BMJ 2005.
[9] Klok RM, Brouwer WBF, Annemans LJP, Bos JM, Postma MJ. Towards a healthier discount procedure. Expert Rev Pharmacoecon Outcomes Res 2005.
[10] Harvey CM. The reasonableness of non-constant discounting. J Public Econ 1994.
[11] Cairns JA. Valuing future benefits. Health Econ 1994;3:221–9.
[12] Haute Autorite de Sante. Choices in methods for economic evaluation. Saint–Denis La Plaine: Department of Economics and Public Health Assessment, Haute Autorite de Sante 2012.
[13] World Health Organization. WHO guide for standardization of economic evaluations of immunization programmes 2008. World Health Organization.
[14] Gollier. Pricing the planet's future: the economics of discounting in an uncertain world. Princenton, NJ: Princenton University Press 2012.
[15] Groom B, Hepburn C, Koundouri P, Pearce DW. Declining discount rates: the long and the short of it. Environmental and resource. Economics 2005.
[16] Livingstone I, Tribe M. Projects with long time horizons: their economic appraisal and the discount rate, Project Appraisal 1995.
[17] Young L. Determining the discount rate for government projects. New Zealand Treasury. Working Paper 2002.
[18] Arrow KJ, Cline WR, Maler KG, Munasinghe H, Squitiere E, Stiglitz JE. Intergenerational equity and rate of the discount rate in long-term social investment. IEA World Congress 1995.
[17] Heal GM, Millner A. Agreeing to disagree on climate policy. Proceeding of the National Academy for Sciences of the United States of America 2014.
[18] Nordhaus ED. Managing the global commons: the economics of climate change.Mimeo, MIT Press Cambridge, MA 1994.
[19] Davidson M. A social discount rate for climate damage to future generations based on regulatory law. Climate change 2006
[20] Shively G. Disappearing future: Discounting and the tyranny of the present. Purdue University, West Lafayette 2002.
[21] Tasset A, Nguyen VH, Wood S, Amazian K. Discounting: Technical issues in economic evaluations of vaccination. Vaccine 1999.