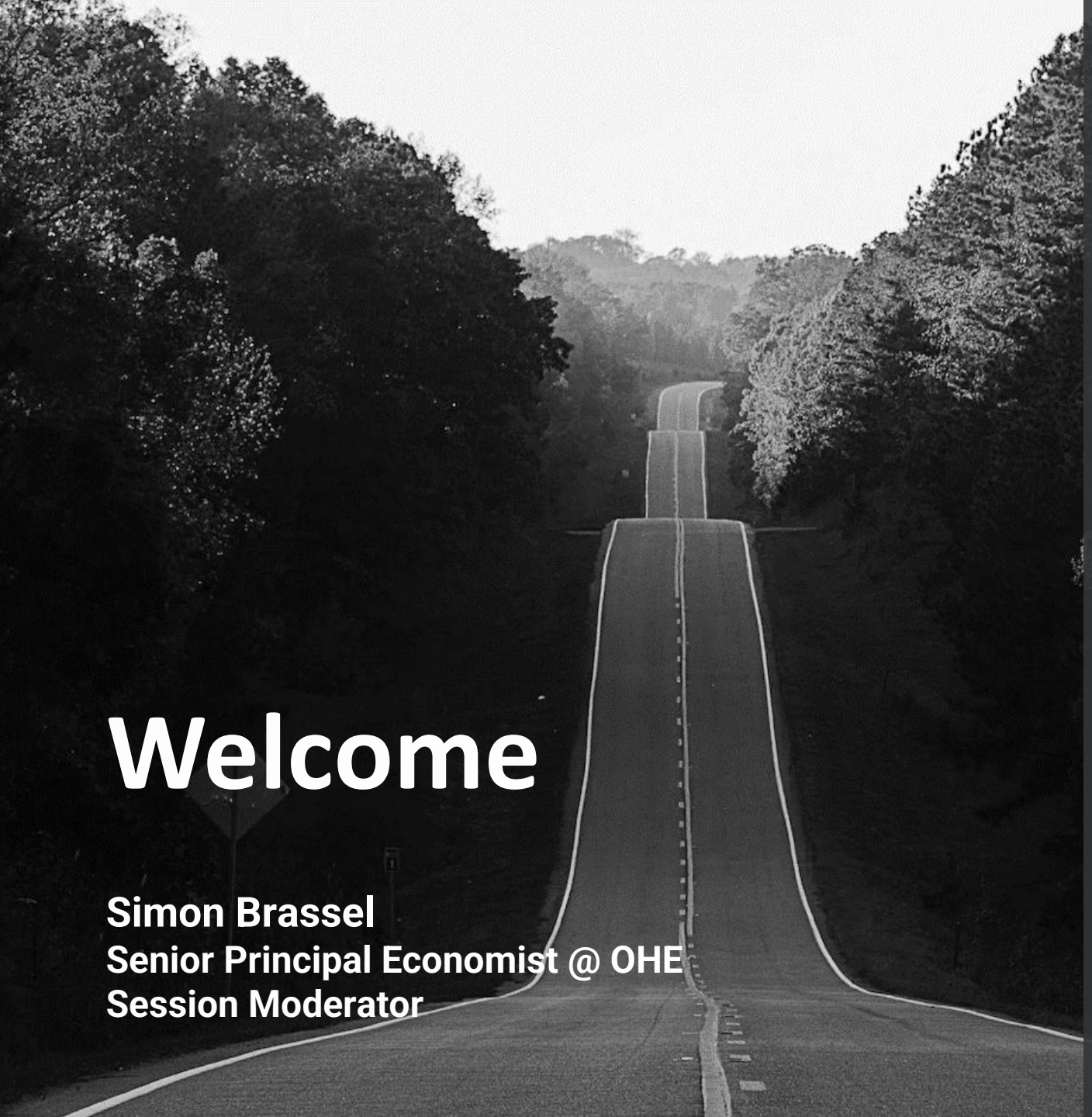
An Eye for the Future:

Does an Interdisciplinary View Help Improve Discounting Approaches for Curative Gene Therapies?

Poll 1



Welcome

Simon Brassel
Senior Principal Economist @ OHE
Session Moderator

OHE

Disclaimer

I am an employee of the Office of Health Economics, a registered charity and Independent Research Organisation, which receives funding from a variety of private and public sector sources.

Speakers & Agenda

Simon Brassel
OHE

Welcome & scene setting

Nicola Trevor
Janssen Pharmaceuticals

The challenge from the perspective of the pharmaceutical industry

Mohamed El Alili
ZIN, Netherlands

An HTA makers insights from the Netherlands

Grace Hampson
OHE

A look beyond the horizon - discounting in environmental economics

Avril Daly
Retina International

How discounting affects a patient's life

Discounting – A Primer

WHICH DISCOUNTING APPROACHES TO CHOOSE?

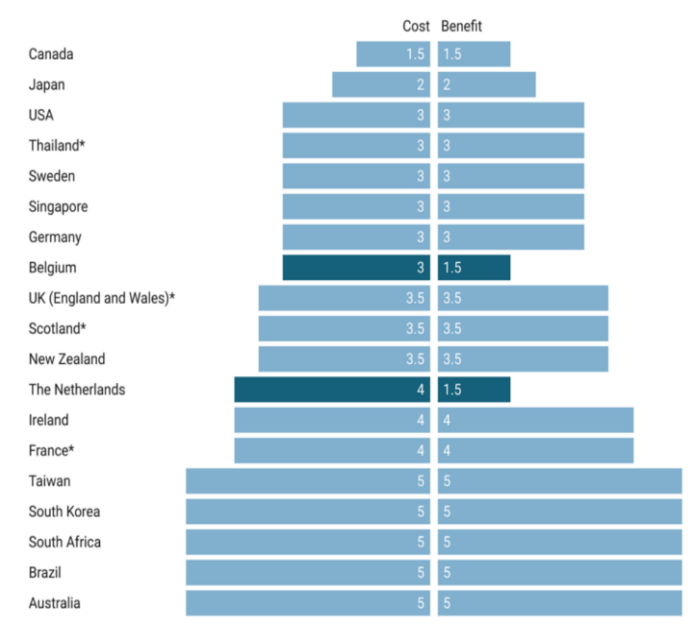
- ✓ Equal vs. differential
- ✓ Constant vs. Stepwise vs. Hyperbolic vs. Time-shifted

HOW SHOULD WE ESTIMATE THE DISCOUNT RATE?

- ✓ equal to the opportunity cost of capital
- ✓ equal to an estimate of the social rate of time preference (SRTP) for consumption

WHAT IS THE IMPACT?

- ✓ highly influential in decisions about reimbursement of health technologies or policies outside the health sector



HTA DISCOUNT RATE BY COUNTRY, EQUAL VS DIFFERENTIAL (2020, 2021)
Source: ISPOR (2022)

Ramsey Rule

Social Rate of Time Preference

$$r = \rho + \eta g$$

Marginal productivity of capital

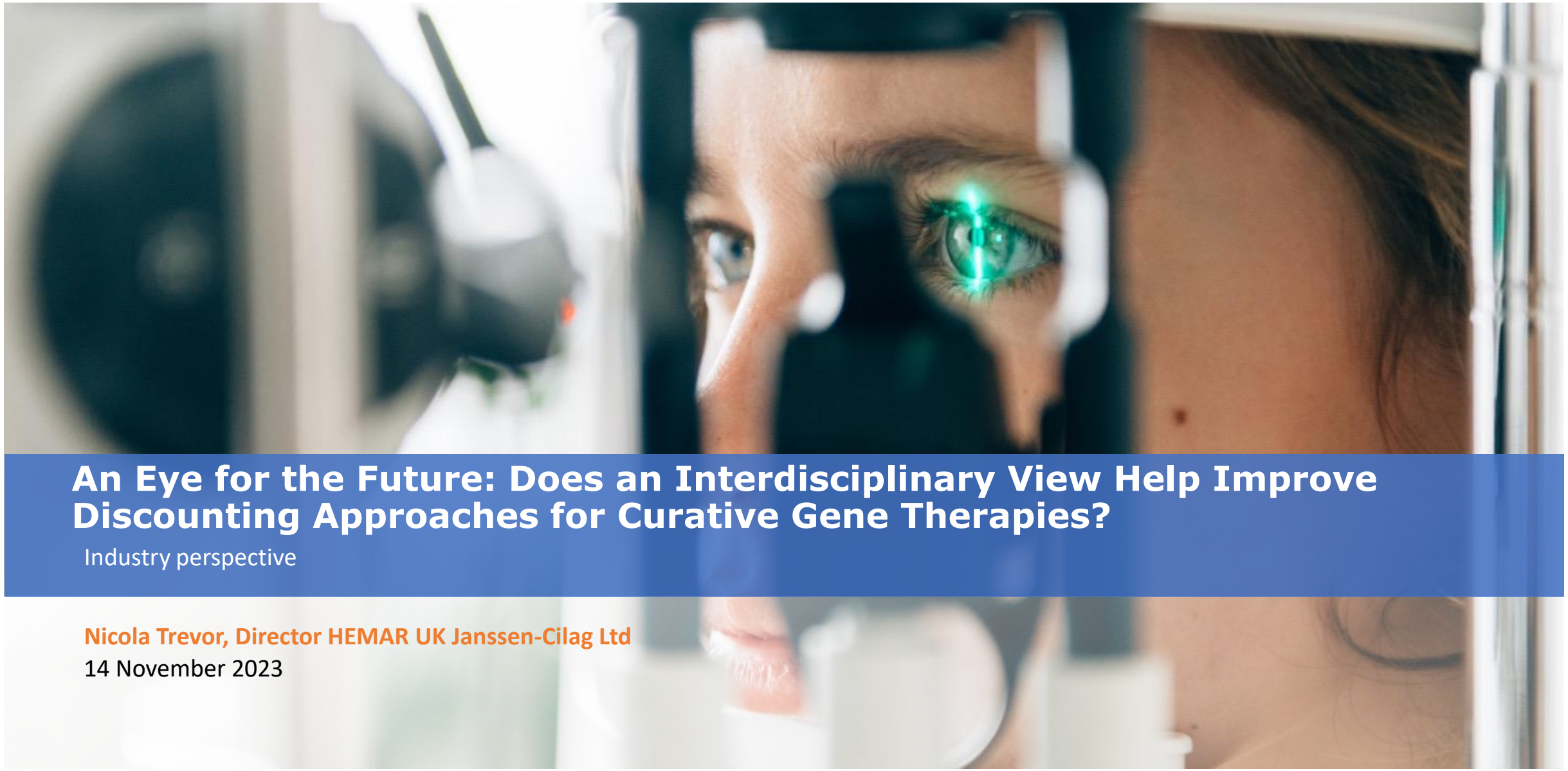
Wealth effect

Rate of pure time preference

		Discount rate for outcomes				
	Discount rate	0.0%	1.5%	3.0%	3.5%	5.0%
	Model outcome	19.74	10.61	6.29	5.39	3.57
Discount rate for costs	0.0% (646,697)	Dominant	Dominant	Dominant	Dominant	Dominant
	1.5% 95,824	$4,854	$9,034	$15,245	$17,792	$26,840
	3.0% 415,205	$21,032	$39,145	$66,057	$77,094	$116,297
	3.5% 476,337	$24,129	$44,908	$75,783	$88,445	$133,420
	5.0% 589,233	$29,848	$55,552	$93,744	$109,407	$165,042

FIGURE 2: SENSITIVITY OF COST-EFFECTIVENESS TO DISCOUNT RATES IN XLRP
Source: pharmaceutical company analysis of a hypothetical gene therapy for XLRP

Poll 1 Results



An Eye for the Future: Does an Interdisciplinary View Help Improve Discounting Approaches for Curative Gene Therapies?

Industry perspective

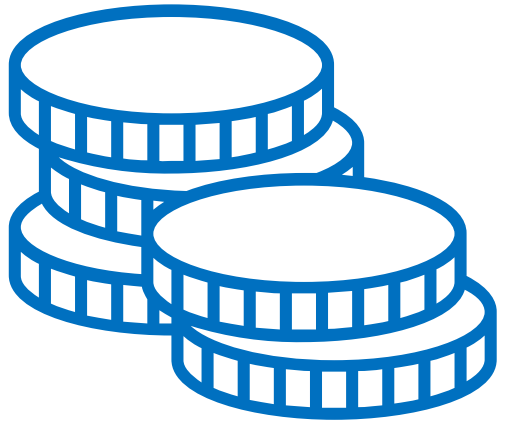
Nicola Trevor, Director HEMAR UK Janssen-Cilag Ltd

14 November 2023

In traditional economic appraisal techniques being used to inform public decision-making, costs and benefits spread over time are weighted according to when they are experienced

Individuals have **a positive time preference** preferring consumption sooner rather than later

Discounting allows for a comparison of **costs** and **benefits** that occur over extended periods



This is applicable for monetary value, but the question is whether it should also be applied to social and health benefits at all?

Sheldon, T. (1992) Discounting in health care decision-making: time for change? Journal of Public Health Medicine Vol 13, 250-256

Discounting weights public decision-making in favour of interventions that have a short-term impact

Current practices to assess preventive interventions such as **ATMPs, Immunization, Climate Change Adaptation and Resilience with long-term benefits and often (one-time) upfront cost** are not fit-for-purpose

Long term benefits

Benefits that happen further in the future are heavily/completely discounted hence the actual long-term benefits are not properly reflected and valued

One-time upfront costs

Not discounted

Example

Gene therapy with the potential to intercept a slowly progressing disease like some Inherited Retinal Diseases. Intercepting the disease would imply one-off administration of a gene therapy in children <10 years of age, while patients develop median legal blindness around the age of 45 and full blindness another decade later. **The benefit of avoiding blindness would be fully discounted with current discounting practices.**

Drummond M. et al. (2019) Analytic Considerations in Applying a General Economic Evaluation Reference Case to Gene Therapy. Value in Health Volume 22, Issue 6, 661-668
Groom, B., et al. (2022). The future, now: A review of social discounting. Annual Review of Resource Economics, 14, 467-491
Jönsson, B., et al. (2018) Advanced therapy medicinal products and health technology assessment principles and practices for value-based and sustainable healthcare. The European Journal of Health Economics, 20, 427–438

Applying differential discounting can help capture some of the unique challenges associated with evaluating the cost-effectiveness of one-off therapies with long-term benefits including gene therapies

- **Long-term benefits**
- **Intergenerational equity**
- **Innovation**
- **Opportunity cost**

Qiu, T. et al. (2022) Gene Therapy Evidence Generation and Economic Analysis: Pragmatic Considerations to Facilitate Fit-for-Purpose Health Technology Assessment. Front Public Health, Vol: 10: 773629.

It may be time to rethink the foundations of discounting and decision-making that has a longer time horizon

In healthcare this particularly applies to COST/QALY archetypes, where discounting is often a pivotal factor in access to preventative/curative therapies

$$\frac{\text{COST}}{\text{QALY}}$$

We would propose to fully consider scenarios where differential discounting is applied without discounting health benefits in future decision-making, or at least scenarios where long-term health benefits (e.g., after 10 or 20 years) are no longer discounted

Conclusion

Investing in prevention

Decision-making with longer time horizon

Rethinking the foundations of discounting

Improving patient access

Discounting in the Netherlands

Mohamed El Alili, PhD

Senior pharmaco-economic advisor

Brief overview of discounting in the Netherlands

- 1999: first guideline for economic evaluations
  - **Optional** cost-effectiveness analysis: equal discounting 4%
  - The exact rate for discounting money was derived in 1995 from figures on the real rates of return on investment and economic growth by the Ministry of Finance.[1]
  - Combination of social rate of return on obligations/private investments (SRRI) and literature.
  - Theoretical arguments:

1. Consistency argument by Weinstein and Stansen[2]
2. Postponement paradox by Keeler and Cretin[3]
3. A perfect economic world

Brief overview of discounting in the Netherlands

- 2006: Second guideline for economic evaluations
  - **Obligatory** cost-effectiveness analysis: differential discounting 4% for costs and 1.5% for effects
  - Discounting **costs** previously determined (SRRI and literature).
  - Discounting **effects** adjusted downwards to take into account increase of value of health over time.[4-6] → $r_h = r_c - g_v$
    - Arguments:

    1. The value of health is expected to increase over time[4,5]
    2. Consistency can be reached under differential discounting as well[6]
    3. Infinite postponing was never observed in practice[7]

- 2015: Third guideline for economic evaluations
  - Differential discounting: 4% for costs and 1.5% for effects

Brief overview of discounting in the Netherlands

- 2024: Fourth guideline for economic evaluations (*to be published, available January 2024*)
  - Differential discounting → 3% for costs and 1.5% for effects
  - Discounting **costs** adjusted downwards based on discount rate recalculated by the Ministry of Finance using both SRRI and social rate of time preference (SRTP).[8]
  - Discounting **effects** adjusted downwards to take into account increase of value of health over time.[4-6] → $r_h = r_c - g_v$
    - Arguments:

1. Same as before
2. In line with Dutch societal cost-benefit analysis → 1% decrease.
3. Too large difference between discount rate for costs and effects → previously assumed health would increase with 2.5%, now assumption 1.5%[9,10]

Illustration

CAR-T/gene therapy	Discounted	Undiscounted
Incremental costs	€672.736	€653.558
Incremental QALY	8,3	12,69
ICER	€80.994 per QALY	€51.488 per QALY

Drug for heart failure	Discounted	Undiscounted
Incremental costs	€48.825	€80.564
Incremental QALY	3,45	4,49
ICER	€14.674 per QALY	€18.194 per QALY

Challenges in assessment of ATMPs

- DISCOUNTING: larger impact on ATMPs than on other types of treatments

But…[11]

- Uncertainty in long-term clinical effectiveness
- Uncertainty in cost and economic effectiveness
- Difficult getting positive recommendation; patient access delayed

Solutions

- Managed entry agreements (already in place)
  - Price negotiations
  - Conditional inclusion (VT traject)

- Not in place (yet):
  - Different discounting methods for ATMPs: example of NICE
    - In line with Ministry of Finance apply lower discount rate of 1.6%?[8]
  - Revise willingness-to-pay for ATMPs
  - Make room for different approaches in guideline for economic evaluations for ATMPs
  - Framework for socially acceptable drug prices in the Netherlands

Thank you

References

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3. Keeler EB, Cretin S. Discounting of life-saving and other non-monetary effects. Manag Sci. 1983;29:300–6.
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What can health economics learn from environmental economics' approach to discounting?

Grace Hampson
Associate Director @ OHE

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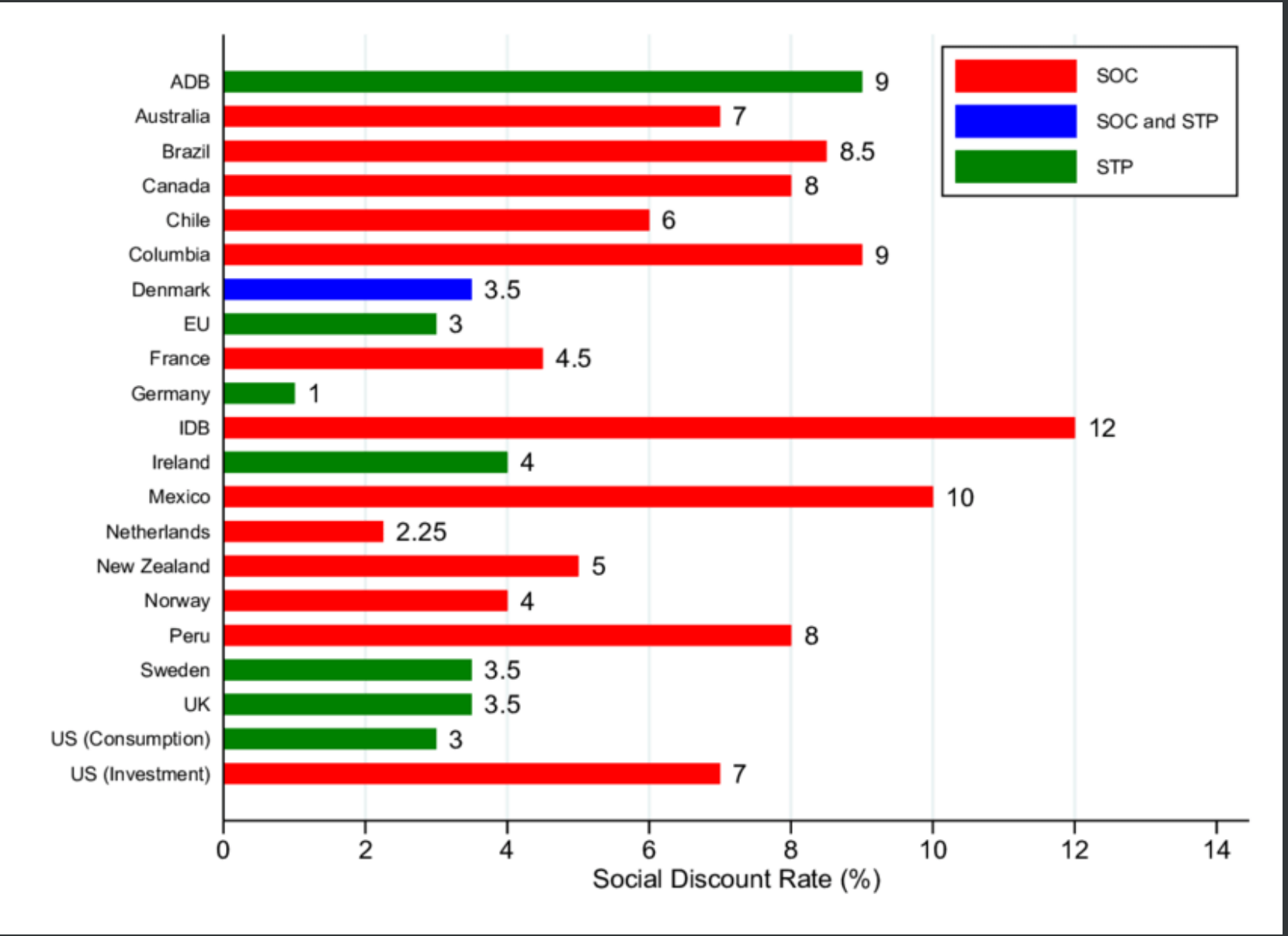
Disclaimer

I am an employee of the Office of Health Economics, a registered charity and Independent Research Organisation, which receives funding from a variety of private and public sector sources.

Discount rates by country



Source: Groom et al., 2022

Contents

- Lower discount rates
  - Ethical concerns – intergenerational equity
  - Ethical concerns – inequality
- Differential discount rates
- Declining discount rates
- Use of the discount rate – non-marginal cases

Lower discount rate #1: intergenerational equity

Rationale

- The welfare of future generations should be on par with our own

➢ **Societal pure time preference, δ = 0**

➢ UK - sensitivity analysis allowed for very long-term effects where δ = 0

'It is, of course, possible that people actually do place less value on the welfare of future generations, simply on the grounds that they are more distant in time. But it is hard to see any ethical justification for this'.

- Stern (2006)

Does this apply to health?

- Herd protection (Jit and Mibei, 2015)

- Health interventions are aimed at individuals

Lower discount rate #2: inequality

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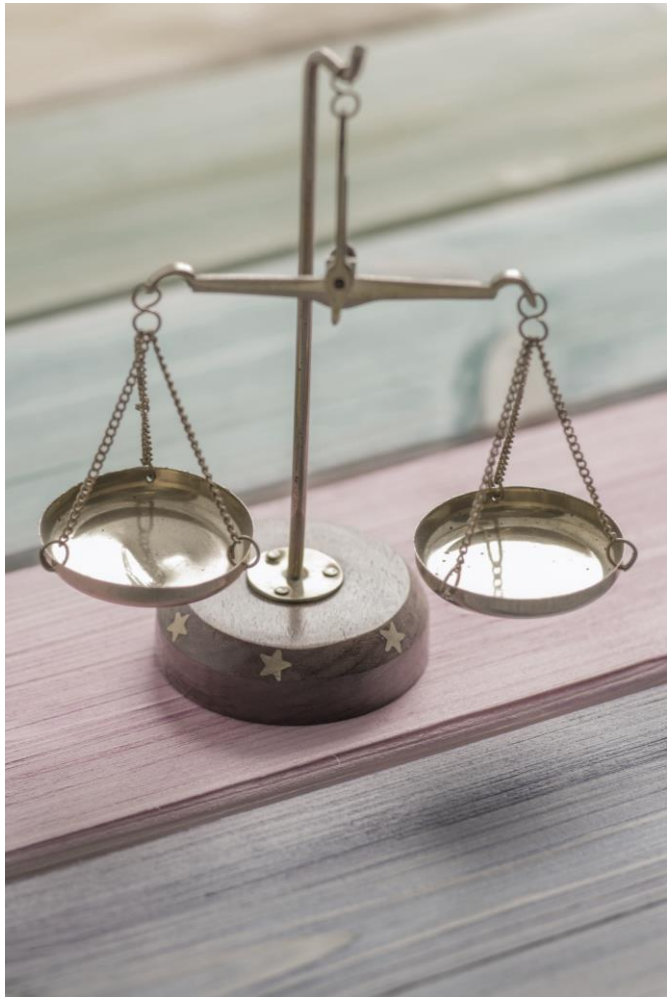
Rationale

- Inequality aversion:
  - 1) lower SDRs compensate future societies for greater inequality
  - 2) lower SDRs prevent exacerbating inequality within generations

➢ **Term accounting for inequality in SRTP → when mean consumption is growing faster than median consumption, discount rate is lower**



Does this apply to health?

☑

- Interventions most affected by discount rates often severe with no alternative strategies
- Lower SDRs → reduce health inequalities

☒

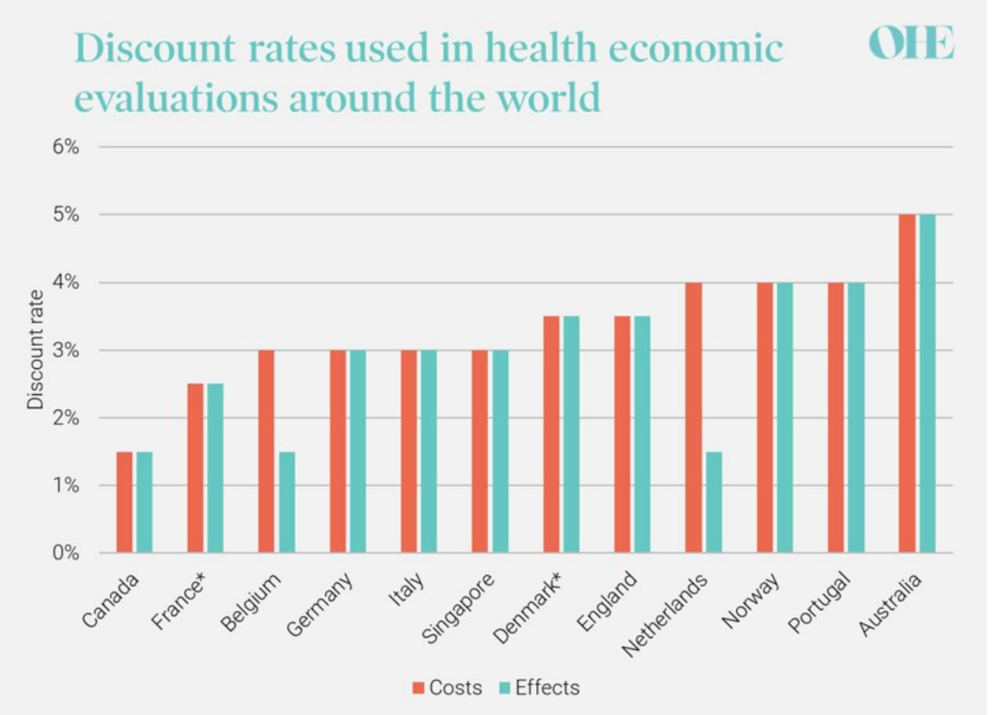
- Most interventions are within individuals so 1) may not apply
- There are other ways for accounting for health inequality

Differential discount rates: wealth effect

Rationale

- Value placed on consumption of goods lower in wealthier, future societies
- 'Wealth effect' does not apply for environmental goods

➢ **UK treasury do not differentially discount environmental effects at a lower rate than consumption goods or costs**



Does this apply to health?

- Substitutability arguments similar for health effects

- In the context of a fixed NHS budget, costs represent health foregone elsewhere

→ Lower discount rates for both costs and health effects

Declining discount rates: uncertainty

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Rationale

- Under uncertainty, the discount rate decreases over time

➢ **Across a range of selected countries, the long-term SDR (after 100 years) has been found to be a percentage point lower than the headline SDR**

Table B1: Present Value of a cash-flow of €1000 received after t years

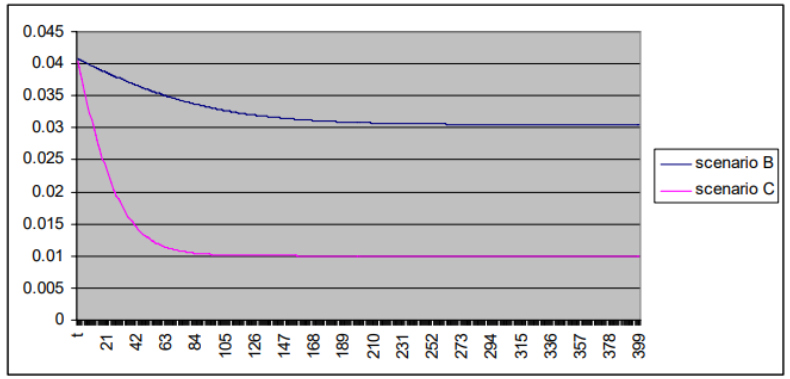
t	Scenario A: 4%	Scenario B: 3% or 5%	Scenario C: 1% or 7%	Percentage difference between A,B	Percentage difference between A,C
1	960.7894	960.8375	961.2218	0.005	0.045
10	670.3200	673.6744	700.7114	0.500	4.534
50	135.3353	152.6076	318.3640	12.763	135.241
100	18.3156	28.2625	184.3957	54.308	906.766
150	2.4788	5.8310	111.5788	135.241	4401.412
200	0.3355	1.2621	67.6681	276.220	20071.564
300	0.0061	0.0619	24.8935	906.766	405054.203
400	0.0001	0.0031	9.1578	2630.823	8137639.571

Does this apply to health?

- Little theoretical reason this logic should not apply to health interventions

- NICE suggests the effect of a recommended decline would be small in practice

Figure B2: The forward discount rates



Use of the discount rate: non-marginal effects

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Rationale

- Climate change is an existential threat – current discounting approaches inappropriate for comparing non-marginal paths

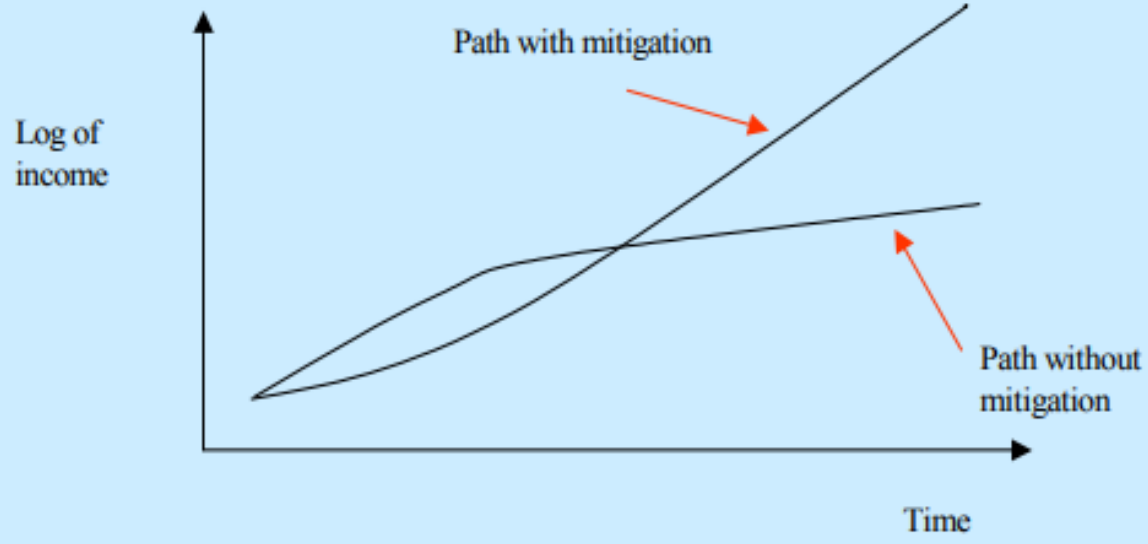
➢ **analysis requires formal comparison between paths**

Does this apply to health?

☒

- Impact of individual health technologies will likely be marginal at the macro level

Figure 2.3 Conceptual approach to comparing divergent growth paths over the long term



Source: Stern review 2006

What can we learn?

Lower discount rates: intergenerational equity	☑	Relevant for health interventions with intergenerational effects
Lower discount rates: inequality	?	
Differential discount rates: wealth effect	☑	'Wealth effect' should not apply for health
Lower discount rates: wealth effect	☑	'Wealth effect' should not apply for health
Declining discount rates: uncertainty	☑	Discount rate should reduce over time
Use of the discount rate: non-marginal effects	☒	Unlikely to be relevant for most health interventions

Retina International

The Patient Perspective

Avril Daly, CEO Retina International

ISPOR – November 14th, 2023

The life trajectory of an individual with IRD

What is the impact of the disease across different domains from birth to end of life?

- What happens when?
- Which domains are relevant?
  - E.g., overall health, wellbeing,
  - education, career, participation in regular activities,
  - family life, etc.

Retina International

The possibility of prevention?

Early intervention has the potential to halt or slow down the degeneration of the retina and hence change those trajectories described above.

- Here, Genetic Testing is the Key to our Future.
- IRDs are ACTIONABLE conditions.
- The burden of IRDs on society is misunderstood but is significant.

Retina International

How to realise the potential that current and future innovation offer?

- In Rare Disease it feels like patients are battling a misperception of the impact of innovation.
- The burden of disease has been determined by stakeholders including patients and their representatives.
- Discounting in combination with narrow value frameworks within HTA is a significant challenge.

Retina International

A call from Patients to Decision Makers

Listen to us!

Learn from our experience!

Lead the change!

Thank you!

Retina International

Poll 2

Poll 2 Results


OIE
Q&A