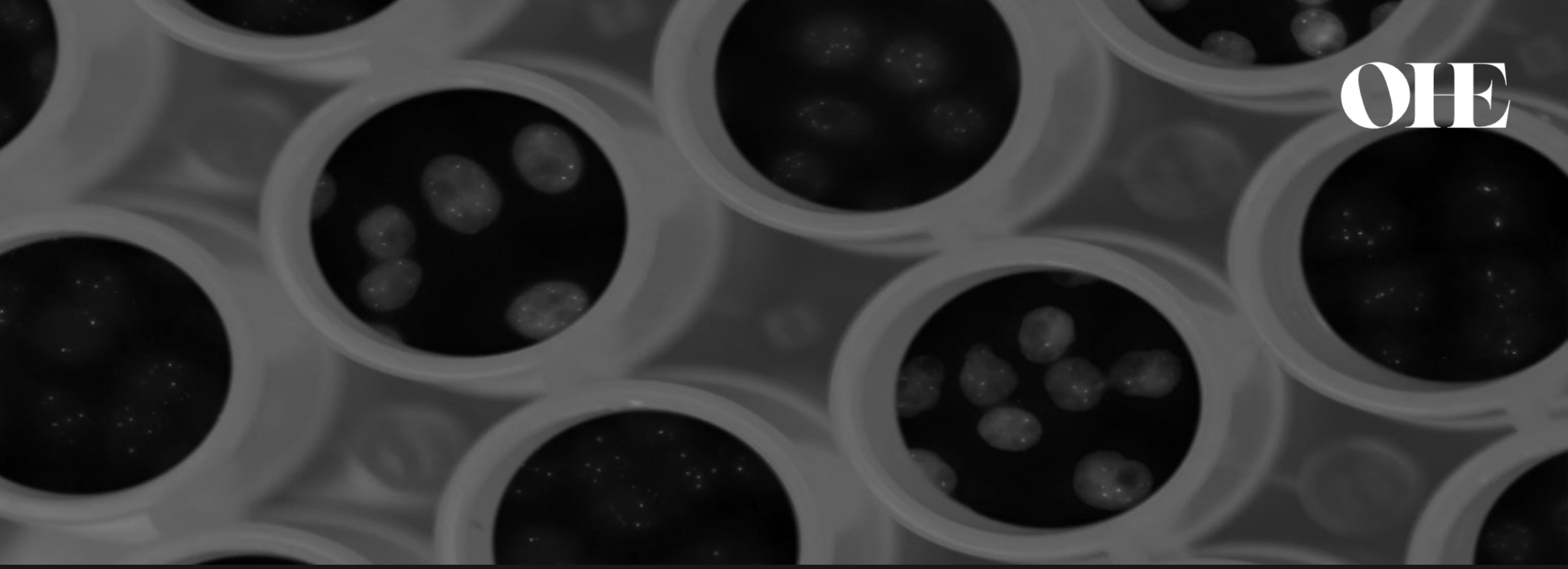

Issues Regarding Pricing and Access to Gene and Advanced Therapy Medicinal Products

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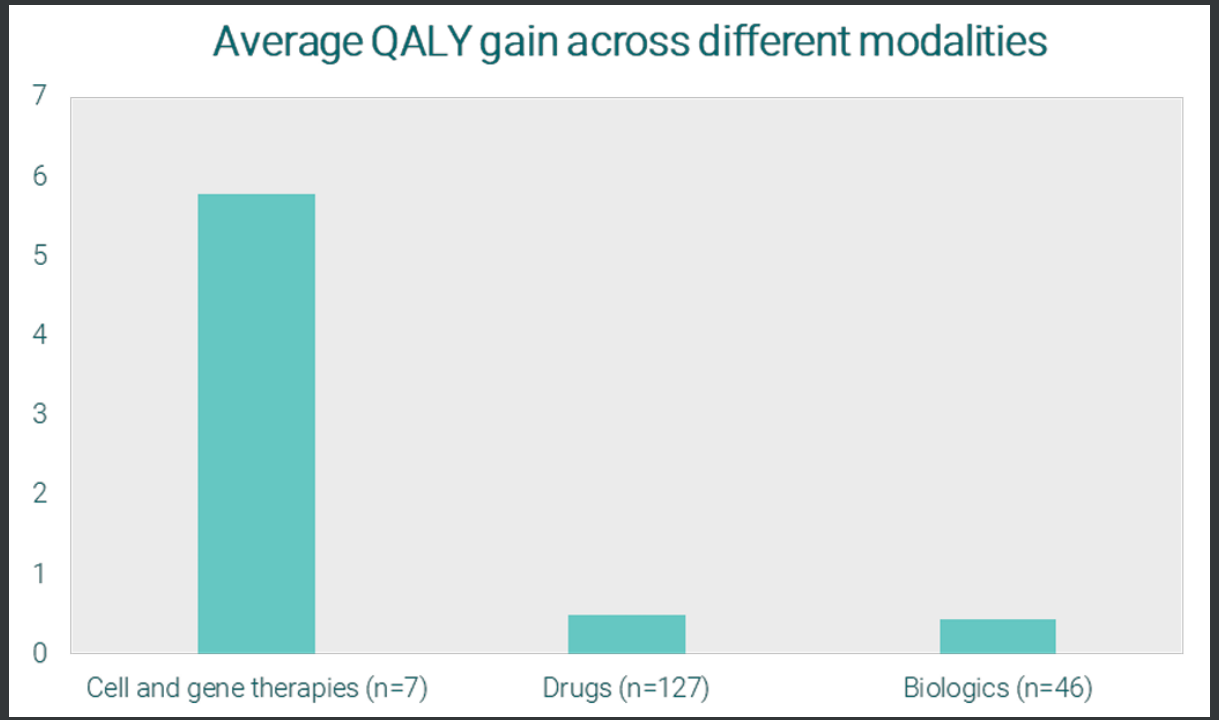
Conflict of Interest

- Lotte Steuten is an employee of the Office of Health Economics, a registered charity and Independent Research Organisation in the UK, which receives funding from a variety of private and public sector sources.
- The Office of Health Economics received funding from various pharmaceutical companies to perform research on the topic of gene therapies and advanced therapeutic medicinal products.
- The opinions and ideas presented here are my own based on 20+ years of experience in HTA, and do not necessarily reflect those of OHE or any of the organisations it receives funding from.

Gene therapies and ATMPS: the health benefits

It is broadly accepted that gene therapies and ATMPs have the potential to transform lives and provide benefits to healthcare systems and society more broadly.

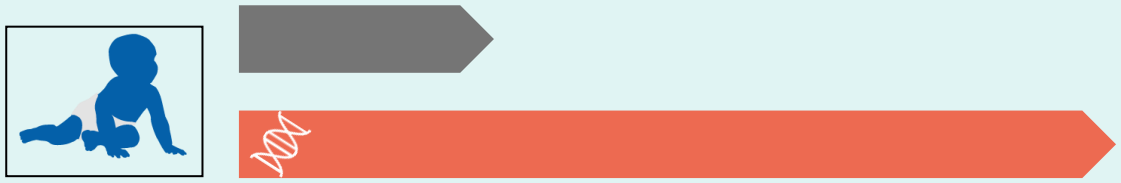
Illustrative example for gene therapies



*Quality adjusted life years (QALYs) Source: Cohen et al 2019

Health gains of gene therapies are not created equal, affecting their potential to deliver health economic value

The economic impact will be affected by whether the health gains are primarily driven by an increase in **length of life** or improvement in **quality of life**.



Rare disease therapies can generate substantial **increases in length of life** by addressing the root cause of diseases with early mortality. **Low cost-offsets to health care systems; high value to society.**

Rare disease therapies that **reduce morbidity** and increase health-related **quality of life** have the potential to generate **cost savings to** the **healthcare system** and **high value to wider society.**

Shared savings?

Length of life after gene therapy

Length of life without next-gen therapy

Quality of life with next-gen therapy

Quality of life without next-gen therapy

HTA of gene therapies and ATMPs aims to inform access and pricing but is challenging for various reasons.

INITIAL ASSESSMENT OF CLINICAL EFFECTIVENESS

- **Generalisability** of clinical trial results
- **Trial design**: alternatives to RCTs
- Appropriate **outcome measures**
- Differing HTA body/payer **evidence requirements** increase the difficulty of designing trials

ASSESSMENT OF COSTS

- One/short duration treatments mean high **irrecoverable costs**
- Does / should **budget impact** affect the value-for-money rule used for reimbursement?
- Patient **portability** (insurance policyholders)

UNCERTAINTY REGARDING LONG-TERM OUTCOMES

- **Short-term follow up** (requires modelling)
- Uncertainty over whether **benefits sustained**
- Uncertainty regarding adverse events & **safety concerns**
- Need for appropriate HTA methods to handle uncertainty
- **Discount rates**

INCORPORATING ADDITIONAL ELEMENTS OF VALUE

- Are potentially **one-time treatments/life-changing therapies** valued more by society?
- Importance of **severity weighting**
- **Spillover effects** on family members/carers and society
- **Other elements,** including equity, insurance value, option value, etc.

Are our HTA methods fit for purpose?

Based on a literature review, qualitative research and insights derived from an international panel of HTA and health economics experts six recommendations were determined and published in a previous report.

Recommendations

Recognise potential lifetime benefits in modelling incl. sens analysis of discount rate.

Recognise additional elements of value in HTA, based on continued research.

Develop transparent standards for the inclusion of RWE and surrogate endpoints in HTA.

Include outcomes-based payment models alongside HTA to mitigate uncertainty whilst enabling patient access.

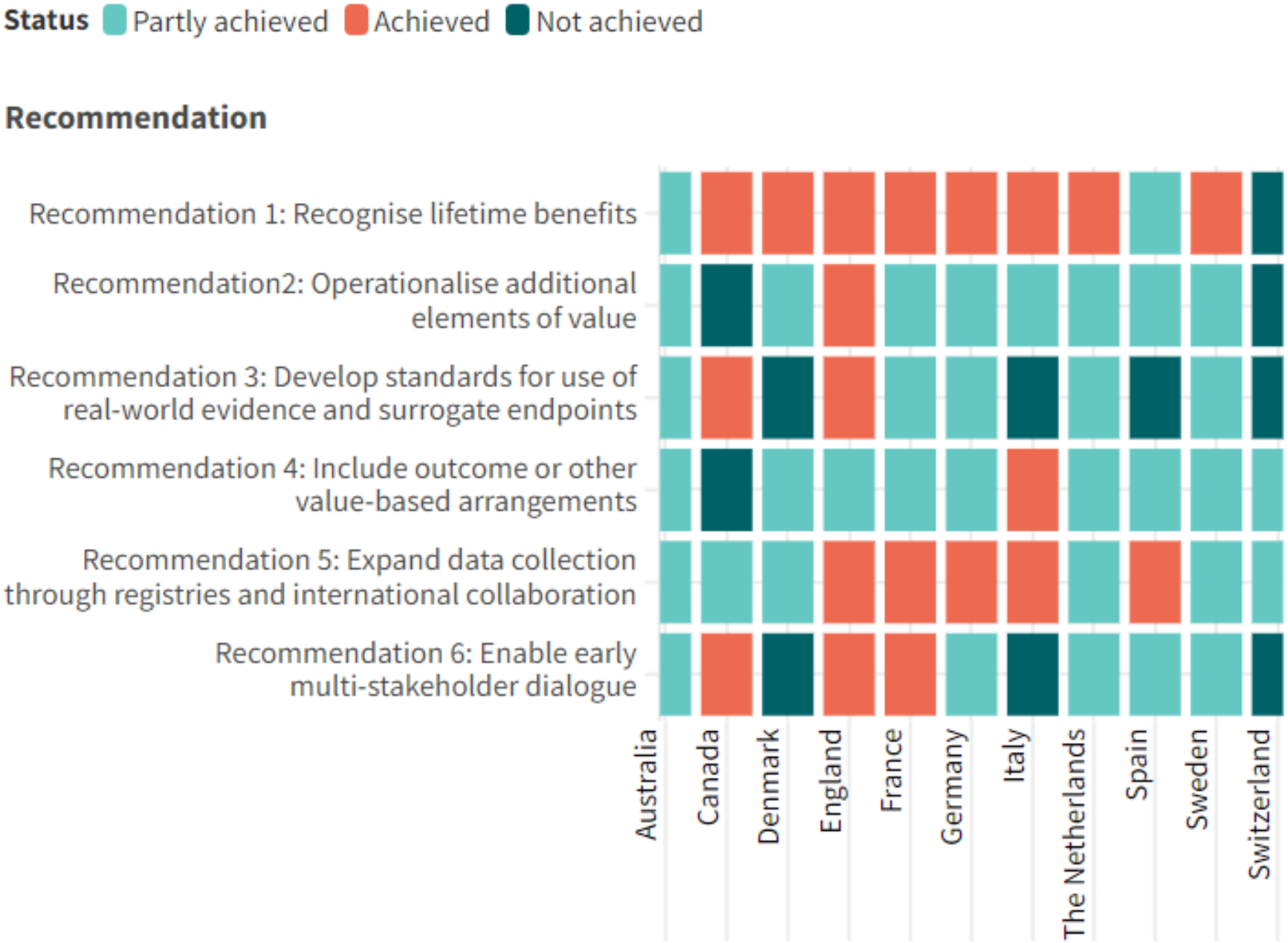
Expand data collection through registries and international collaboration.

Enable early multi-stakeholder dialogue to align on feasible and appropriate HTA evidence packages.

Are Recommendations for HTA of Gene Therapies Achieved?

We developed country scorecards exploring the extent to which these recommendations are achieved in 11 countries: Australia, Canada, Denmark, England, France, Germany, Italy, the Netherlands, Spain, Sweden and Switzerland.

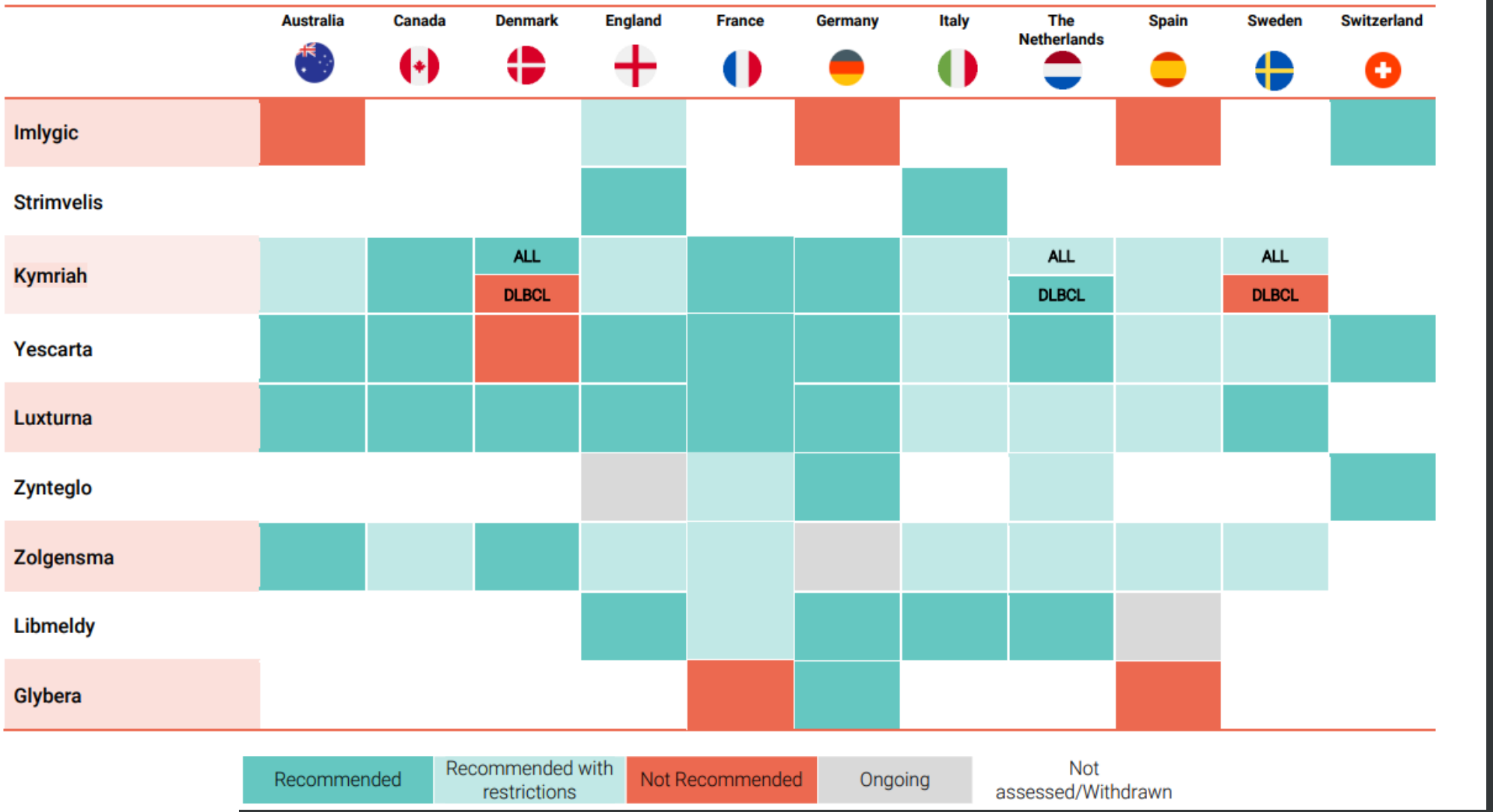
Targeted literature searches, including searches of grey literature and official HTA agency documentation, inputs from an international expert roundtable and pharmaceutical industry were used to determine the extent to which the recommendation was achieved in each country.



In which countries are these recommendations achieved?

Source: https://www.ohe.org/publications/recommendations-for-hta-of-gene-therapies-being-achieved/

HTA recommendations for specific gene therapies



Selected best practice examples (1/3)

1: Recognise potential lifetime benefits in modelling incl. sens analysis of discount rate.

Lifetime horizon: CADTH (Canada), DMC (Denmark), NICE (England), HAS (France), and AIFA (Italy) allow for the time horizon to be long enough to reflect all significant differences in costs and outcomes; ZIN (the Netherlands) mandates the use of a lifetime horizon.

Discount rates: HAS (France) recommends a lower discount rate for costs and benefits after 30 years, and NICE (England) recommends a reduced discount rate for costs and benefits for technologies with benefits that are sustained over a long period of time. ZIN (the Netherlands) recommends the use of differential discounting.

2. Recognise additional elements of value in HTA, based on continued research.

NICE (England) allows to consider severity via a severity modifier that provides an increased weighting of QALYs for severe diseases; G-BA (Germany), assesses rare disease treatments via an orphan medicines pathway

Selected best practice examples (2/3)

3. Develop transparent standards for the inclusion of RWE and surrogate endpoints in HTA.

Good examples are found for CADTH (Canada), which provides detailed guidance on surrogate outcomes and NICE (England), which provides an RWE framework.

Going forwards, with joint clinical assessments on the horizon, a shared commitment to recognising and validating surrogate endpoints and implementing RWE standards will be increasingly important. This should also include generating alignment across regulatory and HTA bodies.

4. Include outcomes-based payment models alongside HTA to mitigate uncertainty whilst enabling patient access.

In Italy many outcomes-based and economic risk sharing agreements have been implemented, making use of their well-established registries. In addition, staged payments linked to individual patient outcomes are being used for two gene therapies.

However, we recognise that recently there has been a decline in the use of outcome-based payments in Italy in favour of confidential price discounts (Cole, Neri and Cookson, 2021).

Selected best practice examples (3/3)

5. Expand data collection through registries and international collaboration.

France has a national database for rare diseases.

Denmark has a nationwide hospital registry and a registry for patients with rare and/or hereditary eye diseases used for an outcomes-based agreement for Luxturna.

Italy has a number of AIFA monitoring registries where data on the use of products has been routinely collected.

International collaboration examples of post-launch evidence generation pilots:

- Left Ventricular Assist Devices in patients with end-stage heart failure involving NICE (England), Avalia-t (Galician Agency for Health Knowledge Management, Spain) and Agenas (Italian National Agency for Regional Health Services, Italy).
- CAR-T products registry (involving AIFA (Italy), G-BA (Germany), HAS (France), NICE (England), and ZIN (the Netherlands)) across a number of indications.

6. Enable early multi-stakeholder dialogue to align on feasible and appropriate HTA evidence packages.

The availability of joint scientific advice, e.g., in partnership with regulators or another HTA body, is particularly advanced, such as the parallel advice offered by CADTH (Canada) and NICE (England) and the joint consultations available through the EUnetHTA that include HAS (France), IQWiG (Germany), G-BA (Germany), AIFA (Italy), AEMPS (Spain), TLV (Sweden) and ZIN (the Netherlands).

Key takeaways

1. Changes to HTA methodologies and evidence generation aimed at capturing the full value of gene therapies and ATMPs should improve value-based access and pricing decisions.
2. Several countries are achieving some of the changes, demonstrating examples of best practice.
3. There is considerable variability in the extent to which recommendations are being achieved between and within countries.
4. None of the countries assessed achieved all recommendations, demonstrating significant potential for improvement in the HTA of gene therapies and ATMPs.

Acknowledgements

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- Poster HTA329: The Race To Improve Health Technology Assessment Of Gene Therapies. Besley et al., ISPOR Copenhagen, 2023 (Wed 9:00am posterboard 5004)


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THANK YOU

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