Unravelling Modelling Challenges in the Economic Evaluations of Gene Therapies: A Global Review

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BACKGROUND

Context: Therapies that can prevent, treat, or cure a disease by changing the expression of an individual's genes are called gene therapies (GTx). The GTx have potential to provide benefits not only to patients but also the society. However, the high costs of GTx pose economic challenges in the decision-making.[1,2]

Aim: To understand the current state of cost-effectiveness models (CEMs) of the available GTx and highlighting the prevalent modelling approaches and challenges encountered by the healthcare sector in making it a standard approach for treatment in the concerned diseases.

METHODS

- A targeted literature review was conducted in the electronic database PubMed to identify the relevant evidence on the CEMs of GTx in the recent years (January 2018 through May 2023).
- The key words used for the searches are shown below:

(Gene therapy* or innovative medicine* or replacement therapy* or regenerative medicine* or advanced therapeutic medicinal product* or ATMP* or curative therapy* or life-extending or potential cure or curative treatment* or curative medicine*)

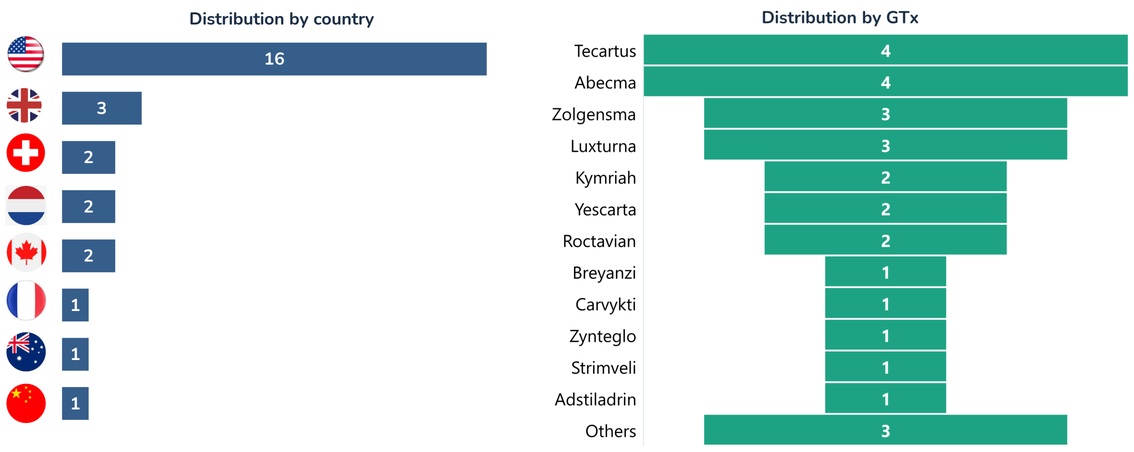
economic evaluation or economic assessment or economic model or economic analysis or cost-effectiveness or Markov or cost-utility or cost-benefit or cost-minimization or decision model or decision-tree or decision analysis or budget impact

- Only full-text articles published in English were included.
- Information on the country of the study, CEM type, modelling approach, results, parameters with most impact and modelling challenges were extracted.
- Data were extracted by one reviewer, and the quality was checked by another reviewer to ensure accuracy.

RESULTS

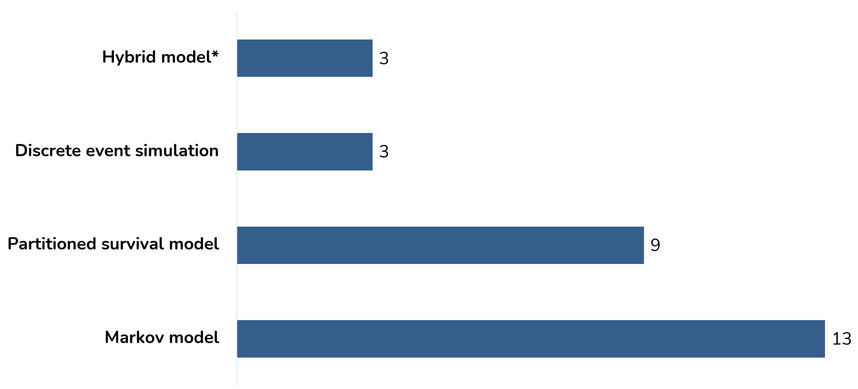
- The search retrieved 375 articles, of which 28 studies met the inclusion criteria and were included for analysis. The distribution of these studies by country and therapy is shown in Fig. 1.

Figure 1. Distribution of studies by country and GTx (N=28)



- Markov model (46%; n=13) was the most commonly used approach for patient simulation, followed by partitioned survival model (32%; n=9) (Fig. 2).

Figure 2. Types of simulation modelling in the CEMs (N=28)



*Hybrid model - combines the decision-tree and Markov model

- Cohort level models (89%; n=25) were more used compared to patient-level approach (11%; n=3). Also, patients were simulated until lifetime in most models (89%; n=25) (Fig. 3).
- Most models used Payer's perspective (89% [n=25]), except three which considered societal perspective.

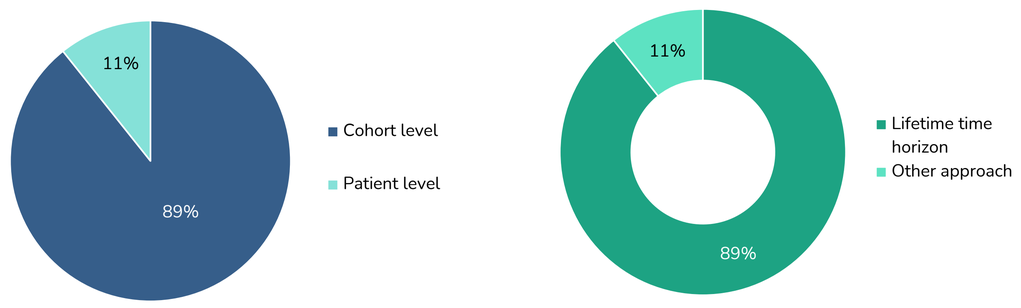
Key challenges in economic evaluations of gene therapy include:

- Utilization of single-arm clinical trials
- Assumptions around treatment durability
- Long-term extrapolations
- Unreliable utility estimates
- Insufficient real-world evidence.

Novel methodological approaches are required to address these modelling challenges to enhance the accuracy and reliability of cost-effectiveness evaluations of gene therapies.

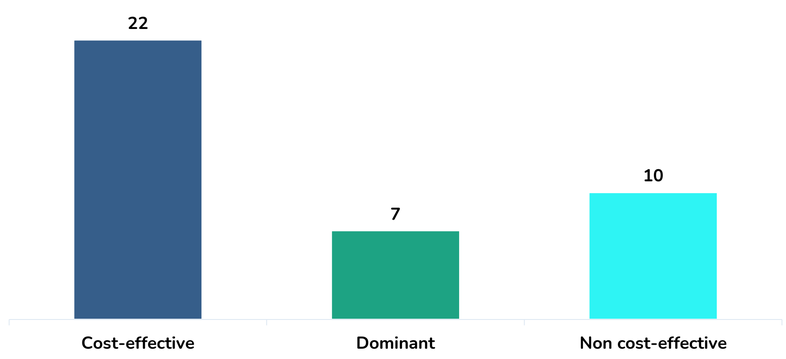
RESULTS cont.

Figure 3. Modelling approaches adopted in the CEMs (N=28)



Among the 39 comparisons made between GTx and standard of care, GTx was found to be cost-effective (56%; n=22) or dominant (18%; n=7) in most cases, with 10 (26%) comparisons indicating non-cost effectiveness (**Fig. 4**).

Figure 4. Cost-effectiveness results of GTx versus standard of care in the CEMs across 39 comparisons



The most influential parameters across the CEMs were related to price of GTx, effectiveness durability of GTx, and utility values.

The main key challenges reported in the modelling of GTx were observed to be the lack of real-world evidence, lack of head-to-head trials, single-arm trial, limited follow-up data, etc. (**Fig. 5**).

Figure 5. Modelling challenge themes reported by authors in the CEMs (N=28)

References

1. Pochopien M, et al. *J Market Access Health Policy*. 2021; 9: 2002006.
2. Gozzo L, et al. *Frontiers in Pharmacol*. 2021; 12: 755052.

Financial Disclosure

The authors are employees of ConnectHEOR Limited and no external funding was received to conduct this research. The authors have no conflict of interest to declare.

Poster presented at the ISPOR EU 2023, November 12-15, Copenhagen, Denmark