

WHAT IS THE IMPACT OF INCLUDING OUTCOMES-BASED AGREEMENTS ON THE COST-EFFECTIVENESS OF CELL AND GENE THERAPIES?

A CASE EXAMPLE OF ZYNTGLO FOR TRANSFUSION-DEPENDENT BETA-THALASSEMIA

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Background

- While interest in outcomes-based agreements has grown, their integration in value assessment is uncommon.
- Outcomes-based agreements offer a potential tool to manage the uncertainties in the clinical evidence and commonly high prices associated with cell and gene therapies and other regenerative medicines.

Objective

- We explored the impact of an outcomes-based agreement on the cost-effectiveness of gene therapies using ICER's review of Zynteglo for transfusion-dependent beta-thalassemia as a case example.

Methods

- A Markov cohort model with an upfront decision tree was used to model a hypothetical cohort of patients with transfusion-dependent beta-thalassemia.
- Patients were treated with Zynteglo or standard of care (SOC) over a lifetime time horizon.
- Analysis was undertaken from a US health care payer perspective.
- A publicly reported Federal Supply Schedule price of US \$2,140,000 was assumed for Zynteglo.
- Cost-effectiveness of Zynteglo was assessed with and without an outcomes-based agreement.

Outcomes-Based Agreement

Full up-front payment: \$2.14 Million

80% payback if transfusion independence (i.e., no transfusions required) was not achieved or maintained over five years.

Transfusion independence = defined as having an average hemoglobin level of 9 grams per deciliter without any red blood cell transfusions for 12 or more consecutive months.

- Outcomes included life years, quality adjusted life years (QALY), costs, cost per QALY, and prices at \$150,000/QALY.
- Optimistic and conservative scenarios were conducted to reflect the uncertainty in the clinical data associated with Zynteglo:
 - Mortality from bone marrow conditioning (1.4% base case; 2.8% conservative scenario)
 - Percentage of patients reverting to transfusion dependent per year after 7 years (0.27% base case; 0.58% conservative scenario)
 - Transfusions per year if loss of treatment effect (7.5 [<18 years] base case; 14.95 [<18 years] conservative scenario)

Results

| | With Outcomes-Based Agreement | Without Outcomes-Based Agreement |
|--|-------------------------------|----------------------------------|
|--|-------------------------------|----------------------------------|

| Zynteglo vs. SOC | |
|---|----------------|
| Incremental Costs | \$508,000 |
| Incremental Effects (LYs) | 2.85 |
| Incremental Effects (QALYs) | 4.98 |
| Incremental Cost Effectiveness Ratio | \$102,000/QALY |
| Probability of being Cost-effective at \$150,000/QALY | 78% |

LYs: life years, QALYs: quality-adjusted life years, SOC: standard of care

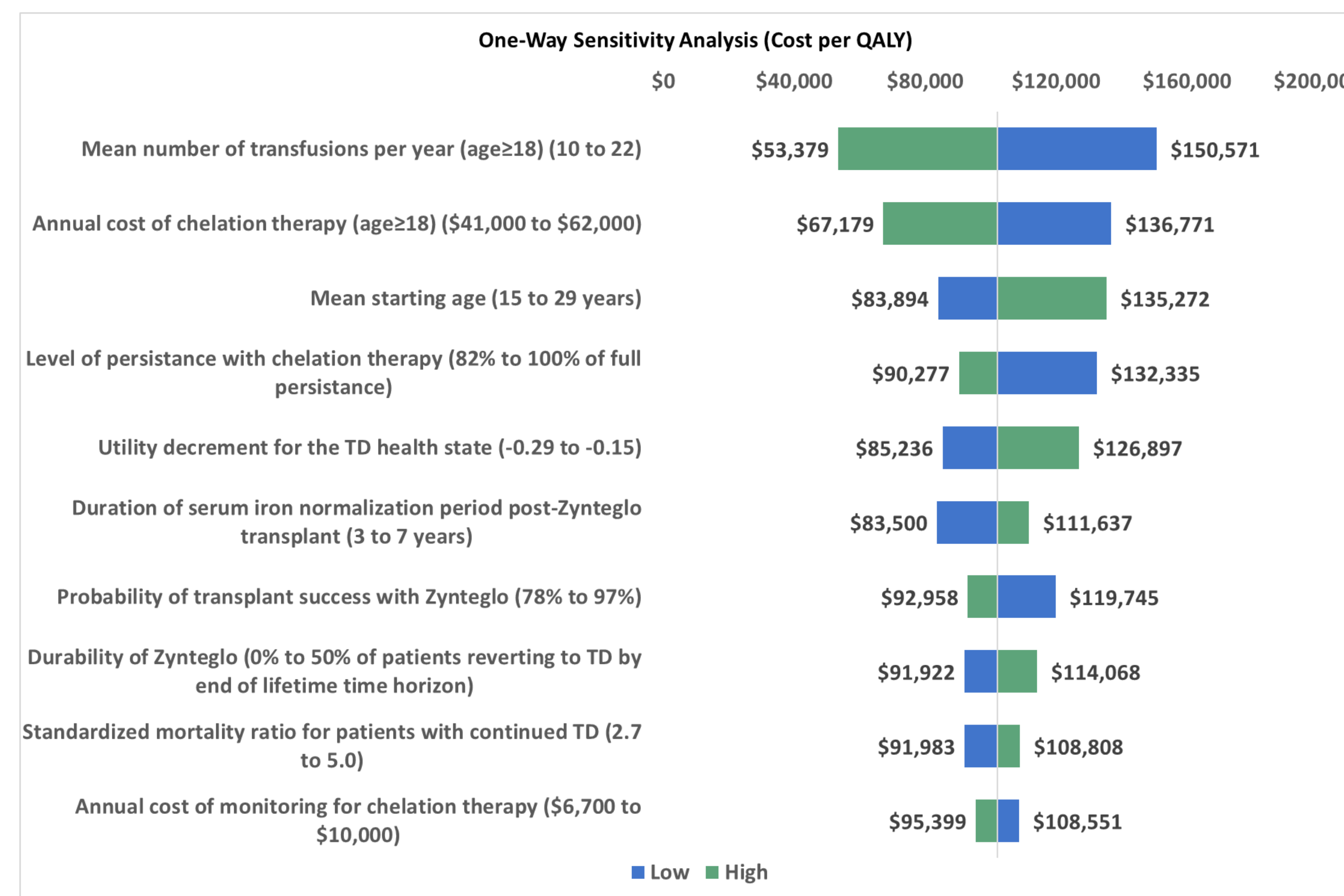
- **With** an outcomes-based agreement, Zynteglo was more effective and more costly compared to SOC with an incremental cost-effectiveness ratio of \$102,000/QALY.
- Under probabilistic analyses, Zynteglo had a 78% probability of being cost-effective at \$150,000/QALY.

| Zynteglo vs. SOC | |
|---|----------------|
| Incremental Costs | \$696,000 |
| Incremental Effects (LYs) | 2.85 |
| Incremental Effects (QALYs) | 4.98 |
| Incremental Cost Effectiveness Ratio | \$140,000/QALY |
| Probability of being Cost-effective at \$150,000/QALY | 54% |

LYs: life years, QALYs: quality-adjusted life years, SOC: standard of care

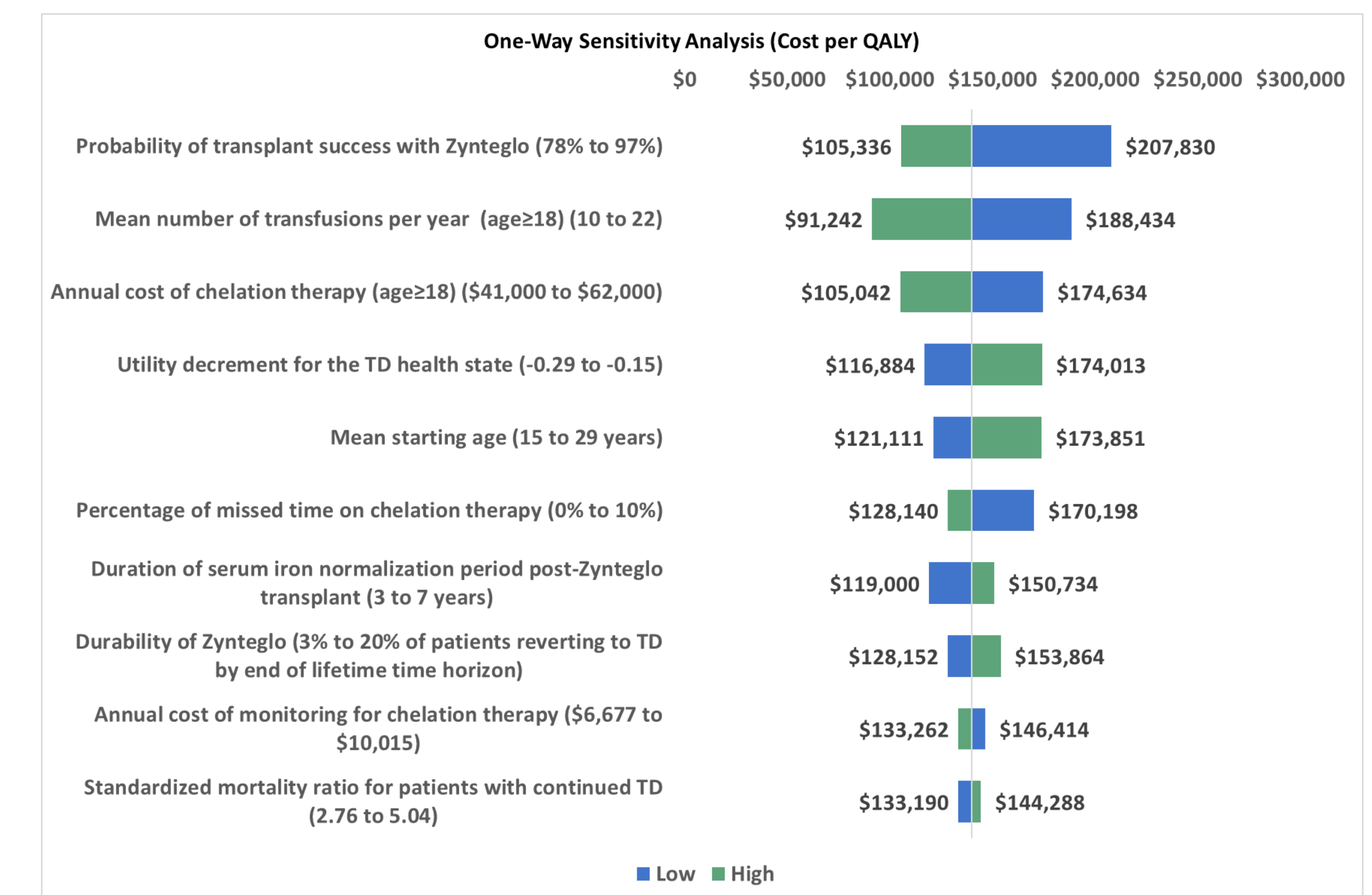
- **Without** an outcomes-based agreement, incremental costs increased by 37% to \$696,000, increasing the incremental cost-effectiveness ratio to \$140,000/QALY.
- Under probabilistic analyses, the probability of being cost-effective declined to 54%.

Price to achieve \$150K/QALY = **\$2,400,000**



QALY: quality-adjusted life year, TD: transfusion dependent

Price to achieve \$150K/QALY = **\$2,180,000**



QALY: quality-adjusted life year, TD: transfusion dependent

- Under conservative assumptions of treatment benefit, the price to achieve \$150K/QALY was **\$2,220,000** with an outcomes-based agreement, with a reduction to **\$2,000,000** without an outcomes-based agreement. Uncertainties were better managed with an outcomes-based agreement in place.

Discussion

- Direct integration of likely outcomes-based agreements in value assessments can allow stakeholders a full understanding of the cost and pricing implications of cell and gene therapies. These agreements can help manage uncertainty in the clinical data, such as the probability of treatment success.
- Further exploration of the implications of such agreements is warranted, especially for interventions with greater uncertainty and/or safety concerns.

References

Beaudoin FL, Richardson M, Synnott PG, Lancaster V, Fluetsch N, Herce-Hagiwara B, Campbell JD, Pearson SD, Rind DM. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review, July 19, 2022. <https://icer.org/beta-thalassemia-2022/#timeline>.

