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Cost-Effectiveness Analysis of Onasemnogene Abeparvovec-Xioi (Zolgensma®) and Best Supportive Care Treatment for Spinal Muscular Atrophy I in the Netherlands With Early-Treatment Scenario

Meijer A.[1], Omar Alsaleh A.J.[2]

[1]Bologna University, Amsterdam, Netherlands, [2]Bologna University, Bologna, Italy

INTRODUCTION

Spinal Muscular Atrophy (SMA)

- A rare genetic disorder (incidence 1 in 10,000) causing progressive muscle weakness and respiratory failure [1, 2].
- Life expectancy around 2 years and infants are not able to achieve any motor milestones (sitting, walking) [3].
- Recent developments:
  - Nusinersen (Spinraza®) [4]
  - Onasemnogene abeparvovec-xioi (OA) (Zolgensma®) [5]
- **Uncertainties** about the **long-term treatment effects** and **high drug costs.**
  - Causes debate about the reimbursement of the drugs and pose challenges for patients and the healthcare systems [6-13].

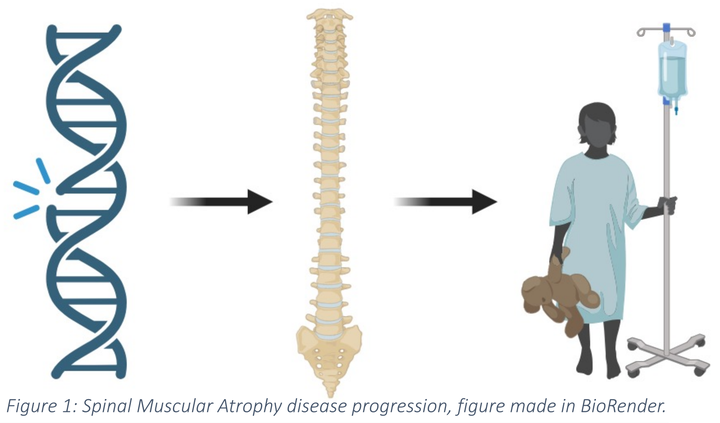


Figure 1: Spinal Muscular Atrophy disease progression, figure made in BioRender.

OBJECTIVE

The aim of this study is to conduct a comprehensive cost-effectiveness analysis of treating SMA Type I patients with OA compared to best supportive care (BSC) (with newly published clinical data [14, 15]) from a societal perspective in the Netherlands with an early-treatment scenario.

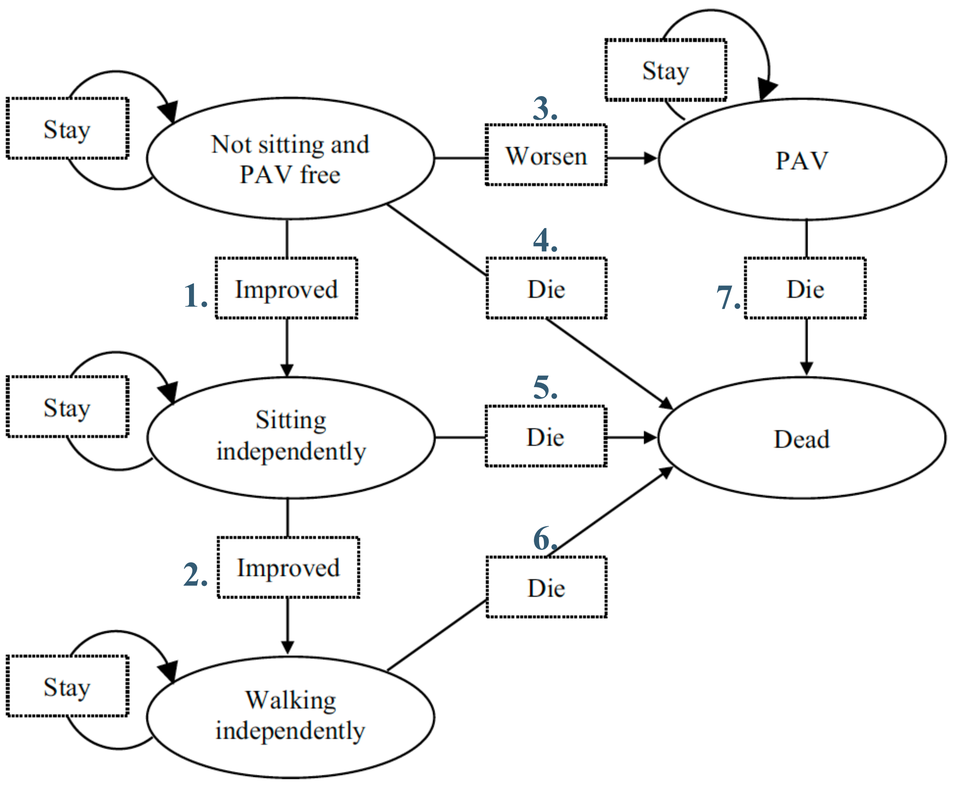


Figure 2: Structure of Markov model for SMA type I [7].

METHODS

- Individual state-transition model, with 5 health states based on **gaining motor milestones**, **needing permanent assisted ventilation (PAV)** and **death** [7].
- Lifetime horizon, with monthly cycles. The model consists of two phases:
  1. A short-term model of 36 months that uses data from clinical trials.
  2. A long-term model that lasts up to 99 years.

Health state transition	BSC	OA treatment
All patients start in 'not sitting and PAV free' state		
1. & 2.	N/A	STR1VE-US and STR1VE-EU (n=42)
3. & 4.	NeuroNEXT (n=16)	NeuroNEXT and STR1VE (n=58)
5.		SMA type II patients (n=240)
6.		National life tables CBS
7.		Patients receiving non-invasive ventilation only (n=24)

Table 1: Data sources used for health state transitions [14, 18-21].

Parameter	Base-case
Utility value PAV	0.095
Utility value not sitting and PAV free	0.190
Utility value sitting	0.600
Utility value walking	0.850
Monthly costs PAV	€ 12,836
Monthly costs not sitting and PAV free	€ 12,836
Monthly costs sitting	€ 12,485
Monthly costs walking	€ 6,935
One-time costs OA drug	€ 2,195,905
Discount rate costs	0.040
Discount rate outcomes	0.015

Table 2: Model inputs [10-13, 16, 17].

Assumptions:

- Motor milestones achieved before 36 months (end of short-term model) sustain until death.
- Regression from higher health states to worse health states is not possible.

RESULTS

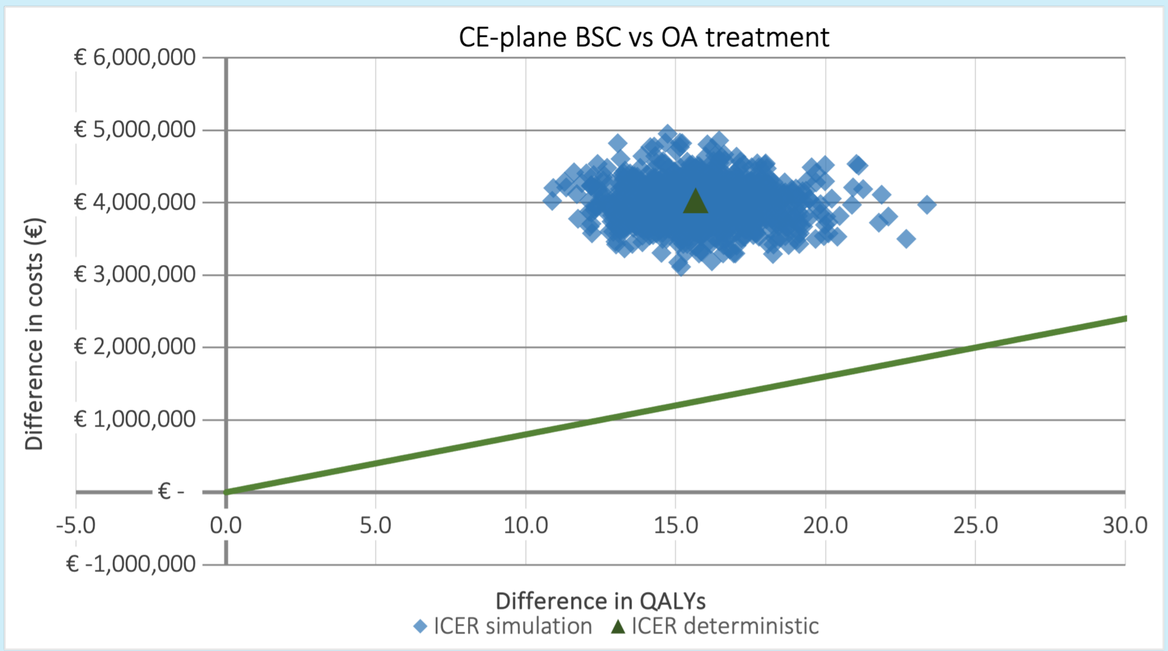
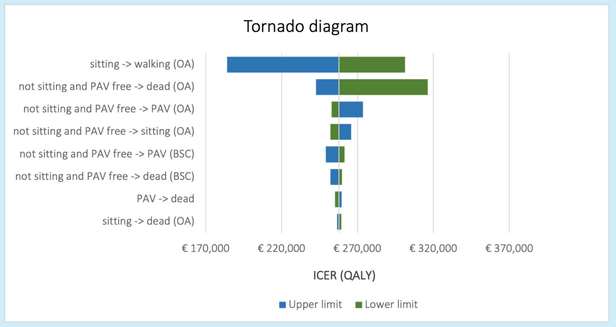


Figure 3: Cost-effectiveness plane based on the PSA.

Outcomes	Base-case	Early treatment
Costs (€)		
BSC	€ 350,878	
OA	€ 4,386,381	€3,951,500
Incremental costs	€ 4,035,503	€3,600,622
Life years		
BSC	2.46	
OA	25.05	34.42
Incremental LYs	22.58	31.96
QALYs		
BSC	0.37	
OA	16.03	28.70
Incremental QALYs	15.66	28.33
ICER (€/QALY)	**€ 257,717**	**€127,107**

Table 3: Outcomes from a societal perspective.



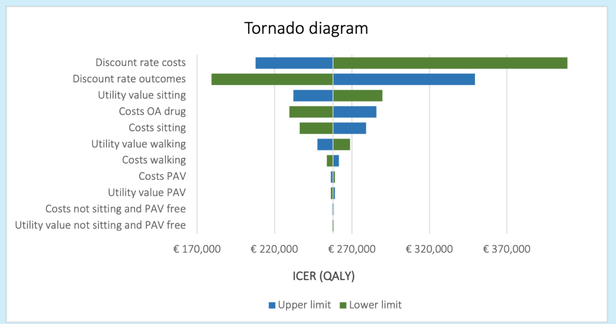


Figure 6 & 7: Outcomes of the DSA presented in a tornado diagram.

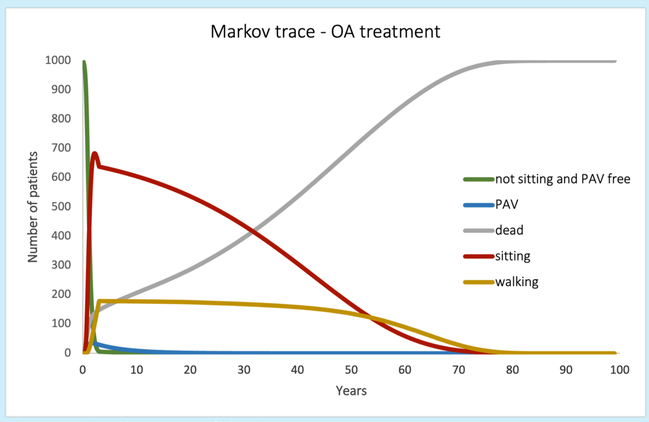


Figure 4: Markov traces of the OA treatment arm.

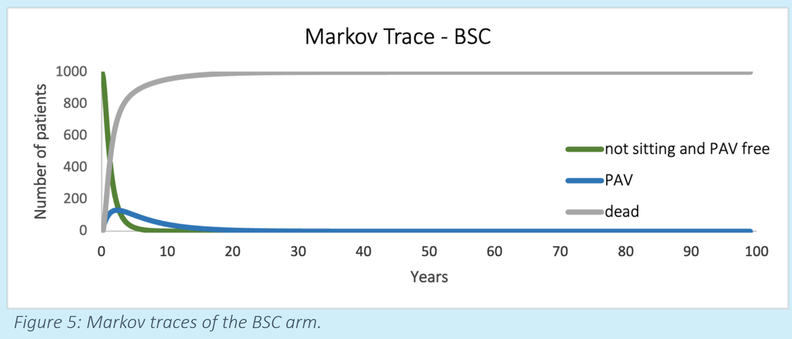


Figure 5: Markov traces of the BSC arm.

- Both ICERs are above the Dutch willingness-to-pay (WTP) reference value of €80,000.
- Key drivers influencing the ICERs were the **costs of OA treatment** and **utility and cost values of 'sitting independently'** health state.

CONCLUSIONS

- ICER of €257,717 > threshold of €80,000 WTP in the Netherlands.
- **Significant improvements** in **disease progression**, **motor skills**, and **quality of life** compared to BSC.
- Substantial gains in life years 22.58 (25.05 – 2.46) and QALYs 15.66 (16.03– 0.37).
- ICER ZIN: €352,095 (~27% reduction).
- Scenario analysis supported the recommendation of the Dutch Health Council for incorporating SMA in the Newborn Screening Program in the Netherlands [12].

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