

# Cost-effectiveness of Cannabidiol (CBD) for the Treatment of Seizures in Patients With Treatment-Resistant Lennox-Gastaut Syndrome or Dravet Syndrome in the Netherlands

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## Introduction

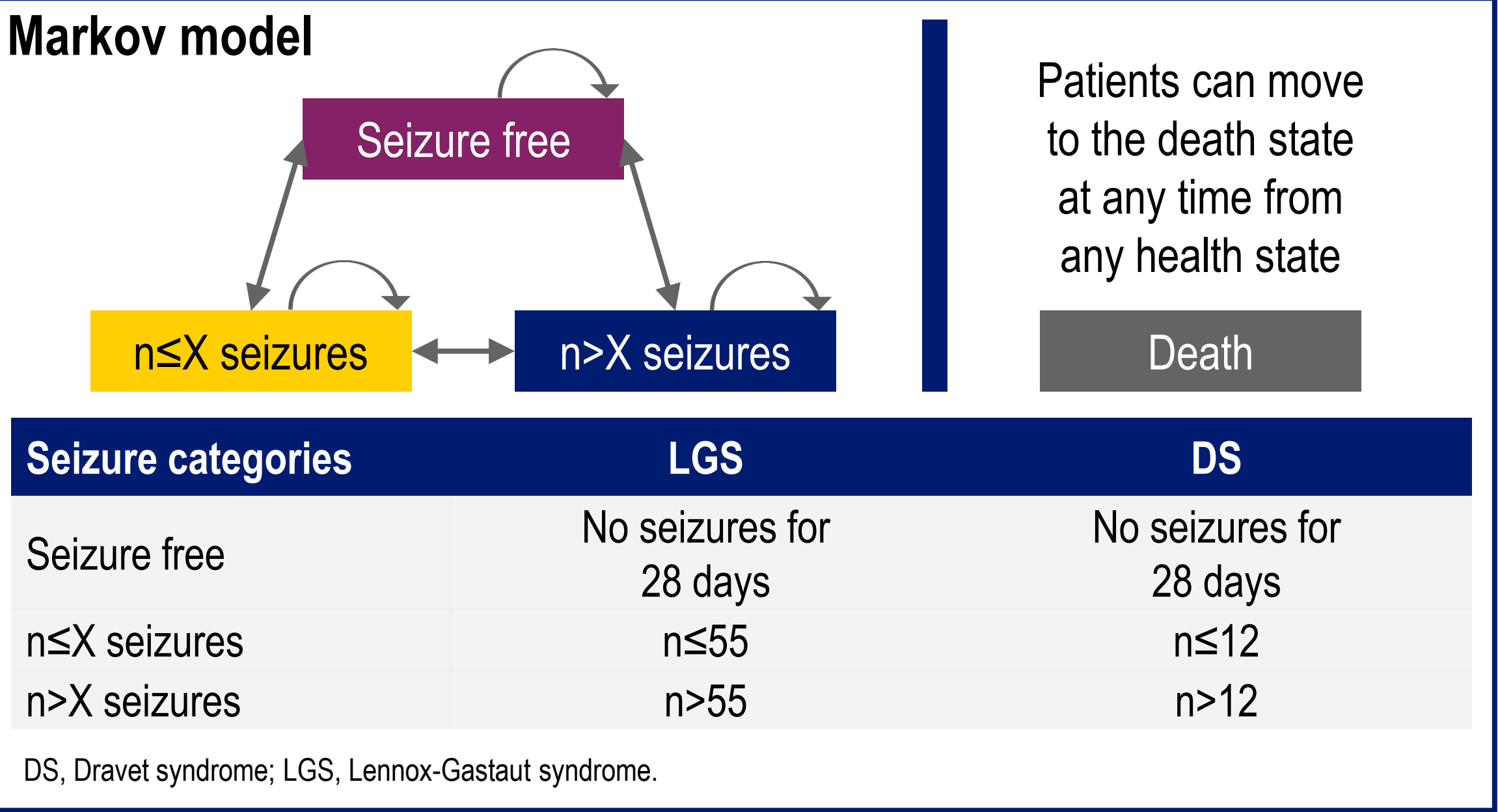
- Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS) are rare, lifelong, treatment-resistant, and life-threatening epileptic encephalopathies that present in infancy or early childhood.<sup>1–3</sup>
- Complete seizure freedom with antiseizure medications (ASMs) is unachievable in most patients, and there remains a significant unmet need for treatments that reduce seizure frequency and severity and improve the overall condition of patients.<sup>4,5</sup>
- Plant-derived highly purified cannabidiol (CBD) medicine (Epidyolex®) is approved in the UK and EU for the adjunctive treatment of seizures associated with LGS or DS, in conjunction with clobazam, in patients ≥2 years of age.<sup>6,7</sup>

## Objective

- This study estimated the cost-effectiveness of CBD plus usual care (established clinical management) compared with usual care alone for the treatment of seizures in patients with treatment-resistant LGS or DS in the Netherlands.

## Methods

- A cohort-based Markov model was developed to determine the average costs and quality-adjusted life years (QALYs) per patient associated with seizure frequency and seizure-free days.
  - Model analysis was performed over a lifetime (90-year) horizon with a 3-month cycle length from a Dutch societal perspective
- Patients entering the model were treated with either highly purified CBD medicine (Epidyolex®; 100 mg/mL oral solution) at 12 mg/kg/day plus usual care, or usual care alone.
  - Usual care consisted of a variety of ASMs including clobazam
- Baseline characteristics for patients entering the model were based on data across all treatment arms of the randomised controlled trials (RCTs) of CBD for each indication.<sup>8–11</sup>
- Model health state transition probabilities were based on patient-level data on seizure frequency and seizure-free days from the RCTs and open-label extension (OLE) associated with CBD.<sup>8–13</sup>
  - Discontinuation and stopping rates associated with CBD treatment were calculated from the RCTs, OLE and/or the US Expanded Access Programme<sup>8–15</sup>



- Drug acquisition, disease management, adverse events, and societal costs were included, with unit costs sourced from published literature.
- A 2019/2020 price year was used, with costs presented in euros (€); discount rates of 4.0% and 1.5% per annum were applied to costs and outcomes, respectively.<sup>16</sup>
- Societal parameters comprised out-of-pocket expenses for both patients and caregivers and included travel costs associated with hospital visits and the time cost of family and professional care.
- Productivity losses were not considered in the analysis since Dutch clinical experts confirmed that most patients with LGS or DS do not work.
- Healthcare resource utilisation data were collected using a UK-based Delphi panel, with estimates validated by Dutch clinical experts.
- Health-related quality of life estimates were collected in Sweden and the UK using vignettes of the general population via time trade-off (TTO) methods<sup>17</sup> and were validated by Dutch clinical experts.
- Parameter uncertainty was assessed via one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA); scenario analyses were conducted to test uncertainty around structural and parametric assumptions.
- This study was conducted with Epidyolex®, and results do not apply to other CBD-containing products.

## Results

- In patients with LGS, CBD plus usual care led to additional costs of €28338 and increased QALYs of 1.318 compared with usual care alone. The resulting incremental cost-effectiveness ratio (ICER) was €21493/QALY.
- In patients with DS, based on the ICER, CBD plus usual care dominated usual care alone, with cost savings of €23642 and increased QALYs of 0.868.
- ICERs for CBD in LGS and DS were in line with the willingness-to-pay (WTP) threshold of €80000/QALY in the Netherlands for these conditions.<sup>18</sup>

### Base-case and key scenario analyses for LGS and DS

Scenario	ICER (€/QALY) of CBD plus usual care vs usual care alone	
	LGS	DS
Base case	21493	Dominating <sup>a</sup>
Alternative seizure thresholds <sup>b,c</sup>	32051	Dominating <sup>a</sup>
Time horizon: 20 years	28538	Dominating <sup>a</sup>
Time horizon: 30 years	24969	Dominating <sup>a</sup>
Number of caregivers: 2	8272	Dominating <sup>a</sup>
Mortality RR in seizure-free health state: 0.71	25028	Dominating <sup>a</sup>
Varying the proportion for ICU admissions within hospitalisations: 50% in general ward vs 50% in ICU	20150	Dominating <sup>a</sup>
Varying the AE disutilities: tripling	21506	Dominating <sup>a</sup>
Varying the AE costs: tripling	21592	Dominating <sup>a</sup>
Number of cycles for which AE disutilities are applied: 9 cycles	21523	Dominating <sup>a</sup>
Utility source: DS utilities (TTO values)	23867	N/A
Utility source: LGS utilities (TTO values)	N/A	Dominating <sup>a</sup>
Apply same hours of care for seizure health states	29465	Dominating <sup>a</sup>

<sup>a</sup>CBD plus usual care was clinically superior and cost saving compared with usual care alone. <sup>b</sup>Alternative seizure thresholds for LGS include the following health states: seizure free, ≤84 seizures and >84 seizures (days with seizures). <sup>c</sup>Alternative seizure thresholds for DS include the following health states: seizure free, ≤25 seizures and >25 seizures (days with seizures).  
€, euros; AE, adverse event; CBD, cannabidiol; DS, Dravet syndrome; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; LGS, Lennox-Gastaut syndrome; N/A, not applicable; QALY, quality-adjusted life year; RR, risk ratio; TTO, time trade-off.

### OWSAs for LGS and DS

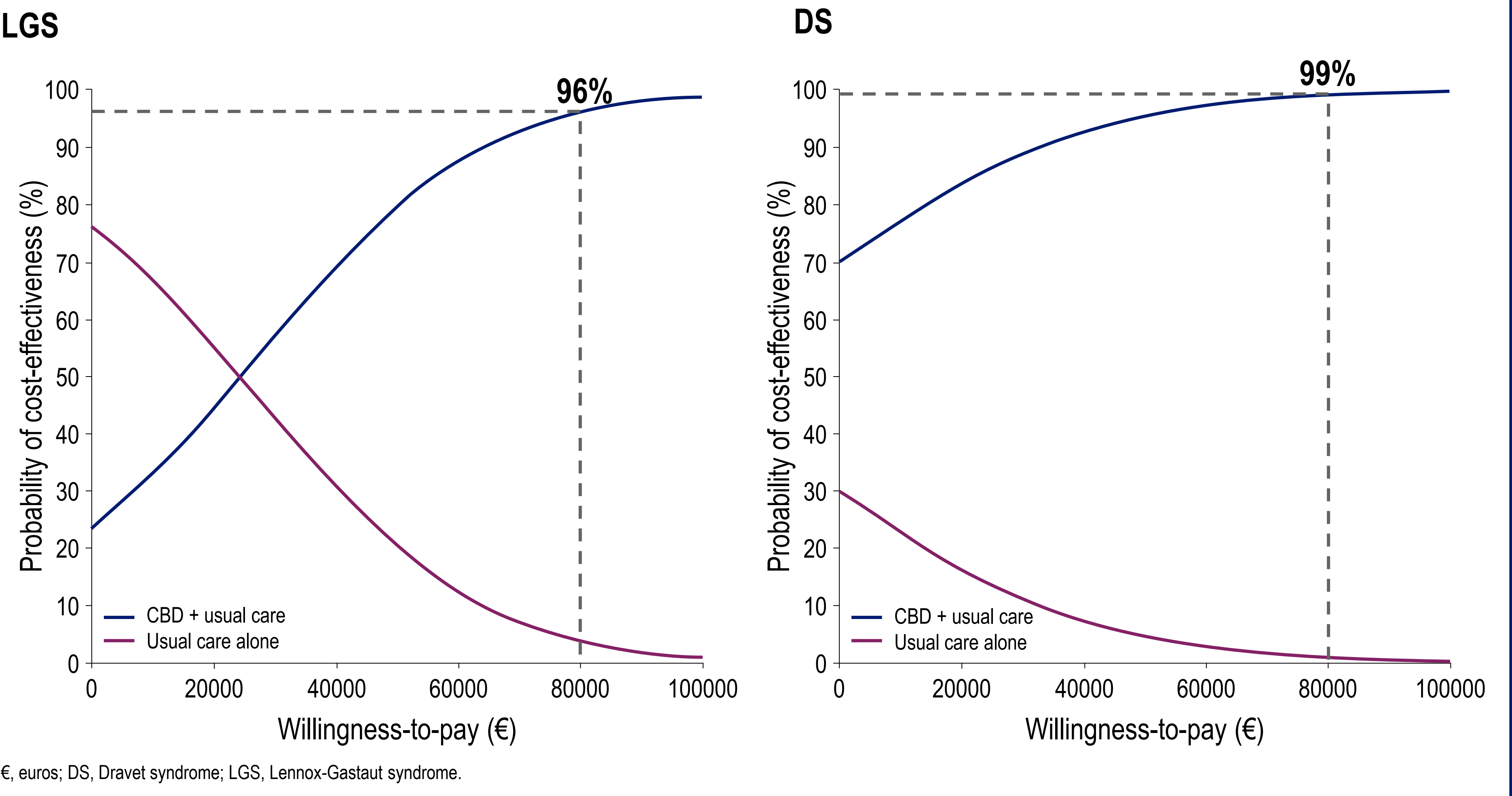
- Within the OWSAs, the ICER was most sensitive to the average dose of CBD for both LGS and DS.
  - The ICER ranged from €9226 to €70561 for LGS, and dominating to €37584 for DS, with all values below the WTP threshold for each indication

### PSAs for LGS and DS

LGS	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)	DS	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Usual care	2,327,078	5.439	-	-	-	Usual care	2,246,536	14.974	-	-	-
CBD	2,357,328	6.772	30251	1.333	22689	CBD	2,223,193	15.850	-23343	0.876	Dominating

€, euros; CBD, cannabidiol; DS, Dravet syndrome; ICER, incremental cost-effectiveness ratio; LGS, Lennox-Gastaut syndrome; QALY, quality-adjusted life year.

### Cost-effectiveness acceptability curves for LGS and DS



## Conclusions

- The analysis demonstrates that treatment with CBD plus usual care is a cost-effective treatment option in patients with LGS or DS when compared to usual care alone in the Netherlands.
  - Results were robust to sensitivity (OWSA and PSA) and key scenario analyses