

Cost effectiveness of Apomorphine in the treatment of advanced Parkinson Disease in the UK and Germany: Results from a multicounty decision analytic model

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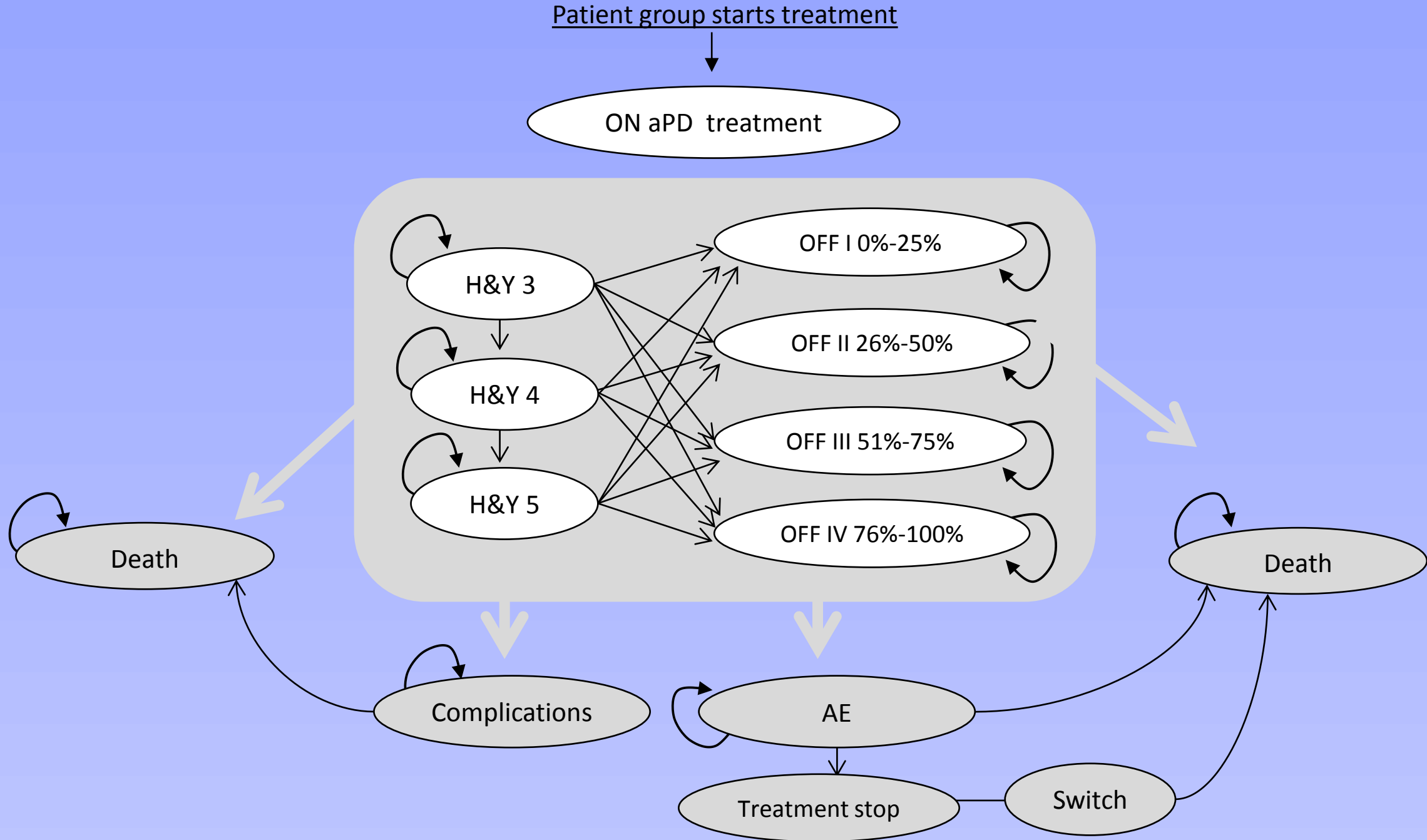
Objectives

Parkinson Disease (PD) is the second commonest cause of neurological disability. Approximately, 5.2 million men and women are affected worldwide. Continuous subcutaneous apomorphine (CSAI) represents an alternative treatment option of advanced PD with motor fluctuation. The purpose of this analysis was to estimate the cost-effectiveness of CSAI compared with Levodopa/carbidopa intestinal gel (LCIG), Deep-Brain-Stimulation (DBS) and Standard-of-care (SOC).

Methods

We developed a Markov-Model to simulate the long-term consequences, disease progression (Hoehn&Yahr-stages 3-5, percentage of waking-time in the OFF-state), complications and adverse-events. The model is adopted based on models which have been published for the UK and Sweden. Complications are different for the alternatives (e.g. pump problems in case of LCIG, temporary/permanent complications in case of DBS). Moderate and severe adverse-events (e.g. motor fluctuation, dyskinesia, nausea, dizziness, hallucination, skin problems, depression, anxiety) and death were included. Including 25 health-states, the model comprises moderate and severe health conditions. Probabilities derived from RCT and open-label studies. Direct costs (2012) were estimated from the perspective of the national health care systems.

Fig. 1: Model Design



Source: developed by IPF

The medical resource use and Utilities are based on literature research.

QALYs, life-years and costs are projected over a life-time horizon and are discounted at 3.5%. Monte-Carlo-simulation accounted for uncertainty.

Cohort definition

The model cohort comprises PD patients aged 50 years or older with Hoehn&Yahr (H&Y) stages 3, 4 or 5 experiencing more than 50% of waking-time (14 hour) in the OFF state at treatment initiation. After treatment initiation with CSAI, LCIG or DBS an improvement in health states in the following cycle may arise; or patients continue SOC. During different therapeutic alternatives adverse events or complications may arise. Due to intolerable adverse events, patients have the opportunity to switch to an alternative treatment. Patients receiving first-line CSAI or LCIG switch to DBS and patients after a DBS either start or increase SOC medication.

Ressource use and costs

The cost assessment is based on the assignment of costs to the health states. The costs of each health state are determined by the resource utilisation associated with a health state. Resource use (e.g. the type and frequency of medical goods and services rendered to the patient) and monetary value (prices, tariffs and/or opportunity costs) for each unit of medical goods and services were used to calculate the total direct costs. In order to estimate the cost of aPD and related costs including the AE and complication costs in the UK and Germany only direct costs were included in the analysis. Health state costs (H&Y and OFF stages) were calculated based on the resource use data of Findley et al. (2011), which were multiplied with national unit costs.

Results

UK life-time costs associated with CSAI amounts to 70,258 £ and generates 2.85 QALYs and 6.28 LYs (106,530 €, 2.92 QALYs and 6.49 LYs for Germany). Costs associated with LCIG are 117,121 £, achieves 3.06 QALYs and 6.93 LYs (178,405 €, 3.18 QALYs and 7.18 LYs for Germany). The incremental-cost per QALY gained (ICER) was 223,052 £ (281,089 €).

Tab. 1: Results of costs QALYs and LYs for the UK

Strategy	Costs C	Diff. DC	QALYs E	Diff. QALYs DE	ICER
CSAI	70,258.28 £		2.85		9,296.41 £ vs. SOC
LCIG	117,121.48 £	46,863.20 £	3.06	0.21	223,051.88 £ vs. CSAI
DBS	88,361.61 £	18,103.33 £	2.75	-0,10	(Dominated by CSAI)
SOC	68,082.92 £	-2,175.36 £	2.62	-0.23	
Strategy	Costs C	Diff. DC	LYs E	Diff. LYs DE	C per LYs gained
CSAI	70,258.28 £		6.28		4,225.64 £ vs. SOC
LCIG	117,121.48 £	46,863.20 £	6.93	0.65	72,075.05 £ vs. CSAI
DBS	88,361.61 £	18,103.33 £	6.38	0.11	170,144.08 £ vs. CSAI
SOC	68,082.92 £	-2,175.36 £	5.76	-0.51	

Source: IPF own calculations

ICER = incremental cost effectiveness ratio

Tab. 2: Results of costs QALYs and LYs for Germany

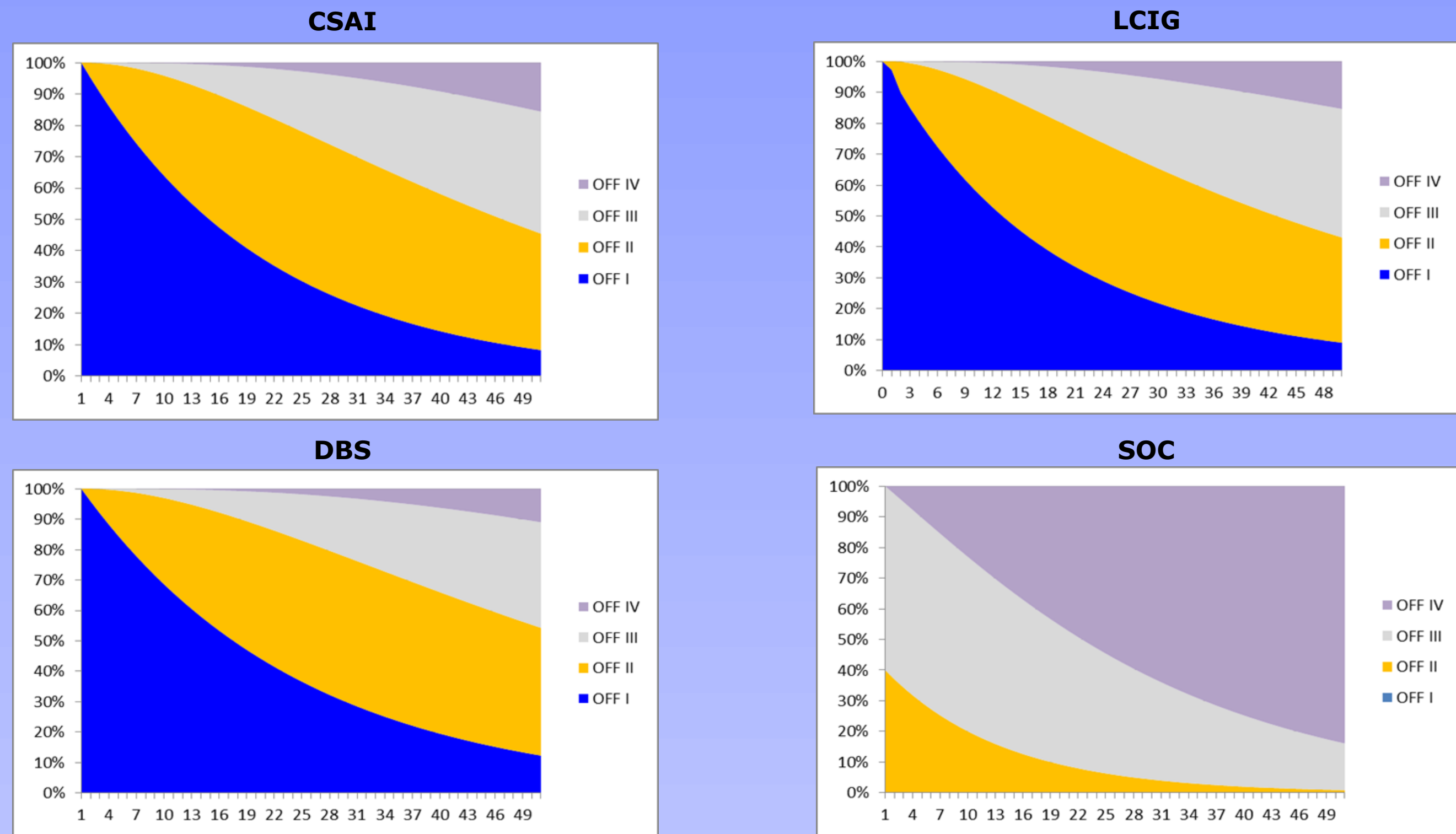
Strategy	Costs C	Diff. DC	QALYs E	Diff. QALYs DE	ICER
CSAI	106,530.75 €		2,92		77,066.79 € vs. SOC
LCIG	178,405.15 €	71,874.40 €	3,18	0.26	281,088.78 € vs. CSAI
DBS	121,987.80 €	15,457.05 €	2,85	-0.08	(Dominated by CSAI)
SOC	91,587.50	-14,943,25 €	2,73	-0.19	
Strategy	Costs C	Diff. DC	LYs E	Diff. LYs DE	C per LYs gained
CSAI	106,530.75 €		6,49		4,225.64 € vs. SOC
LCIG	178,405.15 €	71,874.40 €	7,18	0,69	72,075.05 € vs. CSAI
DBS	121,987.80 €	15,457.05 €	6,61	0,12	170,144.08 € vs. CSAI
SOC	91,587.50 €	-14.943,25 €	6,00	-0,49	

Source: IPF own calculations

ICER = incremental cost effectiveness ratio

Costs for DBS are 88,361.61 £, associated with 2.75 QALYs and 6.38 LYs (121,988 €, 2.85 QALYs and 6.61 LYs for Germany). CSAI dominates DBS. SOC associated UK costs are 68,082.92 £; 2.62 QALYs and 5.76 LYs were reached (91,588 €, 2.7 3QALYs and 6 LYs for Germany).

Fig. 2: Distribution of patients according to OFF time per 6 month



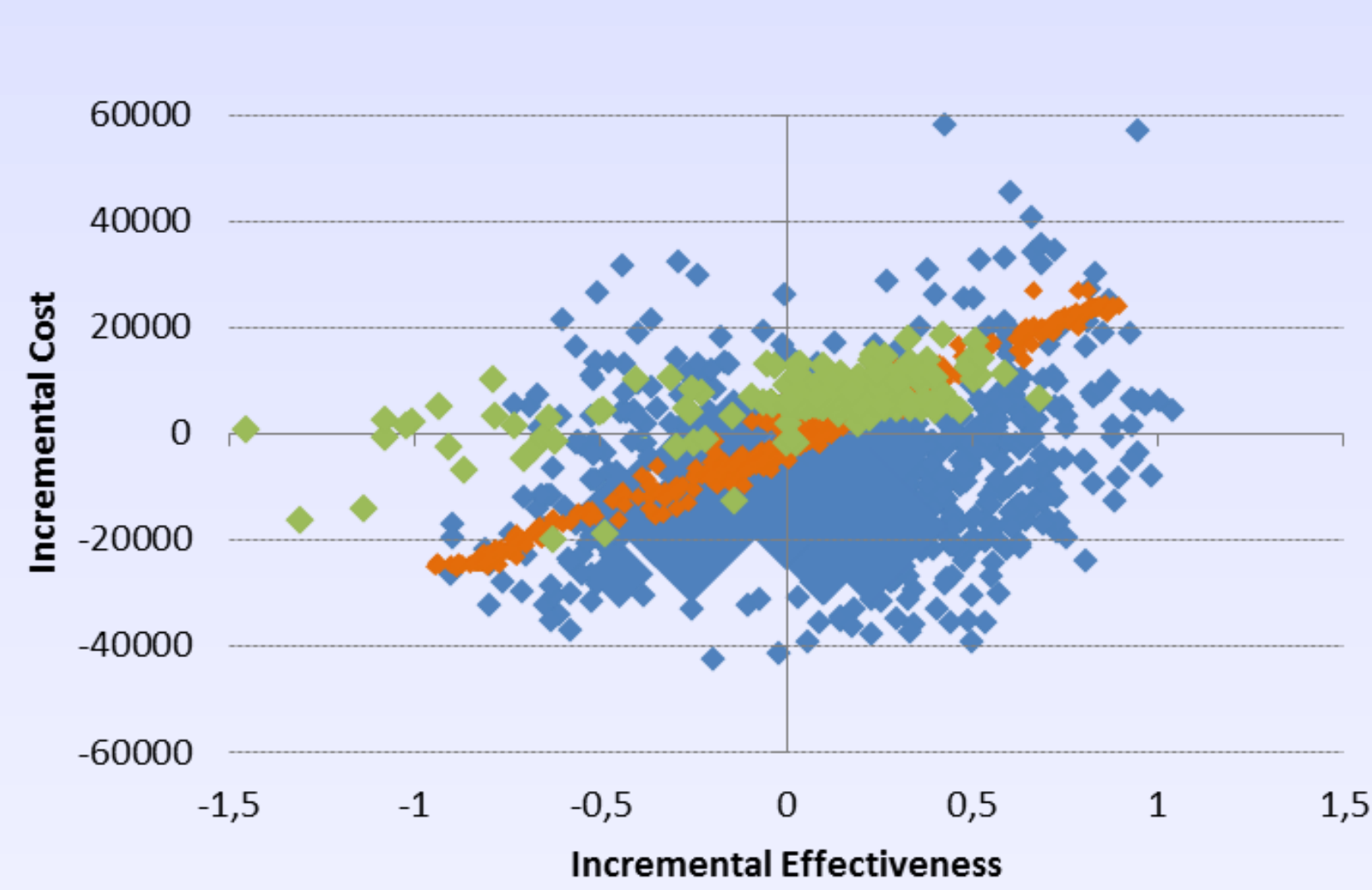
Source: IPF own calculations

CSAI, LCIG and DBS patients spent less time in higher OFF states compared to SOC. Patients treated with CSAI spent 69% of their remaining life-time in OFF I stage, 24% in OFF II, 6% in OFF III and 1% in OFF IV. Patients treated with LCIG spent 76% of their life-time after treatment start in OFF I, 20% in OFF II, 3% in OFF III and 1% in OFF IV; DBS patients spent 78% of time in OFF I state, 19% in OFF II, 2.5% in OFF III and 0.5% in OFF IV. In comparison to that, patients remaining on SOC therapy spend 27% of time in OFF II, 57% in OFF III and 16% in OFF IV stage.

Sensitivity Analysis

Probabilistic sensitivity analysis of 500 trial plots revealed that CSAI is cost effective compared to LCIG in more than 69.6% of the simulations with a willingness to pay of 20,000 £ in the UK and in 98.6% of the simulations in Germany with an willingness to pay threshold of 20,000 €; versus DBS in 25.8% (33%) and versus SOC in 98.7% (16.6%) of all simulations (Fig. 3).

Fig. 3a: Probabilistic Sensitivity Analysis UK



3b: Acceptability curves UK

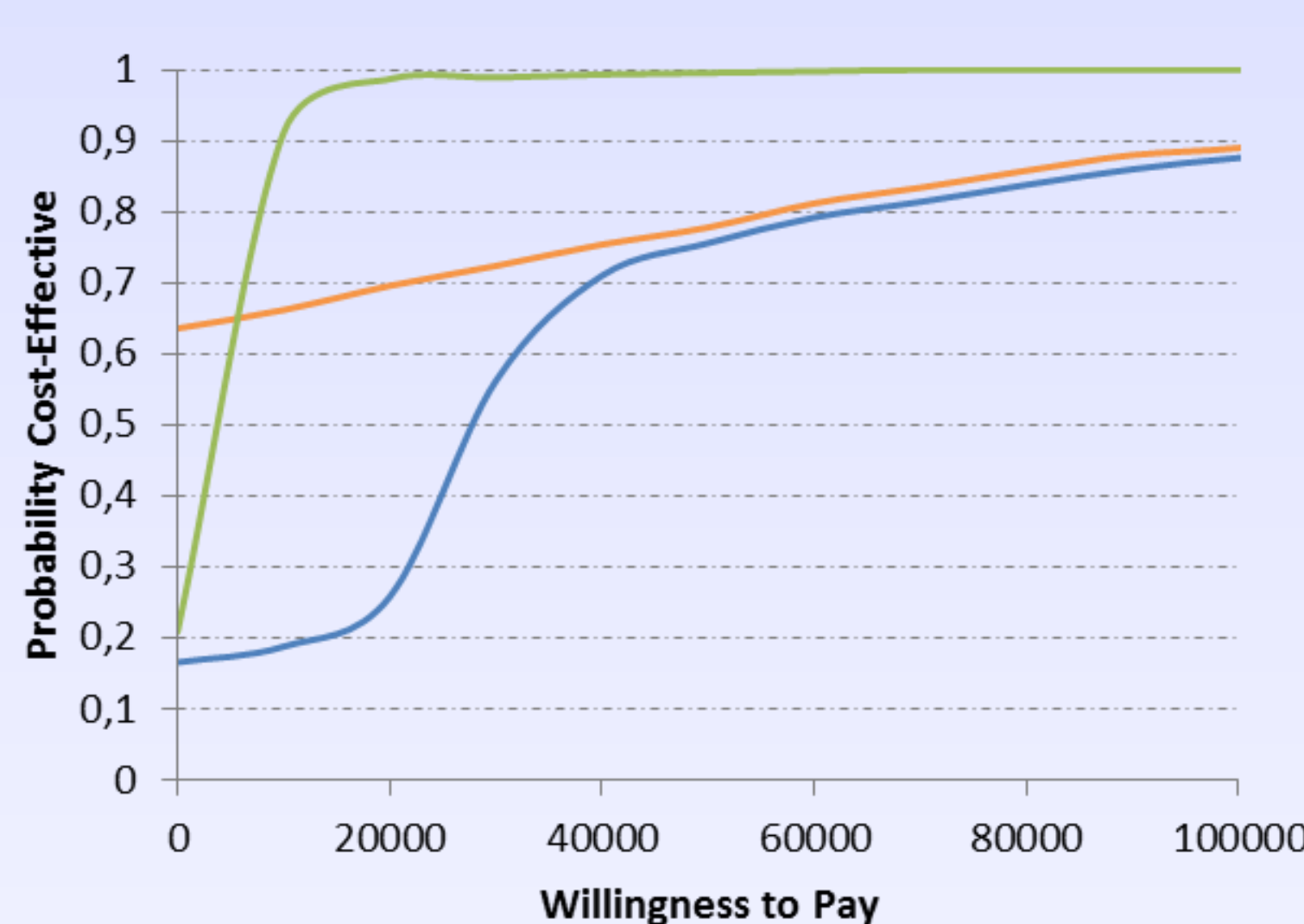
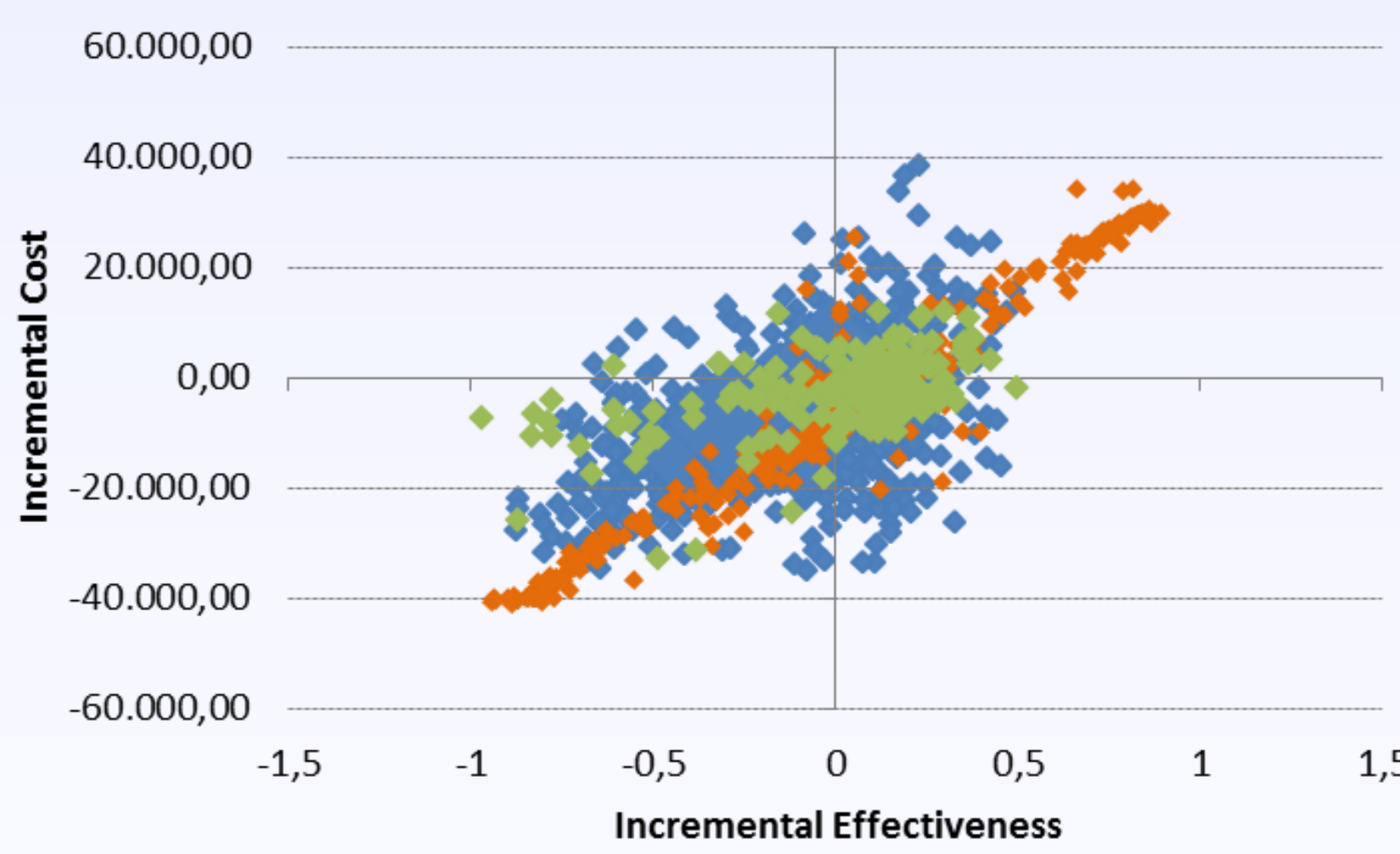
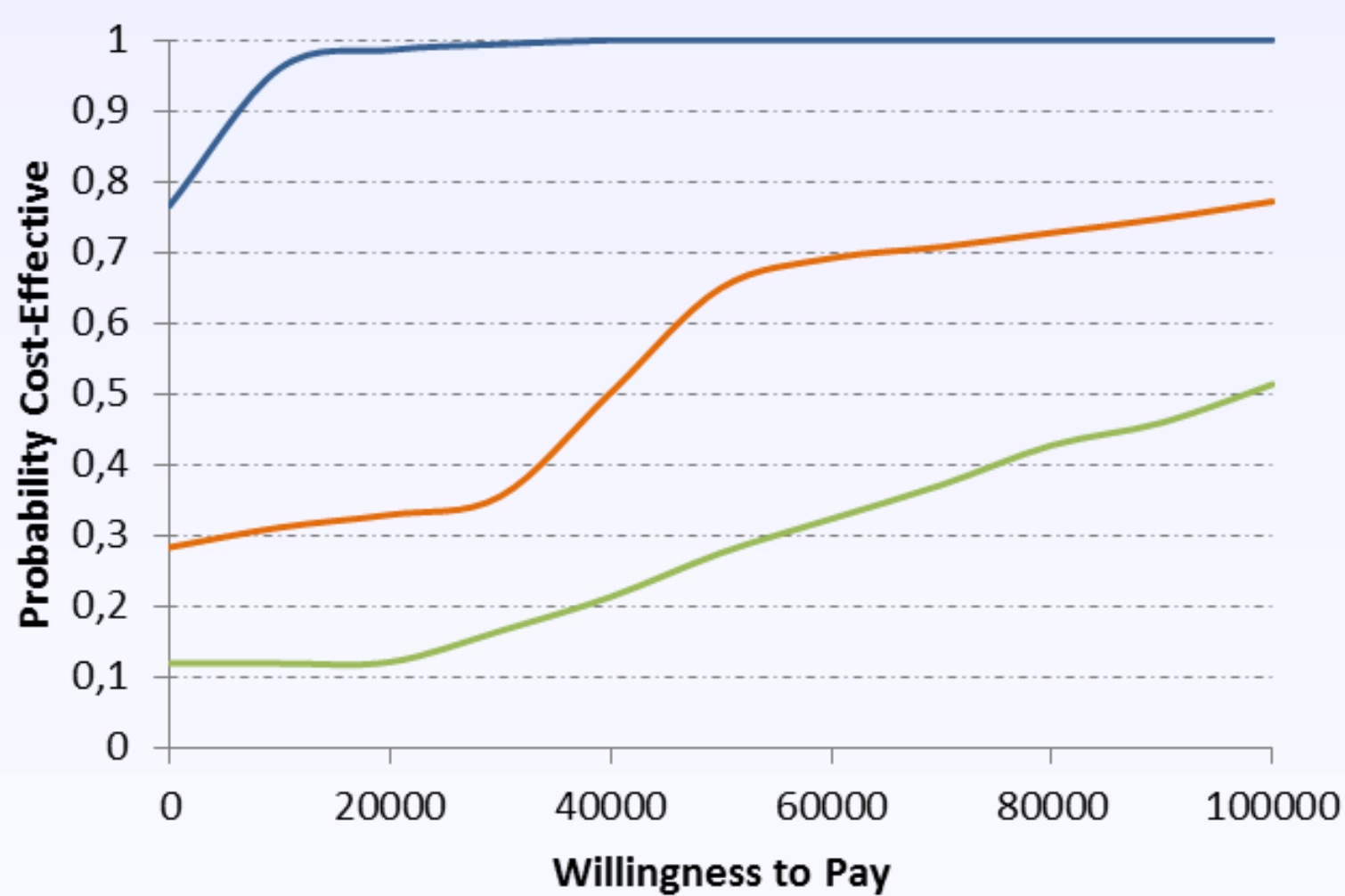


Fig. 3c: Probabilistic Sensitivity Analysis Germany



3d: Acceptability curves Germany



Source: own calculations

Conclusion

Funding the maternal toxoplasma screening saves money and is cost-effective for the society and the Austrian health care system.

References

Lowin J, Bergman A, Ray Chaudhuri K et al. A cost-effectiveness analysis of levo-dopa/carbidopa intestinal gel compared to standard care in late stage Parkinson's disease in the UK. J Med Econ. 2011;14(5):584-93
Willis M, Persson U, Zoellner Y, et al. Reducing uncertainty in value-based pricing using evidence development agreements. The case of continuous intraduodenal infusion of levodopa/carbidopa (Duodopa) in Sweden. Applied Health Economics & Health Policy 2010;8:1-10
Findley LJ, Wood E, Lowin J, Roeder C, Bergman A, Schifflers M. The economic burden of advanced Parkinson's disease: an analysis of a UK patient dataset. J Med Econ. 2011;14(1):130-9
Findley LJ, Lees A, Apajala M, Pitkänen A, Turunen H. Cost-effectiveness of levodopa/carbidopa/entacapone (Stalevo) compared to standard care in UK Parkinson's disease patients with wearing-off. Curr Med Res Opin. 2005;21(7):1005-1014
Ganchev ST, Nutt JG, Woodward WR. Apomorphine infusional therapy in Parkinson's disease: clinical utility and lack of tolerance. Mov Disord 1995;10:37-43.
Katzenschlagel R, Hughes A, Evans A, et al. Continuous subcutaneous apomorphine therapy improves dyskinesias in Parkinson's disease: a prospective study using single-dose challenges. Mov Disord 2005;20:151-157
Egbert K, Schrader C, Hahn M, et al. Continuous jejunal levodopa infusion in pa-tients with advanced parkinson disease: practical aspects and outcome of Deuschl G, Schade-Brittinger C, Krack P. A Randomized Trial of Deep-Brain Stimu-lation for Parkinson's Disease. N Engl J Med 2006;355:896-908
Additional Literature with the author