

Cost Utility Analysis of Empagliflozin in Chronic Heart Failure with Reduced Ejection Fraction: A UK Healthcare System Perspective

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BACKGROUND

- Chronic heart failure (CHF) is a progressive clinical condition with rising prevalence worldwide, including UK, with considerable economic strain on the healthcare system in the years to come¹
- Despite current therapeutic options, patients with HF with reduced ejection fraction (HFrEF) are often under-treated, thereby facing poor prognosis²
- Empagliflozin, a sodium-glucose co-transporter 2 inhibitor (SGLT2i), has been shown to exhibit favorable morbidity and mortality improvements.³ Its economic value in HFrEF remains to be determined

OBJECTIVE

- To conduct a cost utility analysis of empagliflozin versus standard care in UK HFrEF patients

METHOD

- 3-state Markov Model: Stable heart failure; Hospitalization; Death (See Fig 1)
 - Stable patients transit across different New York Heart Association (NYHA) class
 - Hospitalized patients assumed to return to original NYHA stable class after event
- Model assumptions:
 - Perspective: NHS and Personal Social Service
 - Time Horizon: Lifetime; Cycle length: 1 month; Discounting: 3.5% per annum
 - Intervention: Empagliflozin 10mg daily
 - Comparator: Standard care, defined as guideline-directed medical therapy (ESC 2016)
- Outcome: Total and incremental costs, life-years (LYs), quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratio (ICER), defined as cost/QALY gained
- Model inputs:
 - Hospitalization due to heart failure (HHF) / cardiovascular (CV) mortality: extrapolated from published Kaplan-Meier curves from EMPEROR-Reduced³
 - Adverse events (AE):
 - Rate: EMPEROR-Reduced³; Disutility: targeted literature search
 - Health-state utility: EQ-5D-3L from SHI_T trial⁴
- One-way deterministic sensitivity analyses and probabilistic sensitivity analysis to address parameter uncertainty, scenario analyses to address structural uncertainty

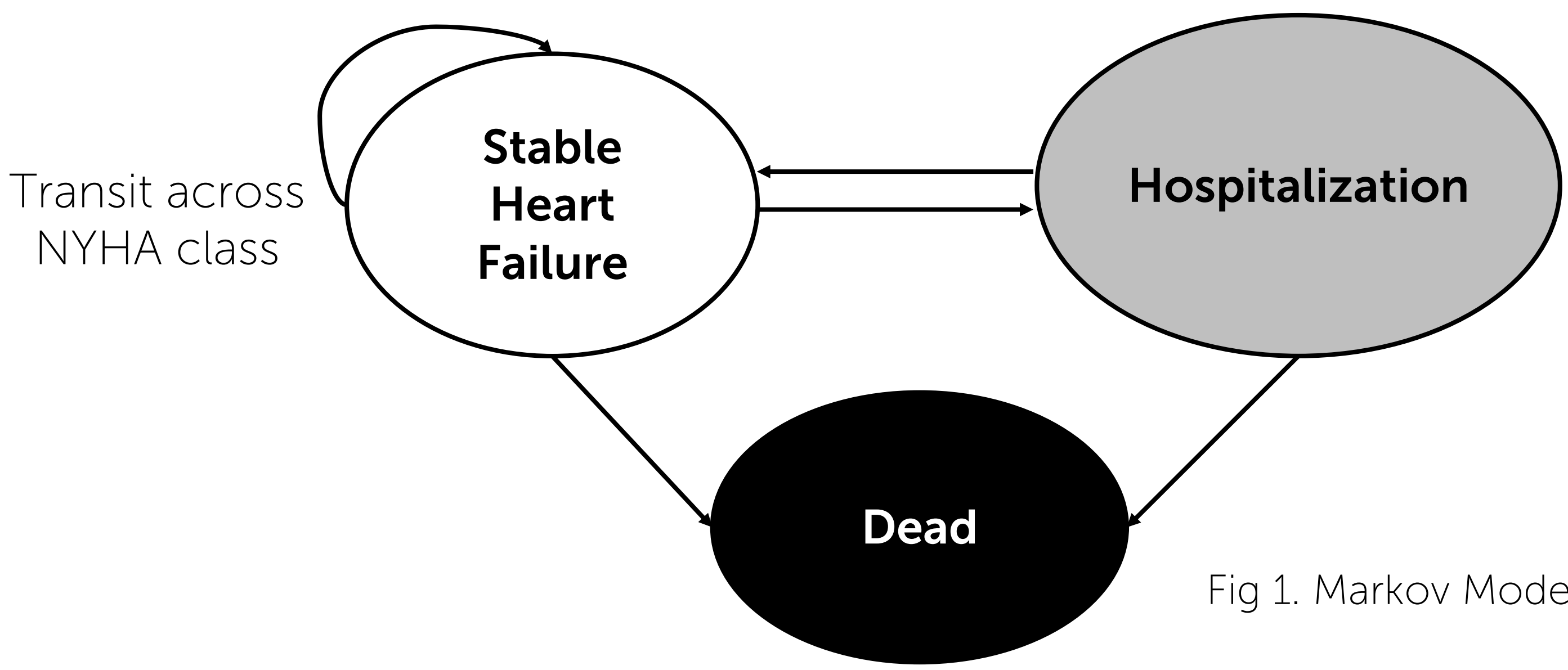


Fig 1. Markov Model

RESULTS

- Add-on empagliflozin prevented 105 HHF events but there were no minimal differences in CV and non-CV mortality
- Add-on empagliflozin was associated with higher costs and a 0.09 QALY gain over standard care, resulting in an ICER of **£26,543**

Table 1. Base-case analysis

Results	Empagliflozin	Usual Care	Incremental
Outcomes			
Hospitalizations due to heart failure	967	1,072	-105
Cardiovascular death	919	920	-1
Non-cardiovascular death	81	80	1
QALYs	3.60	3.51	0.09
Costs			
Medications	£3,703	£1,397	£2,306
Adverse events	£1,523	£1,429	£94
Hospitalizations due to heart failure	£2,469	£2,775	-£306
Healthcare utilization	£5,045	£4,656	£389
Cost-effectiveness			
Total costs	£12,740	£10,257	£2,483
Total QALYs	3.60	3.51	0.09
ICER			£26,543

ONE-WAY SENSITIVITY ANALYSIS

- Baseline utility and cost of empagliflozin were significant drivers for base case results
- In contrast, the model responded less to cost of AEs, AE disutility, and non-CV mortality

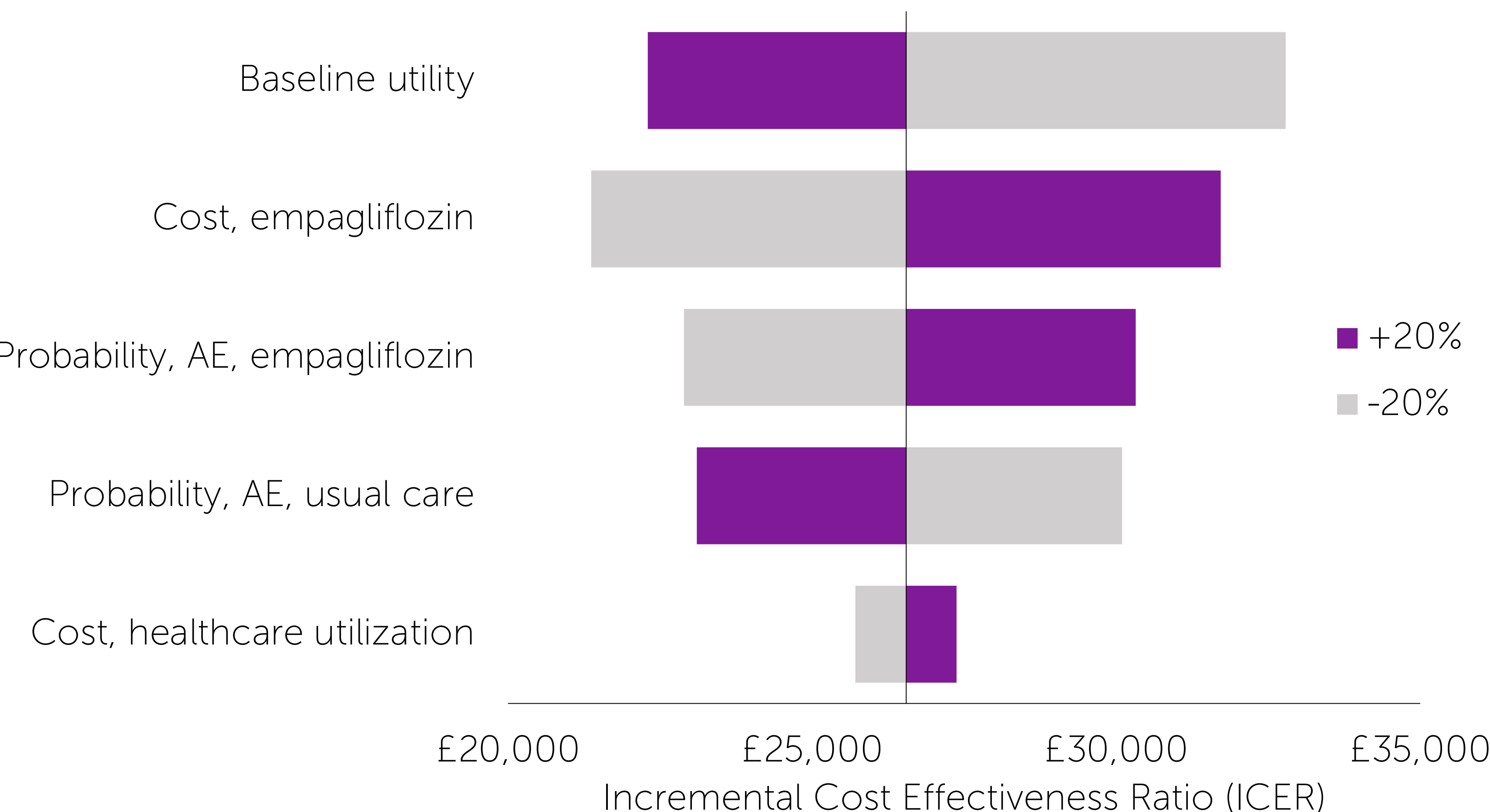


Fig 2. One-way sensitivity analysis. The top 5 significant drivers are depicted here.

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PROBABILISTIC SENSITIVITY ANALYSIS

- Probabilistic sensitivity analysis reveals a wide ellipse; **29.8%** of the 1,000 Monte Carlos simulations had standard care **dominating** add-on empagliflozin

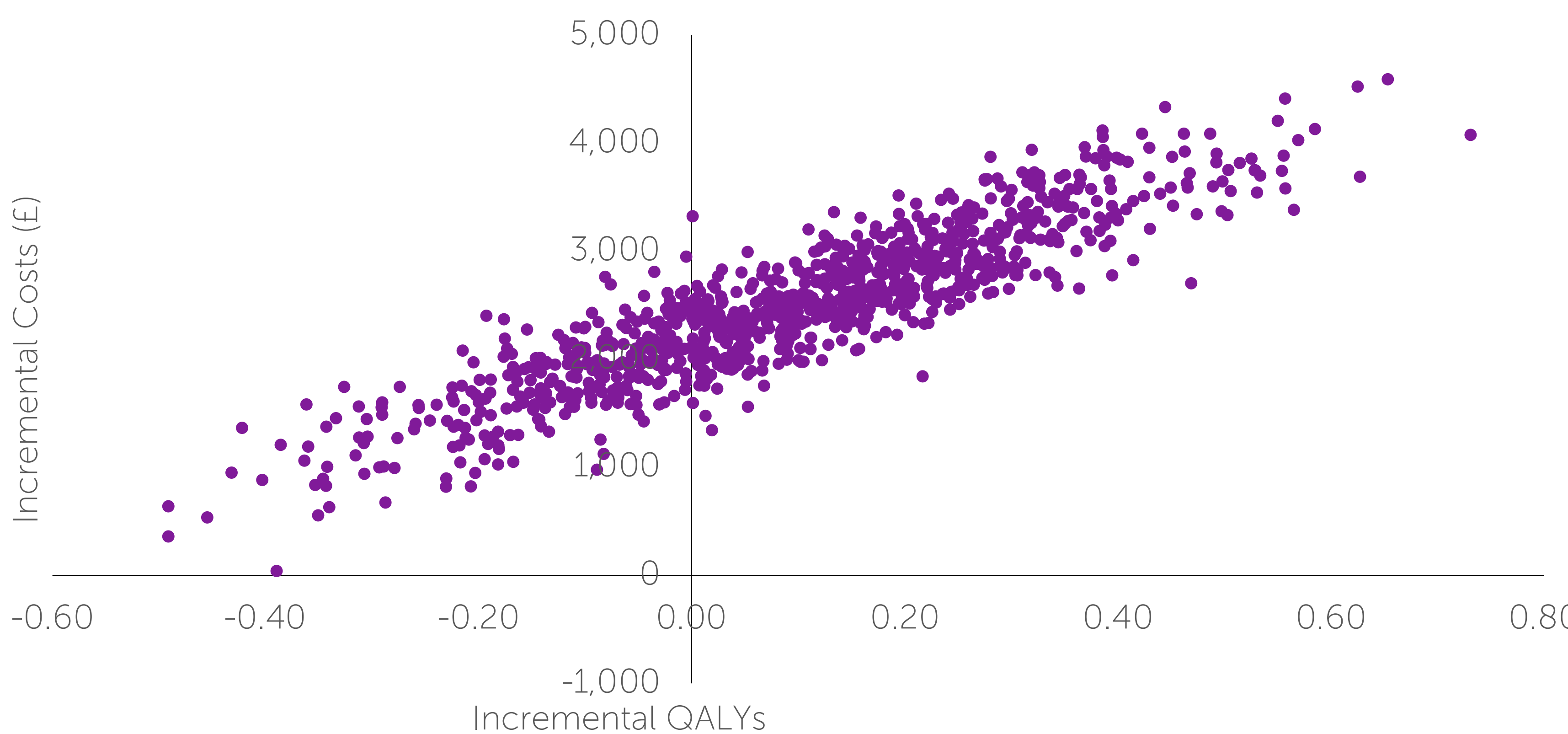


Fig 3. Cost-effectiveness plane

- At a **£30,000** threshold, probability of empagliflozin being cost-effective is **~55%**
- Probability of empagliflozin being cost-effective plateaued at **~65%** at increasing willingness-to-pay (WTP) thresholds

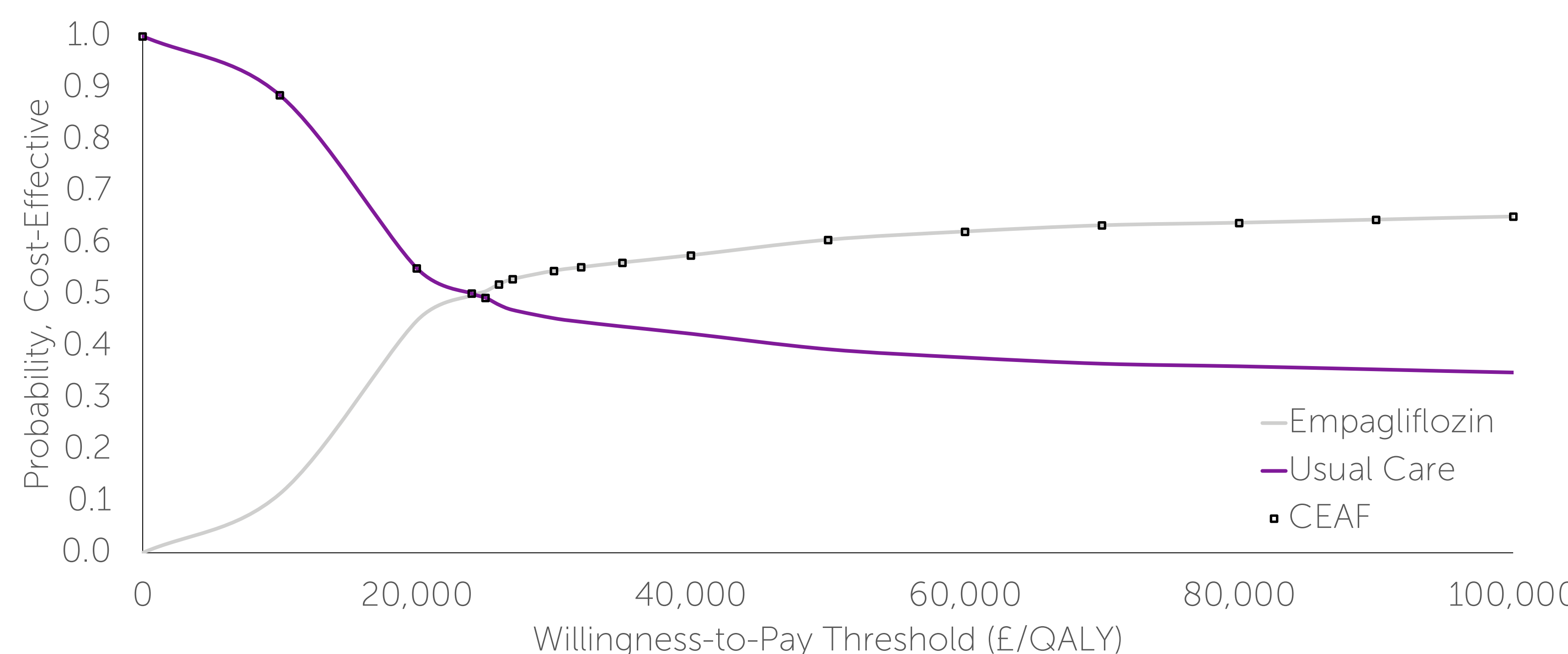


Fig 4. Cost-effectiveness acceptability curve

DISCUSSION AND CONCLUSION

- Add-on empagliflozin may be a cost-effective treatment for HFrEF patients at a £30,000 threshold, but with high uncertainty
- Compared to other analyses on dapagliflozin,^{5,6} another SGLT2i, where it was shown to be cost-effective, divergence in our results and conclusion stem from differences in model design and determination of HHF and CV mortality rates used in model
- More research is warranted before empagliflozin can be recommended, with greater certainty, as a cost-effective treatment against standard care