COST-EFFECTIVENESS AFFORDABILITY CURVES IN EVALUATING CANCER DRUGS IN ENGLAND

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Introduction

> Decision makers are increasingly requiring both cost-effectiveness (CE) and affordability information on new technologies, which has resulted in the use of cost effectiveness thresholds (CET) and budget impact thresholds (BIT).[1-3] In the UK, for example, in addition to the established cost effectiveness threshold (CET) of £20,000-£30,000, the National Institute for Health and Care Excellence (NICE) and National Health Service (NHS) England have established a £20 million BIT since 2017.

> Cost-effectiveness and affordability are typically addressed in separate models using a CE analysis (CEA) and a BI analysis (BIA) respectively, where inconsistent use of methods and data exist. Consideration of both analyses may produce conflicting conclusions as, although a CEA might show the incremental cost-effectiveness ratio (ICER) for a new technology is below a CET, it may still be beyond the affordability of a payer.[4]

> Moreover, both CEA and BIA results are characterised by uncertainty, due to the nature of economic modelling and the assumptions required. Cost-effectiveness acceptability curves (CEAC) have been widely used to summarize CE results under uncertainty. However, this method ignores the budgetary resources necessary to fund the technology.[5]

> Affordability curves (AC) have been used, though less often, to present the probability that an intervention is affordable at different budget levels.[6] However, this ignores whether the technology is deemed cost-effective.

> Cost-effectiveness affordability curves (CEAfC) are a useful tool to simultaneously consider both cost-effectiveness and affordability, combining these results graphically in a single curve and showing the joint probabilities of an intervention being both cost-effective and affordable at varying CETs and BITs.[5]

> CEAfCs have been used in economic evaluations, mainly focusing on preventive interventions in developing countries.[7] To the authors' knowledge, this CEAfCs has not been applied to treatments in developed countries.

> The objective of this study is to apply CEAfCs to the evaluation of cancer drugs in England and understand the added value of this methodology in this setting.

Methods

> A combined CEA and BIA model was built and populated with publicly available data on trastuzumab emtansine (T-DM1) versus lapatinib in combination with capecitabine (LC) as 2nd line treatment for human epidermal growth factor receptor 2 -positive (HER2+), unresectable, locally advanced or metastatic breast cancer (mBC) in England.

> T-DM1 is an antibody-drug conjugate recommended in 2017 as an option for treating HER2+ mBC in adults who previously received trastuzumab and a taxane, separately or in combination.

> A commonly used three-state partitioned survival model consisting of progression-free survival (PFS), progressed disease (PD) and death was built from the NHS and personal social services (PSS) perspective.

> Key inputs for the model were taken from the published NICE single technology appraisal (STAs), with assumptions made on the market share parameters (Table 1).[8-11]

> Probabilistic sensitivity analyses (PSA) were performed and the results are presented using CEACs, ACs and CEAfCs. The CEAfCs at different price levels were explored.

Table 1. Key model inputs

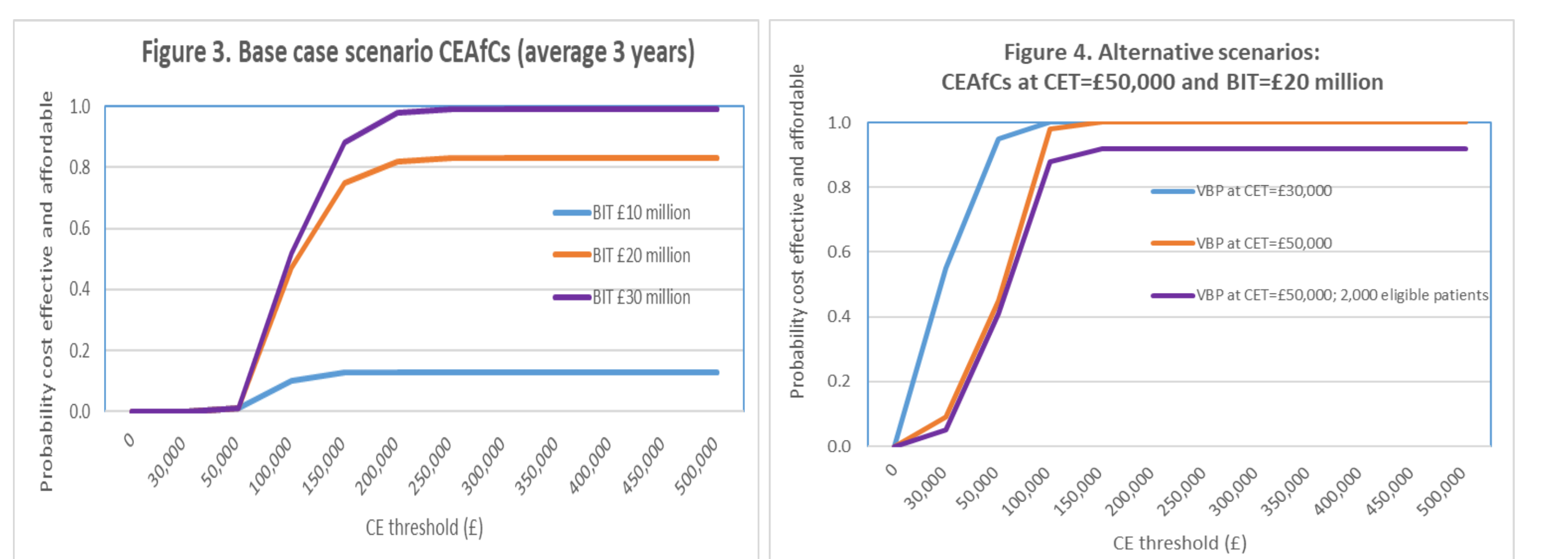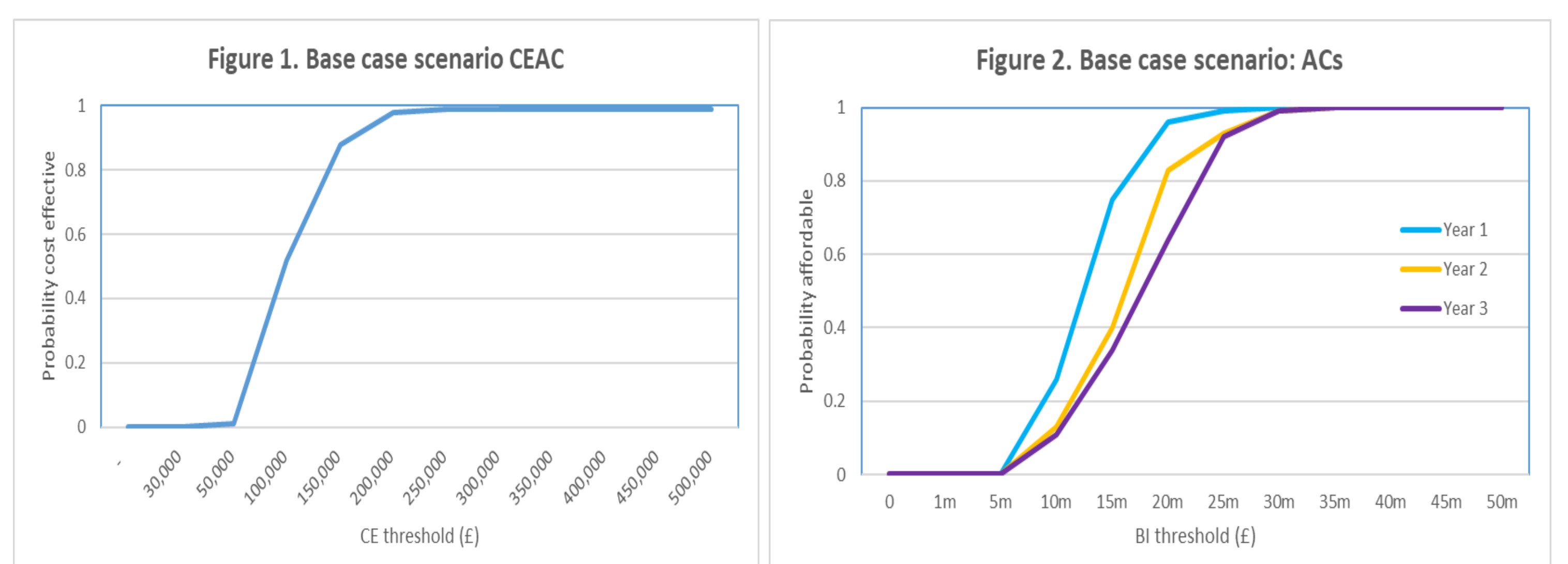|	Parameters	T-DM1	LC	Sources
Efficacy	PFS	KM with Gamma tail	KM with Gamma tail	
	OS	KM with Gamma tail	KM with Gamma tail	
Costs	Drug dose(3-week cycle)	IV 3.6 mg/kg	Orally; L: 1250mg once daily; C: 1000mg/m2 twice daily (days 1-14)	8-11
	List price	1641.01 (100 mg vial); £2625.62 (160 mg vial)	L: £965.16 (250 mg 84 tablet) and £1206.45=(250 mg 105 tablet); C: £30 (150 mg 60 tablet	
	Administration cost	£329 (1st cycle); £362 (subsequent cycles)	£0	
	Pharmacy cost	£18 per cycle	£6 per cycle	
	Follow up costs	£130 every three months		
	PF state cost	£172.67 per month		
	PP state cost	£172.67 per month		
	End of life care cost	£4,032.94		
Utility	Utility_PF state	0.807	0.8	
	Utility_PD state	0.53		
BIA inputs	Number of eligible patients	1200 to 2000		
	T-DM1 uptake	50%		Assumptions

Results

> The results at T-DM1's list price (base case scenario) are presented in Table 2. At this price, T-DM1 is not cost-effective compared with LC, with an ICER of £100,252 per QALY gained.

> Based on T-DM1's list price, expected eligible population and assumed uptake, the annual budget impact is estimated to be over £12 million in year 1 and over £18 million in year 5.

Table 2. Base case results

CEA results (Lifetime of 15 years outcomes and costs; discounted)							BIA results (Annual budget impact; undiscounted)		
	T-DM1		LC		Incremental			Mean	(95% CI)
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Year 1	12,693,831	6,129,138; 21,137,756
Total cost (£)	71,767	57,229; 92,397	28,157	25,203; 31,394	43,609	32,026; 61,002	Year 2	16,254,338	7,998,171; 27,901,092
Effectiveness (QALYs)	1.6911	1.339; 2.0096	1.2561	0.9326; 1.531	0.4350	0.4064; 0.4786	Year 3	17,577,710	8,692,321; 28,136,976
Incremental cost-effectiveness ratio (ICER)					100,252	78,811; 127,466	Year 4	17,542,822	9,171,368; 29,242,641
							Year 5	18,173,236	9,214,873; 30,667,108

> PSA results are presented in Figures 1 to 3. Adopting an end-of-life (EOL) CET of £50,000 per QALY gained and a BIT of £20 million, T-DM1 has 0% probability of being cost-effective and 96% to 64% probability of being affordable, given the annual BI over 3 years. Combining both CEA and BIA results, the CEAfCs show that, at the list price, T-DM1 has 0% probability of being both cost-effective and affordable at a £50,000 CET and a £20 million BIT, over 3 years. The CEAfCs in Figure 3 show how the joint probability varies based on different BITs and CETs.

> CEAfCs under alternative scenarios are presented in Figure 4. If a value-based price (VBP) approach based on the £30,000 CET was adopted, the probability of T-DM1 being both cost-effective and affordable increased from 55% at a £30,000 CET to 85% at a £50,000 CET. If a VBP was set according to a £50,000 CET, yielding a higher price reflecting EOL considerations, the probability of T-DM1 being cost-effective and affordable reduced to 9% at a £30,000 CET and 45% at a £50,000 CET, respectively. At this VBP, if the number of eligible patients increased to 2,000, based on the upper limit of the range explored in the NICE STA, the probability of T-DM1 being both cost-effective and affordable reduced slight to 41%, at a £50,000 CET.

Figure 1. Base case scenario CEAC

Figure 2. Base case scenario: ACs

Figure 3. Base case scenario CEAfCs (average 3 years)

Figure 4. Alternative scenarios: CEAfCs at CET=£50,000 and BIT=£20 million

Discussion and conclusions

> The model found that, whilst T-DM1 was not cost-effective at its list price compared with LC, it was affordable given the BIT. The CEAfC showed T-DM1 had a 0% probability of being simultaneously cost-effective and affordable at this price. If a value-based price approach was adopted, the joint probability of T-DM1 being both cost-effective and affordable greatly increased.

> This study shows that CEAfCs can be used in evaluating innovative treatments such as cancer drugs. CEAfCs can produce an unambiguous single value to estimate the joint probability that an intervention is both cost-effective and affordable at different CETs and BITs under uncertainty.

> CEAfCs can only be used when CEA and BIA are combined in a single probabilistic model. Although there are continued recommendations on keeping BIA separate from CEA on the basis that the two analyses have different complexities and time horizons, support for combining both analyses is growing and many combined models have been published.[12] The advantages of a combined CEA and BIA model include sharing common underlying assumptions, increasing consistency in methods and data, and presenting a more comprehensive economic evaluation of a new technology.

> PSA has become a standard requirement for good quality economic evaluations. Adding probabilistic BIA to a probabilistic CEA is not complex, while providing added value. Whenever there might be conflicting results from the integrated analyses shown as a low joint probability of cost-effectiveness and affordability, the combined analysis can be used to explore the factors affecting the results and identify the ranges of changes in pricing and other inputs.

> BITs are increasingly used by HTAs and payers to trigger discussions and negotiations with manufacturers at the appraisal stage.[2] Conducting a comprehensive assessment of the uncertainty around a treatment's affordability early in the process would allow manufacturers to play a more proactive role in such negotiations and achieve faster market access.

> As increasingly stricter CETs and BITs are applied globally, CEAfCs can inform decision-makers on the probability of an intervention being both cost-effective and affordable. Furthermore, increased use of CEAfCs as a complementary analysis to CEACs and ACs would provide a clearer understanding of the uncertainty associated with CEAs and BIAs.

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