BETTER OFF DEAD: MITIGATING FOR SITUATIONS WHERE IMPROVING SURVIVAL ISN'T COST-EFFECTIVE

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BACKGROUND

- Long-term therapies for progressive, fatal diseases with no active treatment face significant barriers for cost-effectiveness due to incremental costs of both drug and healthcare resource over the model time horizon.
- In extreme cases, a new therapy that substantially increases survival would not be cost-effective even if it were provided free of charge.

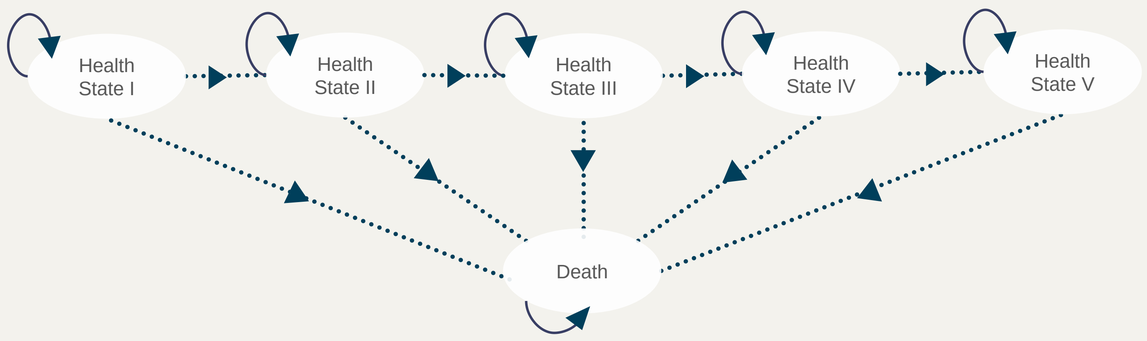
OBJECTIVE(S)

The objective was to explore potential policies for chronic treatments that might reduce the negative impact of improving survival on cost-effectiveness.

METHODS

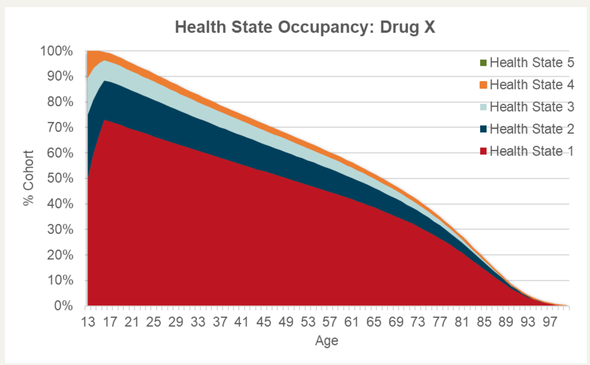
- A simple 6-state model (including death) was adapted to model the cost-effectiveness of a new treatment, Drug X, vs. current standard of care (SoC) for a putative progressive and fatal disease (**Figure 1**).
- The model considered a UK National Health Service perspective and was based on National Institute for Health and Care Excellence (NICE) methods guidelines[1].

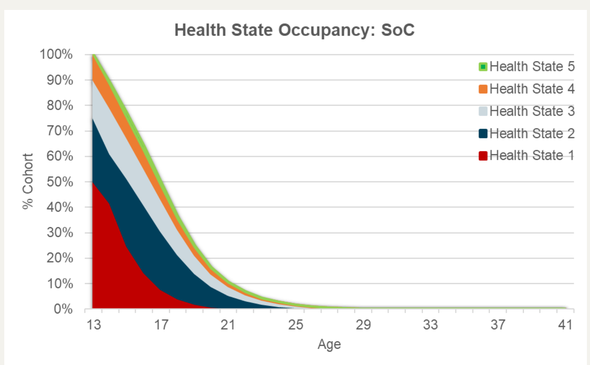
Figure 1 Model diagram



- The disease was assumed to have increasing mortality and disease management costs and decreasing utility by health state (**Table 1**).
- It was assumed that patients initiating Drug X could have existing comorbidities, thus patients entered the model in all health states other than Health State V (**Table 1**).
- Drug X would be initiated in adolescence and continued into adulthood, with dosing being weight-based.
- Drug X was assumed to initially improve health state occupancy followed by stabilisation when administered chronically (**Figure 2**).
- In addition to preventing progression, Drug X was assumed to increase 'within-state' survival (i.e. lower standardised mortality ratios) due to decreased risk of fatal acute events. Overall, Drug X was predicted to increase mean survival by 17.5 discounted life years (**Figure 3**).
- Incremental cost effectiveness ratio (ICER)-reducing scenarios were explored including population restrictions, quality-adjusted life year (QALY) and life years gained (LYG) weights, differential discounting, and reducing costs of incremental survival.

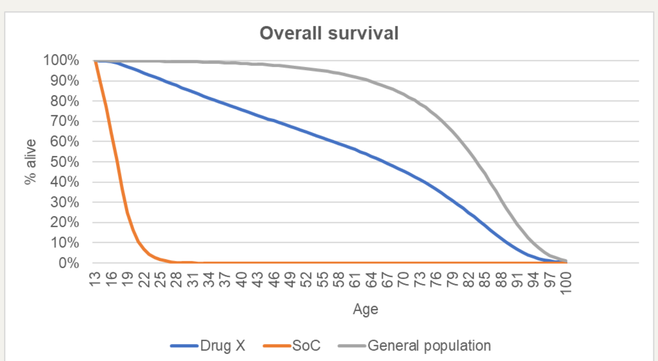
Figure 2 Health State Occupancy Charts – Drug X & SoC





Key: SoC, standard of care

Figure 3 Overall Survival Chart – Product X, SoC and General Population



Key: SoC, standard of care

Table 1 Key Model Inputs by Health State

	Health State I		Health State II		Health State III		Health State IV		Health State V	
Baseline health state distribution	50%		25%		15%		10%		0%	
Health State Utilities	0.9		0.6		0.3		-0.05		-0.1	
Health State Costs	£6,000		£6,000		£9,000		£12,000		£26,000	
	Drug X	SoC	Drug X	SoC	Drug X	SoC	Drug X	SoC	Drug X	SoC
Standardised Mortality Ratios	1.1	900	1.3	1000	1.8	1500	2.0	2000	8	6500

Key: SoC, standard of care

RESULTS

- The ICER was £505,681/QALY with drug costs included and £33,080/QALY assuming no drug costs (**Table 2**). Thus, treatment was not cost-effective at NICE's upper standard threshold of £30,000/QALY, even when provided free.
- The most impactful scenario was applying an uncapped QALY weight equal to 10% of the undiscounted incremental LYG, which reduced the ICER to £114,733 per QALY (**Table 2,** Scenario 1).
- Another scenario applied drug costs only over the anticipated LYs of SoC, in order to exclude costs incurred due to excess survival in the treatment arm. This scenario resulted in a similar reduction in the ICER to £120,620 per QALY. (**Table 2,** Scenario 2).
- Other scenarios reduced the ICER to between £221,214 and £493,670 per QALY (**Table 2**).

Table 2 Base Case and Scenarios

#	Scenario	Inc. Costs (Drug X)	Inc. QALYs (Drug X)	ICER	Change from base case ICER
	Base case	**£7,030,512**	**13.903**	**£505,681**	**N/A**
	Drug provided free	**£459,919**	**13.903**	**£33,080**	**-93%**
1	Uncapped QALY weight equal to 10% of undiscounted incremental LYG	£7,030,512	13.903	£114,733	-77%
2	Exclude drug costs associated with excess survival in Drug X arm during each cycle	£1,676,985	13.903	£120,620	-76%
3	Remove discounting of QALYs after 10 years (in both arms)	£7,030,512	31.782	£221,214	-56%
4	Discount of 50% on Drug X after 10 years (e.g. due to generic/biosimilar competition)	£4,997,468	13.903	£359,451	-29%
5	Remove drug associated costs in Drug X arm once all SoC patients are dead	£5,104,583	13.903	£367,155	-27%
6	Only Health State I patients treated at baseline	£7,028,314	15.661	£448,781	-11%
7	Exclude HRU costs associated with excess survival in Drug X arm during each cycle	£6,559,452	13.903	£471,799	-7%
8	Annual discount rate of 1.5% applied to QALYs (discounting of costs remains at 3.5%)	£7,030,512	14.405	£488,044	-3%
9	Remove incremental HRU costs once all SoC patients dead	£6,863,526	13.903	£493,670	-2%

Key: HRU, healthcare resource use; ICER, incremental cost effectiveness ratio; Inc. incremental; LYG, life years gained; N/A, not-applicable; QALYs, quality-adjusted life years, SoC, standard of care

DISCUSSION

- Currently, decision modifiers to reduce the impact of additional costs of increased LYG are rare in health technology assessment, and in some markets LYG are *de facto* penalised.
- For example, in their recent methods update the Netherlands now require inclusion of indirect costs in LYs and have reduced their cost discount rate while maintaining the existing QALY discount rate[2]. This makes cost-effectiveness less achievable with higher LYG.
- NICE's severity modifier rewards low QALYs on SoC, not incremental QALYs or LYG on treatment (in contrast with NICE's ultra-orphan QALY modifier[1]).
- Consequently, in many markets it is common and necessary to restrict access to more cost-effective subgroups of patients to increase QALYs and reduce ICERs.

CONCLUSIONS

- Several policy options were identified that improved cost-effectiveness without restricting access for such patients.
- Applying uncapped QALY modifiers based on LYG would help treatments which improve survival to be cost-effective more effectively than capped modifiers based on QALY gain or cost discounting approaches.

REFERENCES

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