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Is less more? Aggregating health states in state transition models

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Background

- State transition models (STMs) are structured around a set of mutually exclusive and collectively exhaustive health states capturing the key features of the disease and treatment [1,2].
- Guidelines recommend using the simplest type of model that remains consistent with the underlying decision problem and theory of disease [3,4].
- Determining the validity of simplified model structures is crucial. If they are accurate, simpler models can enhance decision-making through improved transparency, and easier interpretation [5,6].

Objectives

- To investigate the impact of aggregating health states on modeling outcomes, using an example in coronary heart disease (CHD).

Methods

Model design

- Three STMs with 4, 6, and 10 health states were constructed based on published CHD model structures [7,8] (Figure 1).
- Simpler models grouped different types of stroke and heart failure. The event states were tunnel states.
- The models were programmed in R (code available on Github) with analyses were run over a 50 using annual cycles.

Stroke and heart failure rates

- The STMs used a synthetic dataset of 10,000 UK adult patients reflecting primary care data on heart attacks and strokes over a 10-year follow-up period, representing 'standard of care' [9].
- The annual transition probabilities are presented in Table 1 and broadly align to those observed in CHD models [7,10].
- A hypothetical treatment effect (Table 2) was calculated from pseudo trial data and was applied to baseline transition probabilities.

Probability	10 health states	6 health states	4 health states
IS	0.48%	0.57%	0.68%
HS	0.09%		
Hosp. HF	0.02%	0.11%	
Non-hosp. HF	0.08%		

Table 1: Transition probabilities

Relative risk	10 health states	6 health states	4 health states
IS	0.167	0.175	0.200
HS	0.179		
Hosp. HF	0.500	0.250	
Non-hosp. HF	0.206		

Table 2: Hypothetical treatment effects

Mortality rates

- Standardized mortality ratios (SMRs), obtained from NICE hypertension guidelines were applied to stroke and HF states [8].
- In all three STMs, post-event states used a simplified 2.00% mortality risk regardless of age.
- For health states that were grouped, SMRs were calculated using weighted averages. For example, in the 6-health state model:

$$SMR_{stroke} = P_{IS}SMR_{IS} + P_{HS}SMR_{HS}$$

- where P_{IS} is the probability that a stroke is an IS and P_{HS} is the probability that a stroke is a HS.

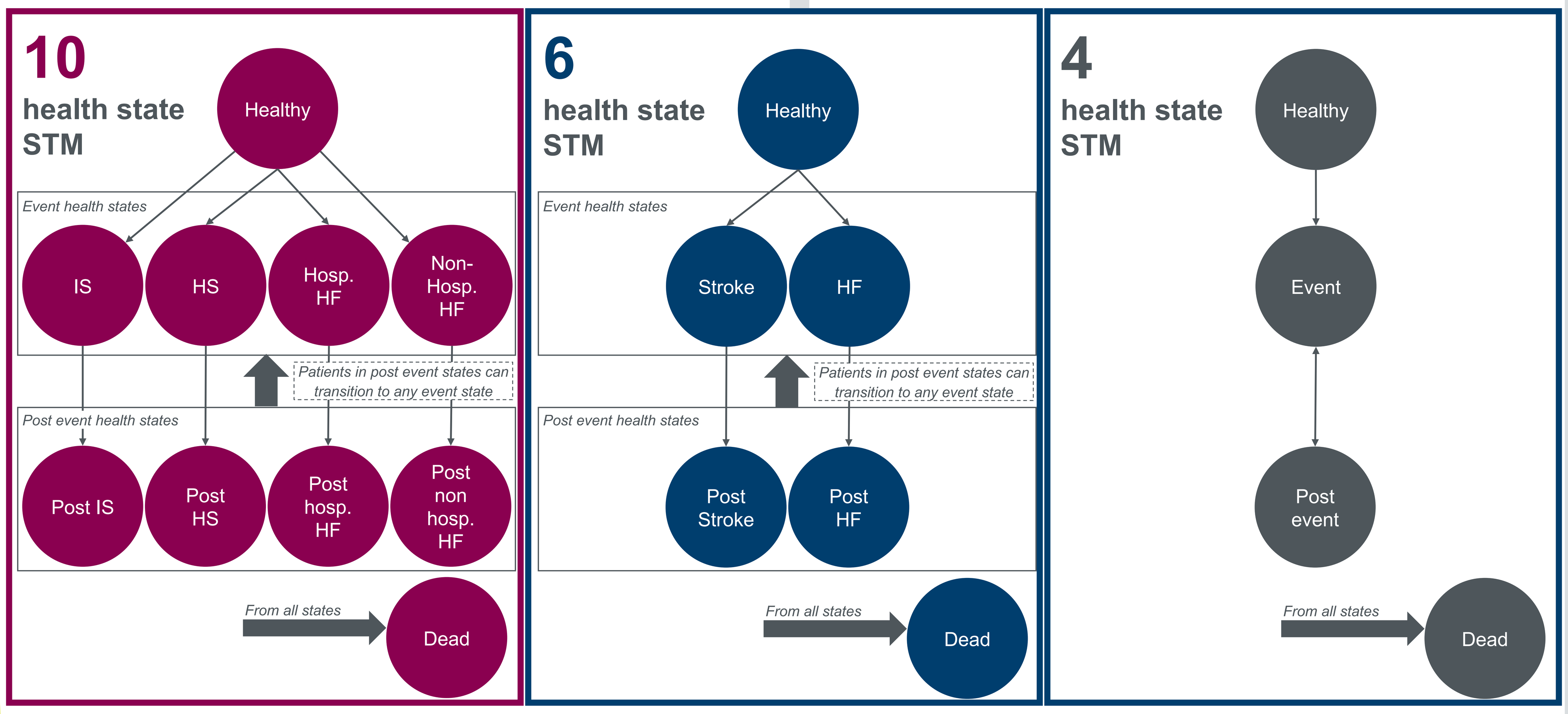

Figure 1: Model structures for the STMs with 10, 6 and 4 health states

Costs and utility values

- One-off event costs, annual post-event costs, and health state utility values used plausible ranges based on the NICE guidelines for hypertension [8]. Treatment was assumed to be associated with a one-off cost of £10,000.
- The 6 and 4 health state STMs derived costs and utility multipliers using the same weighted average approach as for mortality SMRs.
- Healthy states were assigned perfect health (utility = 1), with no associated costs.

Parameter	IS	HS	Hosp. HF	Non-Hosp HF
Event cost	£16,746	£23,076	£4,641	£2,719
Post event cost	£587	£1,749	£706	£203
Event UM	0.756	0.628	0.770	0.683
Post event UM	0.816	0.628	0.924	0.820

Table 3: Cost and utility values used in all three STMs

Results

Base case analysis

- Undiscounted incremental costs and QALYs were very similar across all three models (Table 4).
- In the base case analysis, the difference between the highest ICER (£7,898.99; 4-state STM) and the lowest ICER (£7,549.33; 10-state STM) was £388.65 per QALY.

	Costs	QALYs	ICER
10 health state STM			
Intervention	£11,105.98	31.75	-
Comparator	£5,950.13	31.07	-
Incremental	£5,155.85	0.68	£7,549.33
6 health state STM			
Intervention	£11,111.73	31.76	-
Comparator	£5,932.81	31.08	-
Incremental	£5,152.37	0.68	£7,510.34
4 health state STM			
Intervention	£7,510.34	31.74	-
Comparator	£5,957.34	31.07	-
Incremental	£5,284.73	0.67	£7,898.99

Table 4: Outcomes obtained in the three STMs

One-way sensitivity analysis

- To evaluate their impact on outcomes, all individual inputs were varied by an arbitrary range of ±20% (one parameter at a time; in the three STMs simultaneously).
- In this one-way sensitivity analysis, the difference between the highest and the lower ICER observed in the three models ranged from a minimum of £205.36 to a maximum of £672.46 per QALY (compared to £388.65 per QALY for the base case).
- This difference was most sensitive to the post-ischaemic stroke utility multiplier and the number of events in the hypothetical treatment arm used to calculate the relative risks in Table 2.

Conclusions

- This study suggests that aggregating health states in an STM may not necessarily lead to meaningful impacts in terms of model outcomes.
- In any cost-effectiveness model, a balance must be struck between simplicity / transparency and ensuring that the model accurately reflects relevant stages and events associated with the disease.
- Having a good understanding of underlying data might be more important than developing more disaggregated or complex model structures.
- There are some obvious limitations to our analysis:
  - The synthetic dataset provided us with perfect clinical information, allowing data to be easily aggregated for health states that were grouped in the simpler STMs.
  - Clinicians would argue that, because they have different etiology and consequences, IS and HS events should not be lumped together. It would be easier to find inputs associated with each event separately, than for both stroke types combined.
  - Even the 10-state STM is still a relatively simple model with simplified inputs (for costs, utilities, mortality and treatment effect), non-time varying transition probabilities and health states not accounting for stroke severity.
- Further research on this topic may look to increase the complexity of the most granular model, evaluate models in other disease areas, and/or look at using real-world rather than synthetic data.

ABBREVIATIONS

IS; ischaemic stroke, HS; haemorrhagic stroke, Hosp; hospitalized, Non hosp.; non-hospitalised, HF; heart failure, QALY; quality-adjusted life year, ICER; incremental cost-effectiveness ratio, UM; utility multiplier, STM; state transition model

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GITHUB LINK

https://github.com/JettingerParexel/CHD_model