

Development of a Novel Economic Modelling Approach for Asthma



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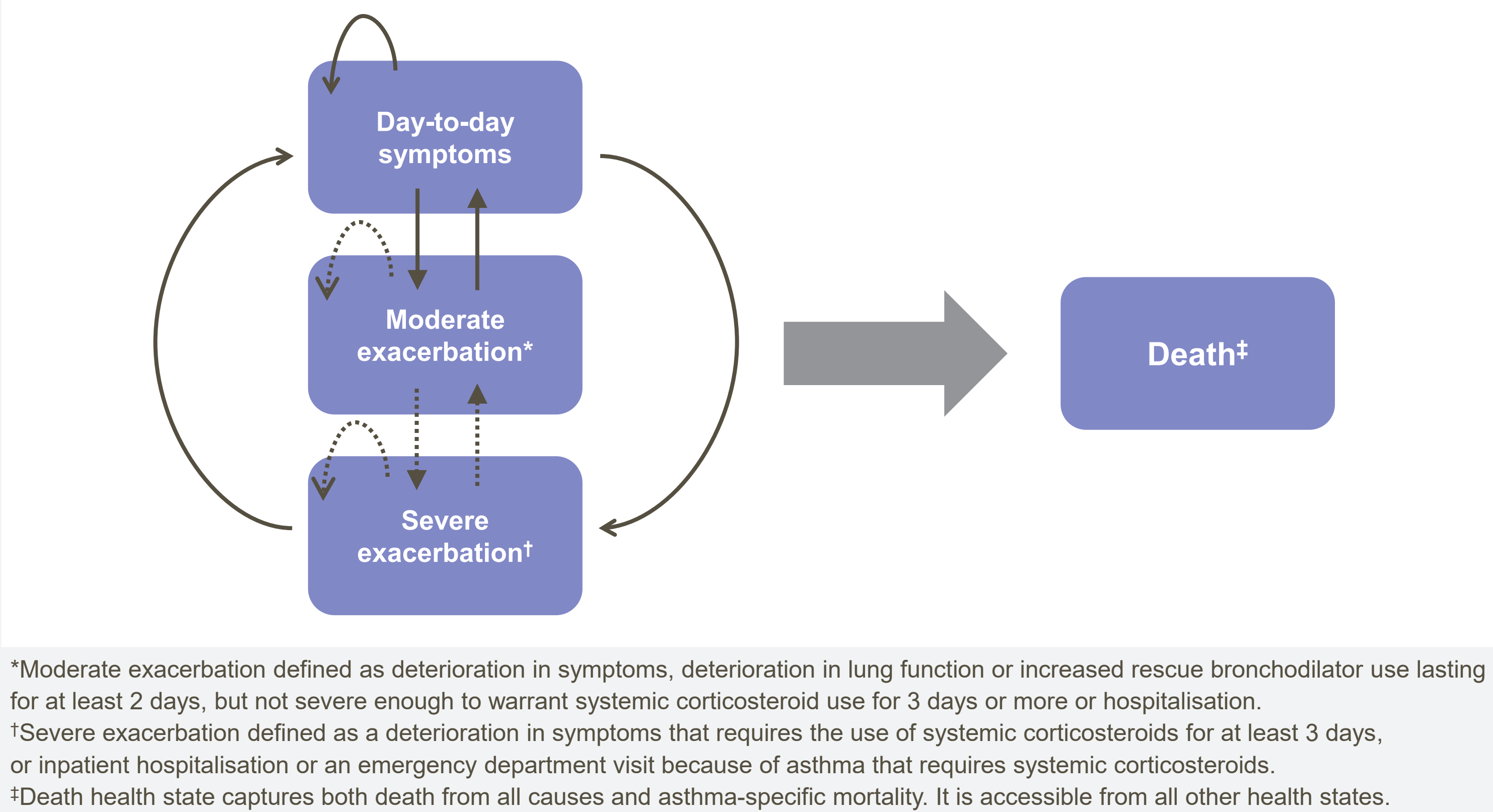
Objectives

- Asthma is a common respiratory disease affecting approximately 300 million people worldwide. The aim of asthma management is to achieve asthma control, as uncontrolled asthma is associated with increased risk of exacerbation, reduced health-related quality of life (HRQoL) and greater healthcare resource utilisation (HRU).^{1, 2}
- The cornerstone of asthma maintenance therapy is inhaled corticosteroid (ICS)/long-acting β_2 -agonist (LABA) combination therapy, with treatment guidelines recommending a stepwise approach to achieve asthma control.¹
- Assessment tools such as the Asthma Control Questionnaire (ACQ) are used to quantitatively assess patients' level of asthma control and guide treatment decisions.³
- A positive relationship between increased ACQ score and risk of disease exacerbation has been demonstrated, with poorly-controlled asthma requiring a greater demand on HRU and impacting on work productivity.²
- Here, we present a novel economic modelling approach for asthma based on ACQ score trajectories that captures treatment effects observed in clinical trial data which may not be captured in previous models. To demonstrate the use of this new approach, we conducted an analysis comparing triple ICS/LABA plus long-acting muscarinic antagonist (LAMA) therapy versus dual ICS/LABA therapy.

Methods

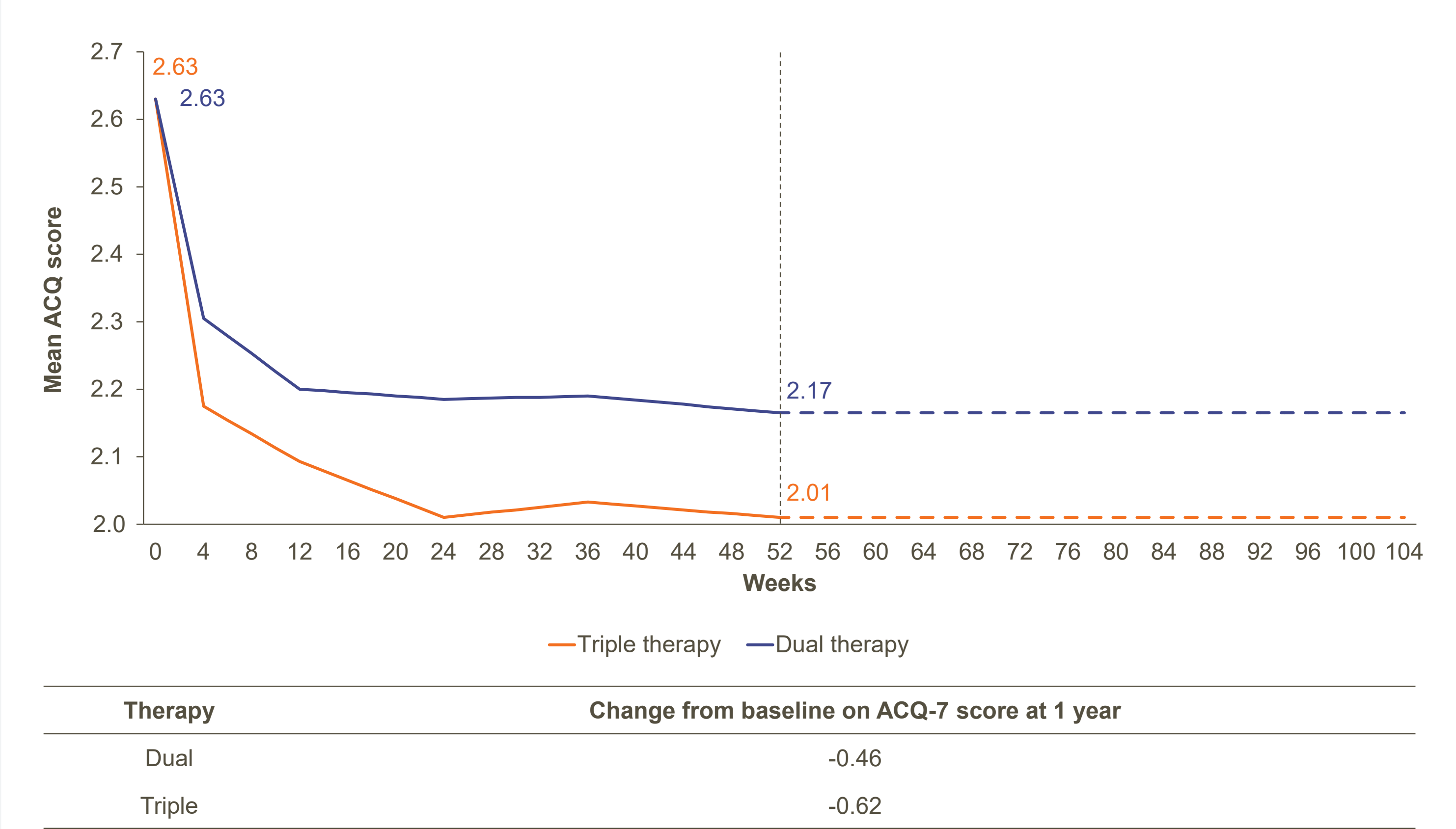
- A targeted literature review of published cost-effectiveness models and health technology assessments for asthma treatments was conducted to identify approaches to modelling the relationships between asthma control, exacerbation risk and HRQoL, including the impact of treatment on these relationships.
- To account for changes in asthma control that were not captured by discrete states in published models, a hybrid approach was developed. The approach used a day-to-day symptoms health state with embedded treatment-specific ACQ score trajectories to track patient's asthma control, with separate health states for moderate and severe exacerbations and death (**Figure 1**). The probability of exacerbation risk, HRU and HRQoL (utility) was linked to ACQ score via risk equations.

Figure 1. Model structure



- To explore the validity of the modelling approach for use in economic evaluations of asthma maintenance therapies, the model was populated with published clinical trial data comparing triple versus dual therapies (**Figure 2**).⁴
- The relationships between differences in ACQ scores and patients' 2-week exacerbation risks and utility values were estimated from the published literature (**Table 1**).^{5, 6}
- Moderate and severe exacerbation outcomes and discounted quality-adjusted life-years (QALYs) were estimated over 1- and 5-year time horizons for the base-case ACQ-7 extrapolation assumption and a range of alternative ACQ extrapolation scenarios.

Figure 2. Mean ACQ-7 score trajectories*



*The ACQ trajectories were generated by pooling data from two clinical trials reported in Kerstjens, et al, 2012.⁴ Changes from baseline at 48 weeks in the trials were assumed to apply at 1 year in the model. Dashed lines indicate extrapolated data.

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Table 1. Relationships between ACQ score and outcomes

Exacerbation risks (2-week transition probabilities from day-to-day symptoms)	At baseline* (ACQ-7 = 2.63)	Increase per 1 point ACQ increase ⁵
Moderate exacerbations	0.090	+50%
Severe exacerbations	0.030	+50%
Utility values (EQ-5D [United Kingdom])	At baseline* (ACQ-7 = 2.63)	Increase per 1 point ACQ decrease ⁵
Day-to-day symptoms ^{6†}	0.758	+0.066
Moderate exacerbations ⁷	0.649	n/a
Severe exacerbations ⁸	0.533	n/a

*Derived from clinical trial outcomes⁴ and a published relationship with ACQ-7⁵ with an assumed ratio of 3:1 between moderate and severe exacerbations. [†]Linear relationship between utility values and ACQ-5 estimated from a published study⁶ and assumed to apply for ACQ-7 scores from the clinical trials.⁴

Results

- The economic models identified in the literature typically utilised Markov-based approaches with discrete asthma control health states with state-specific exacerbation risks and utility values.^{7, 9, 10}
- However, these models did not capture ACQ improvements within states that may be considered clinically significant. Required data is not always publicly available to estimate treatment-specific Markov transition probabilities. They also did not appear to test uncertainty in extrapolating clinical trial outcomes over longer time horizons.^{7, 9, 10}
- Predicted number of moderate and severe exacerbations and discounted QALYs over 1-year and 5-year time horizons in patients receiving triple versus dual therapy with the novel ACQ-7 trajectory-based modelling approach are shown in **Table 2**. Clinical trial outcomes per-patient year are included for comparison.
- The model-generated exacerbation estimates at 1 year were lower than the estimates reported in the clinical trial publication. This difference stems from the structural modelling assumption that patients return to the day-to-day symptoms state in the cycle following an exacerbation. Future research on estimating re-exacerbation risks may inform the validity of this assumption and improve the accuracy of model outcomes.
- The model design allows for exploration of the impact on outcomes of alternative assumptions about the trajectory of ACQ scores after 1 year. Differences from the base-case analysis in incremental exacerbation and QALY outcomes between triple and dual therapy are shown in **Table 3**. These scenarios demonstrate the ability of the model to capture the impact of potential changes in asthma control status over time that might not be easily modelled by discrete asthma control states.

Table 2. Validation of model

Scenario	Total exacerbations*	Severe exacerbations	Moderate exacerbations	QALY
Clinical trial outcomes; ⁴ number per-patient year (95% confidence interval)				
Dual therapy	2.835 (2.511-3.200)	0.663 (0.573-0.768)	2.172 (NA)	NA
Triple therapy	2.145 (1.866-2.466)	0.530 (0.450-0.625)	1.615 (NA)	NA
Model prediction; time horizon 1 year				
Dual therapy	2.233	0.558	1.675	0.755
Triple therapy	1.816	0.454	1.362	0.766
Model prediction; time horizon 5 years				
Dual therapy	11.499	2.875	8.624	3.503
Triple therapy	9.304	2.326	6.978	3.561

*Defined as episodes of asthma worsening in Kerstjens et al, 2012⁴; NA, not available

Table 3. ACQ extrapolation scenarios*

Scenario; model prediction; time horizon 5 years	Severe exacerbations	Moderate exacerbations	QALY
Base case: ACQ trajectories remain flat after 1 year			
Triple therapy vs dual therapy	-0.549	-1.646	+0.058
Scenario 1: Triple and dual therapies revert to baseline ACQ after 5 years (i.e., triple therapy changes more rapidly) Rate of change for dual therapy = 0.0045 per 2 weeks; rate of change for triple therapy = 0.0060 per 2 weeks			
Triple therapy vs dual therapy	-0.525	-1.574	+0.040
Scenario 2: Dual therapy reverts to baseline ACQ after 5 years; triple therapy changes at the same rate Rate of change for both triple and dual therapies = 0.0045 per 2 weeks			
Triple therapy vs dual therapy	-0.583	-1.750	+0.058
Scenario 3: Dual therapy reverts to baseline ACQ after 5 years; triple therapy changes more slowly Rate of change for dual therapy = 0.0045 per 2 weeks; rate of change for triple therapy = 0.0030			
Triple therapy vs dual therapy	-0.640	-1.921	+0.075

*All outcomes are incremental.

Conclusions

- This novel hybrid modelling approach for asthma based on ACQ trajectories with Markov-based exacerbation health states allows a more detailed exploration of treatment effect over time and provides additional flexibility compared with previous economic models for asthma.
- This approach shows promise for use in economic evaluations and health technology assessments of asthma maintenance therapies, including emerging triple therapies.