EE583

Model Structure Variability in NICE HTAs: Evidence From Asthma and TMA Appraisals to Support the Need for Disease-Specific Reference Models

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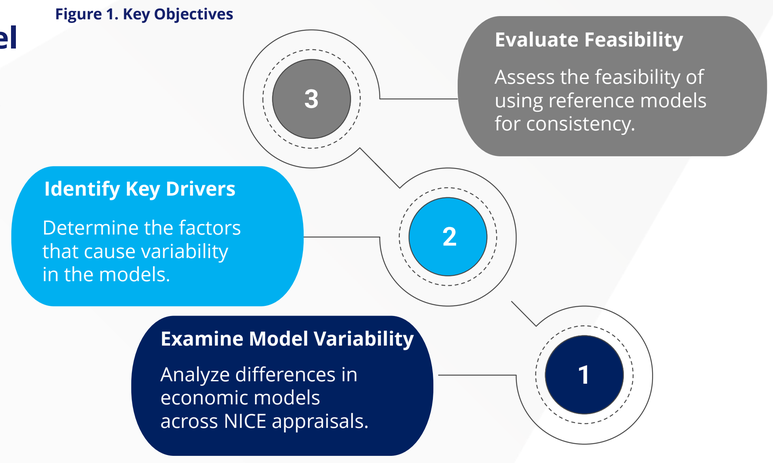
BACKGROUND

- **Economic models are central to HTAs**, guiding decisions on cost-effectiveness and reimbursement.
- **Model structure variability across appraisals** reduces comparability and decision efficiency.
- **Variability** stems majorly from **evolving evidence**, **disease and treatment pathway**, and **differing methodological assumptions**.
- NICE appraisals provide an informative dataset for understanding how **structural variability** affects consistency across diseases areas.
- This study **examines structural variability in NICE HTAs** for chronic **asthma** and rare thrombotic microangiopathies (TMAs), including Atypical Hemolytic Uremic Syndrome (aHUS) and Acquired Thrombotic Thrombocytopenic Purpura (aTTP).

OBJECTIVES

- **Examine economic model structure variability** across NICE appraisals for asthma and TMAs.
- **Identify key drivers** of model variability.
- **Evaluate** whether such variation supports developing **reference models** for consistency.

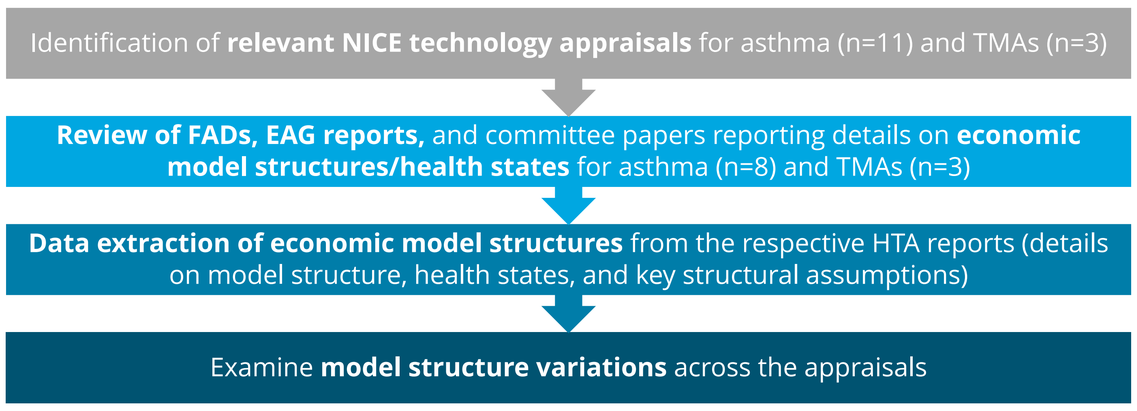
Figure 1. Key Objectives



METHODOLOGY

- **Targeted review:**
  - Conducted using publicly available NICE Single Technology Appraisals and Highly Specialized Technologies for asthma and TMAs.
- **Inclusion criteria:**
  - Final Appraisal Determinations (FADs), Evidence Assessment Group (EAG) Reports, and Committee papers were reviewed.
  - Reports providing sufficient detail on model structure, reasons for revision through the appraisal process etc. were considered.
- **Data extraction:**
  - Model structure, health states, key structural model assumptions, time horizon, comparators etc. were documented.
- **Identification of key drivers of model variability:**
  - Rationale for key structural variations (e.g., new trial data, methodological or clinical guideline updates, expert opinion) were identified.

Figure 2. Flowchart of approach



RESULTS

Asthma (n=8)

- **88% (7 of 8)** employed distinct model structures.
- Early evaluations (e.g., inhaled corticosteroids) used simpler **Markov or decision-tree** models.
- Later **biologic appraisals** adopted **more complex Markov structures**, with explicit modelling of **treatment response, asthma control,** and **exacerbation** events.
- **Structural heterogeneity** led to **limited cross-appraisal consistency**, even within similar intervention classes.

Figure 3. Proportion of asthma appraisals having

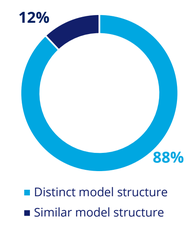
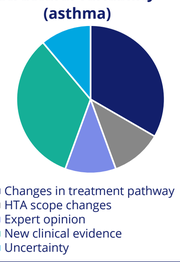


Figure 4. Key drivers of structural variability (asthma)



TMAs (n=3)

- All three models used **distinct structural approaches** with differences in:
  - handling of **acute vs. chronic** phases,
  - inclusion of **plasma exchange**, and
  - representation of **relapse events.**
- Model design was often informed by limited clinical data or expert opinion, reflecting **uncertainty** typical of rare diseases.
- Model reuse was rare, even when disease context remained similar.

Figure 5. Proportion of TMA appraisals having

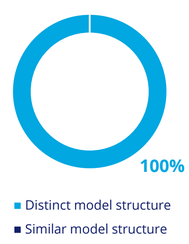


Figure 6. Key drivers of structural variability (TMAs)

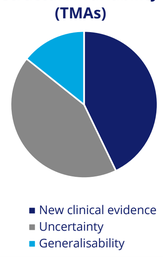


Table 1. Summary of model structures based on the NICE technology appraisals reviewed

Appraisal	Publication date	Intervention	Comparator	Model structure	Health states
Chronic: Asthma					
TA131[1]	Nov 2007	ICS/LABA	ICS and ICS/LABA compared with each other	5 state Markov	Controlled asthma, GP/self-managed exacerbation, hospital exacerbation, treatment failure, step down[3]
TA138[2]	Dec 2008				
TA278[4]	Apr 2013	Add-on omalizumab	Standard of care	5 state Markov	Day-to-day symptoms; omalizumab responders, day-to-day symptoms; Standard therapy, clinically significant non-severe exacerbations, clinically significant severe exacerbations, death: all-cause and asthma related
TA431[5]	Jan 2017	Add-on mepolizumab	Standard of care	5 state Markov	Day-to-day symptoms; on treatment, day-to-day symptoms; responders, day-to-day symptoms; non-responders or standard of care, exacerbations: oral corticosteroid (OCS) burst, emergency department (ED) visit, hospitalization, Death: all-cause and asthma related
TA479[6]	Apr 2017	Add-on reslizumab	Standard of care	5 state Markov	Uncontrolled asthma, controlled asthma, moderate exacerbation and severe exacerbation, death: asthma/all-cause mortality
TA565[7]	Jun 2019	Add-on benralizumab	Standard of care	4 state Markov	Uncontrolled asthma, controlled asthma, exacerbations: OCS burst, ED, hospitalization, death: all-cause and asthma related
TA751[8]	Dec 2021	Add-on dupilumab	Add-on: benralizumab, reslizumab, mepolizumab, omalizumab, and standard of care alone	5 state Markov	Uncontrolled asthma, controlled asthma, moderate exacerbation, severe exacerbation, death: asthma/all-cause mortality
TA880[9]	Apr 2023	Add-on tezepelumab	Add-on: benralizumab, mepolizumab, omalizumab, dupilumab and standard of care alone	5 state Markov	Controlled asthma, uncontrolled asthma, exacerbation, previously controlled asthma, exacerbation, previously uncontrolled asthma, death: asthma/all-cause mortality
Rare: TMAs (aHUS and aTTP)					
HST1[10]	Jan 2015	Eculizumab	Standard of care	5 state Markov	3 health states based on levels of kidney function, temporary state for kidney transplant, death
TA667[11]	Dec 2020	Caplacizumab	Standard of care	Decision tree + 3 state Markov	Remission, true relapse, death
TA710[12]	Jun 2021	Ravulizumab	Eculizumab	4 state Markov	Initiate treatment, discontinuation, relapse and reinitiate treatment

DISCUSSION

- Observed structural variability indicates **fragmented modelling practices** within and across disease areas (asthma and TMAs).
- **Lack of model reuse** reduces methodological efficiency and increases analytic burden for each new technology.
- For rare diseases, **evidence uncertainty and clinical expert input** often dominate model structure decisions, compounding inconsistency.
- Establishing **reference model frameworks**, validated and adaptable within similar disease areas, could **streamline future evaluations**.
- Such reference frameworks could improve: (i) **cross-technology comparability** (ii) **decision transparency** and (iii) **efficiency** in HTA review processes.

LIMITATION

- **Fewer NICE TMA appraisals** may **limit generalizability,** and reliance on public documents may omit internal rationale for model structure variations.

CONCLUSIONS AND POLICY IMPLICATIONS

- **Frequent model structure variation** across NICE appraisals, as evidenced with asthma and TMA appraisals, **highlight** the **need for greater structural alignment**.
- **Disease-Specific reference models** may help mitigate inconsistency and inefficiency in HTAs arising due to model structural variability.
- **Further work is warranted** to evaluate the feasibility, acceptability, and governance of reference models among key stakeholders.
- **NICE and other HTA agencies** could establish **adaptable reference model frameworks,** encourage **model reuse** and **transparent documentation** of **model structure rationale**, foster **structural alignment** and enhance **reproducibility/comparability** across technologies.

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9. https://www.nice.org.uk/guidance/ta880
10. https://www.nice.org.uk/guidance/hst1
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