Model Types Submitted to NICE: What Is Considered Appropriate by Evidence Review Groups?

PRM118

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Objective

- A review of Evidence Review Group critiques of models in recent NICE submissions was conducted to determine any associations between model type and Evidence Review Group criticisms.

Background

- Novel and complex model types are being used more regularly in economic evaluations. However, it is not yet clear how these are received by Evidence Review Groups (ERGs).
- Knowledge of common criticisms relating to specific types of model could be invaluable to those involved in developing economic models for Health Technology Assessment (HTA) submissions.

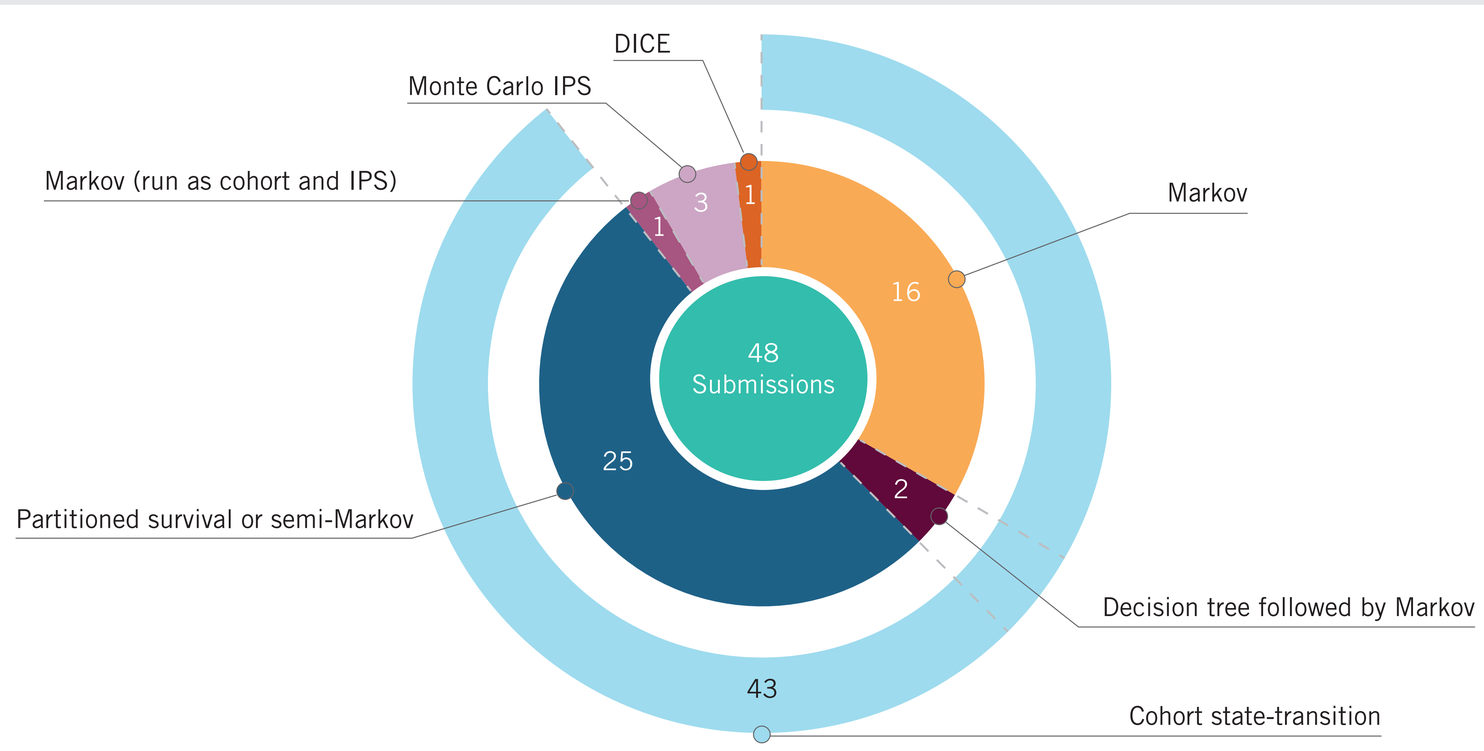
Methods

- All National Institute of Health and Care Excellence (NICE) single technology appraisals published between May 2016 and May 2017 were reviewed.
- Data extracted included indication, model type, the program used for model development, whether the ERG considered the model type appropriate, and details of the ERG critique.
- Cancer Drugs Fund rapid reconsiderations, multiple technology appraisals, and appraisals which had been subsequently replaced or updated were excluded from the analysis, in order to focus on the most recent novel models submitted by companies.
- When the ERG considered the model structure to be appropriate for the decision problem, this was assumed to also apply to model type.

Results

- The 48 submissions reviewed included 43 cohort state-transition models (Markov, partitioned survival, semi-Markov and decision tree/Markov models), 1 Markov model run as both a cohort and microsimulation model, 3 Monte Carlo individual patient simulations (IPS) and 1 Discretely Integrated Condition Event (DICE) model **(Figure 1)**.

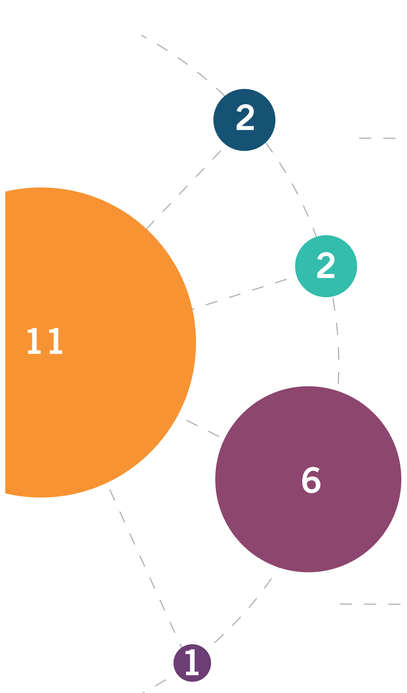
Figure 1| Breakdown of analysed submissions by model type



DICE: Discretely Integrated Condition Event; IPS: Individual Patient Simulation.

- Of the 35 (72.9%) submissions which stated the program used to build the model, almost all used Excel. Only 1 was built in another program (C++), and this resulted in the ERG being unable to check the model implementation.
- In 27 (56.3%) submissions, 14 of which were partitioned survival models in oncology indications, the ERG agreed the model type was appropriate, typically due to alignment with previous models in the same indication or in similar indications.
- In 12 (25.0%) submissions, the ERG critique of the model type was unclear or not stated.
- In the remaining 9 (18.8%) submissions, the ERG was unsatisfied with the model type to some extent:
  - In 2 of these cases, a dynamic modelling approach was considered more appropriate than a Markov model (in infectious diseases),[1, 2] and in 2 other cases, patient heterogeneity was believed to be important where a cohort model had been used.[3, 4]
  - A total of 6 models were criticised for inflexibility in capturing key evidence (2 partitioned survival models),[5, 6] or for unnecessary complexity and lack of transparency (2 Markov, 1 DICE and 1 partitioned survival model).[1, 5–9]
  - Furthermore, the DICE model was criticised for impractical implementation and lack of clear benefit over a Discrete Event Simulation (DES) model.[9]
  - Illustrative examples of ERG critiques are presented in **Figure 2**.

Figure 2| Examples of ERG critique when the model type was unsatisfactory



Disease transmission relevant

"Even though the model structure reflects the key elements of the hepatitis C disease progression with and without treatment, there could be more suitable modelling types than a static Markov model."
TA413, chronic hepatitis C[2]

Patient heterogeneity important

"There could be more suitable modelling types such as patient level simulation, which would reflect the patient heterogeneity."
TA407, ankylosing spondylitis[3]

"As there is variation in the treatment sequence between patients this model structure is inappropriate."
TA404, prostate cancer[4]

Overly complicated/inflexible

"It should be considered whether simpler approaches (e.g. an individual-level state transition model) would have been more appropriate to reflect this decision problem, given the gain in transparency."
TAG486, overweight and obesity[9]

"A key concern related to the…inflexibility associated with the modelling approach chosen by the company (partitioned survival model) which meant that correlations between outcomes are not captured in the model."
TAG504, idiopathic pulmonary fibrosis[6]

Impracticality

"The ERG considers the model as unfit for purpose, due to its extremely long run times, the fact that it crashes on many computers, and the inability to perform PSA."
TAG486, overweight and obesity[9]

Quotes are taken from selected submissions as illustrative examples of ERG critique types. ERG: Evidence Review Group; PSA: Probabilistic Sensitivity Analysis.

Conclusions

- In the majority of cases, ERGs include an explicit review of model type in their critique.
- Cohort state-transition models are generally considered appropriate by ERGs, with the justification that they have previously been used in the disease area.
- Other model types are more common in disease areas with fewer submissions, and are generally considered appropriate if their implementation is transparent and user-friendly.
- Practical implementation with reasonable model run times is an important factor when considering new model types such as DICE and DES.

References

1. NICE TA430: Sofosbuvir–velpatasvir for treating chronic hepatitis C (January 2017); **2.** NICE TA413: Elbasvir–grazoprevir for treating chronic hepatitis C (October 2016); **3.** NICE TA407: Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors (September 2016); **4.** NICE TA404: Degarelix for treating advanced hormone-dependent prostate cancer (August 2016); **5.** NICE ID753: Ibrutinib for treating relapsed or refractory mantle cell lymphoma (In progress); **6.** NICE ID837: Pirfenidone for treating idiopathic pulmonary fibrosis (review of TA282) (In progress); **7.** NICE TA423: Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (December 2016); **8.** NICE TA442: Ixekizumab for treating moderate to severe plaque psoriasis (April 2017); **9.** NICE ID757: Naltrexone-bupropion (prolonged release) for managing overweight and obesity (In progress).

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