EE150

Conceptual Approach to Economic Modeling in Retinal Diseases: A Review and Critique of Two NICE Clinical Guidelines

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OBJECTIVES

The National Institute for Health and Care Excellence (NICE) published clinical guidelines for diabetic retinopathy (DR) and diabetic macular edema (DMO) in 2024 (NG242)[1] and for age-related macular degeneration (AMD) in 2018 (NG82)[2]. We examined the economic models used to inform these guidelines.

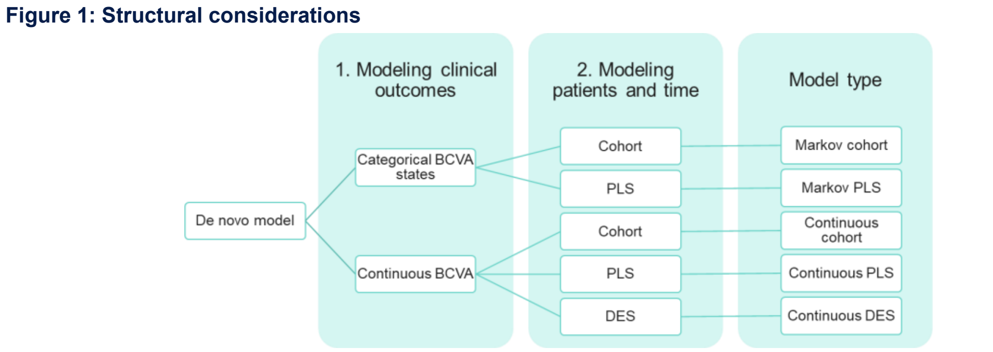
METHODS

As well as considering how the patient's vision was modeled, we reviewed the modeling approaches taken in NG82 and NG242, using the following categories:

- Modeling clinical outcomes (best corrected visual acuity [BCVA])
  - Model as categoric (Markov) health states
  - Model as a continuous variable
- Modeling patients and time
  - Cohort model with discrete time cycles
  - Patient-level simulation (PLS) with discrete time cycles
  - PLS with continuous time (discrete event simulation [DES])

These are also summarized in Figure 1. Following completion of our review, we considered the benefits and pitfalls of potential alternative approaches.

Figure 1: Structural considerations



Key: BCVA, best corrected visual acuity; DES, discrete event simulation; PLS, patient-level simulation.

RESULTS

Health states

NG82 used a two-eye Markov PLS structure with six BCVA health states (Table 1), resulting in 36 BCVA-related health state combinations. Simultaneously, each eye could also be in one of five or six treatment-related health states (Table 1), resulting in 30 treatment-related health state combinations. Death was also included as an absorbing state. As NG82 adopted a PLS approach, one patient was simulated through the structure at a time, and the average health state occupancy across a simulated cohort of patients was then calculated to generate costs and quality-adjusted life years (QALYs) for the cohort. Movements between health states were limited to a maximum of two health states in any given cycle.

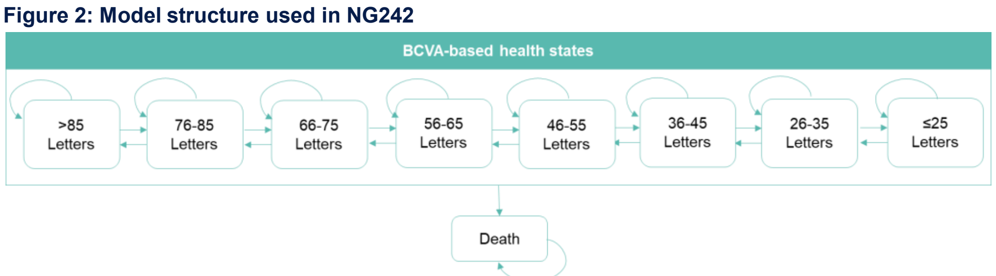
Table 1: Health states used in NG82

First eye (has AMD at baseline)	Second eye (may not have AMD at baseline)
Health states defined by BCVA	
> 85 letters	> 85 letters
85–71 letters	85–71 letters
70–56 letters	70–56 letters
55–41 letters	55–41 letters
40–26 letters	40–26 letters
≤ 25 letters	≤ 25 letters
Health states defined by AMD or treatment status	
–	No AMD
Pre-treatment, with AMD	Pre-treatment, with AMD
First year of treatment	First year of treatment
Second year of treatment	Second year of treatment
Subsequent year of treatment	Subsequent year of treatment
Post-treatment (discontinued)	Post-treatment (discontinued)
Death	

Key: AMD, age-related macular degeneration; BCVA, best corrected visual acuity.

NG242 presented a one-eye Markov cohort structure with eight BCVA health states (ranging from 'BCVA ≤ 25' to 'BCVA ≥ 85') plus death to model the vision in one eye only, with costs for treatment of the second eye approximated but not explicitly modeled. Movements between health states were limited to a maximum of one health state in any given cycle.

Figure 2: Model structure used in NG242



Key: BCVA, best corrected visual acuity.

Model structure

PLS structures, modeling vision in each eye as a continuous variable, in similar retinal diseases have been published (such as Claxton et al. 2016[3] and McCarthy et al. 2019[4]). These approaches apply a sampled mean change in BCVA in each time cycle directly to the vision in the previous cycle. Despite this, previous NICE cost-effectiveness technology appraisals in retinal indications have also typically used a one-eye[5–8] or two-eye[9–13] Markov (categorical) cohort structure. However, the approaches taken by the guideline developers have limitations, as called out in the guideline reports (Box 1).

Box 1: Structural limitations discussed in the NICE clinical guideline economic reports

NG82

- By using mean change in BCVA to inform a distribution of patients across categorical health states, it was necessary to place those mean changes on an underlying distribution
- All eyes are, on average, at the mid-point of their BCVA health state. The probability of moving up one health state is the probability of gaining between 7.5 and 22.5 letters, on average, which is an oversimplification of reality

NG242

- Modeling only one eye may not accurately reflect the disease profile, and previous NICE TAs took a more granular approach to modeling the fellow eye. However, "*given the lack of publicly available data it was not possible for the guideline development team to use this type of structure*"

Key: BCVA, best corrected visual acuity; NICE, National Institute for Health and Care Excellence; TA, technology appraisal.

Health state transitions

Both guideline models estimated transitions between the BCVA states using a network meta-analysis that estimated a (relative) treatment effect on mean change in BCVA.

- The mean BCVA change from baseline by treatment was assumed to be normally distributed as a simplifying assumption, and this distribution was used to estimate the probability that an eye would gain, or lose, any given number of letters – which, in turn, was used to estimate the probability that a patient would transition between the different BCVA health states

We argue that adopting a Markov structure introduces unnecessary complexity by grouping vision into health states.

- This requires transformation of reported trial and/or indirect treatment comparison endpoints (i.e. mean change in BCVA) into transition probabilities, imposing artificial limits on possible transitions and imposing an assumed underlying distribution around the mean BCVA change from baseline

Sources of evidence

The authors of the NG242 economic analysis further suggest that the lack of publicly available data prohibited a more granular exploration of the fellow eye.

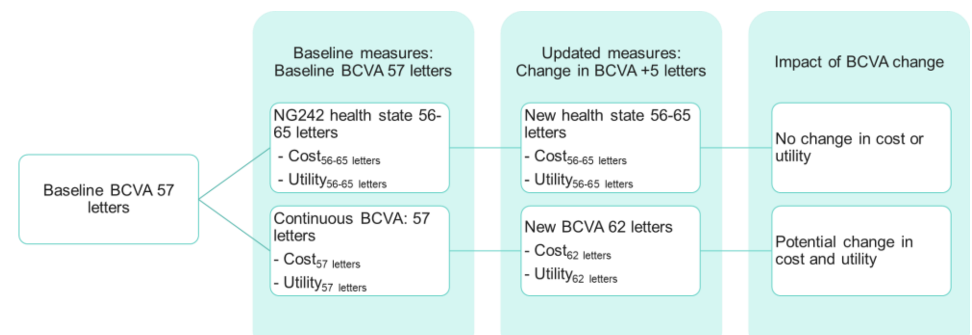
- While this may be a relevant consideration when adopting a Markov state-transition approach, we argue that were a PLS based on continuous BCVA in each eye adopted, evidence requirements would be lessened
- Similarly, computational expense would be lowered, since the number of health states required is significantly increased when modeling two eyes in a Markov health state structure, whereas modeling continuous vision in each eye requires tracking only two variables over time

Interpretation

While often considered more complex, we believe a PLS approach modeling vision as a continuous variable presents a more realistic representation of the disease while reducing the model complexity:

- Reported primary trial outcomes can be used directly in statistical analyses to estimate changes in vision on a continuous scale within the model, enabling the full BCVA benefit of treatment to be captured without requiring transformation into transitions between health states
- Any change in BCVA as well as the resulting impact on patient quality of life (and, if applicable, costs) will be reflected directly in the model. The same differences would not be captured to the same extent in a health state structure without significantly increasing the number of health states (Figure 3)

Figure 3: Impact of small BCVA change in health state and continuous BCVA structures



Key: BCVA, best corrected visual acuity.

We also believe it is easier to visualize and test alternative efficacy assumptions when considering vision on a continuous scale than within a Markov health state structure.

- If an HTA body wanted to understand the impact of alternative mean changes in BCVA, within the PLS based on a continuous BCVA structure, an alternative number of letters gained and assumed standard deviation can be input directly into the model, and the model re-run. Within a Markov health state structure, the same scenario would require additional steps to derive transition probabilities

CONCLUSIONS

- When modeling retinal conditions, we believe that a PLS based on continuous vision in each eye provides the most accurate model of the condition, while providing a flexible framework to test alternative assumptions

REFERENCES

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All NICE TA references were accessed on 14 October 2025

An electronic version of the poster can be viewed by scanning the QR code.

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