The use of NNT modelling to improve the clinical relevance of economic analysis

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Background and objectives

- Incremental cost effectiveness ratios (ICERs) using quality adjusted life years (QALYs) are the main measure of cost-effectiveness used in decision making as part of health technology assessments (HTAs).
- As these measures have many underlying assumptions and technical methodology, they could be misinterpreted by non-health economists (e.g. clinicians and policy makers).
- Outside of health technology assessments, many decision makers within the healthcare system are not expected to have the knowledge or experience to evaluate and interpret these methods. Therefore there is a need to provide additional evidence that could allow such decision makers to for the contextualise clinical and economic outcomes to provide more accessible value messaging.
- Other health economic outcomes, such as number needed to treat (NNT) and cost of preventing an event (COPE) could provide a practical interpretation of the clinical and financial effectiveness of treatments for specific stakeholders.
- Objective of this study: To conduct a landscape review of publications, literature reviews and HTAs to determine where NNT and COPE the is used in decision making, and to determine whether there are appropriate guidelines in place to inform these analyses and associated decision making.

Methods

- A desktop search was conducted to identify publications, literature reviews and HTA submissions containing information on the use of NNT and COPE and the disease areas or economic analysis that these analyses are conducted alongside.
- Literature searches of PubMed and technology appraisals within NICE were conducted to determine publications that had included NNT as part of a health economic study. Any study that included NNT within its decision making were included in the search.
- The literature review focused primarily on systematic reviews previously conducted across different disease areas due to the volume of potential clinical studies and associated outcomes that would be captured within the review when including individual treatment evaluations.

Results

- Across the identified health economic studies that included NNT analyses the majority focused on treatments for neurological conditions and rheumatoid arthritis (RA).
- Within RA, NNT measures generally focused on ACR20 or Paulus criteria improvements, which provide consistent and well-defined endpoints that may be used across the included treatment options in the analysis.
- Across many of the disease areas where NNT has been utilised , in particular neurological conditions, the use of QALY measures may be unable to fully capture the symptom implications when using the EQ-5D dimensions.
- Within publications identified, NNTs and COPE were included within cost effectiveness analyses and were used to determine the cost effectiveness ratio per event.
- Although these outcomes were used it was stated that NNTs have limitations and primarily will help with decision-making, indicating including NNT information alongside cost effectiveness may help clinicians better understand and apply results. No publications were found that included NNTs within budget impact models.

NNT: number needed to treat; COPE: cost of preventing an event

Results

- There were multiple approaches identified to approach the implementation of NNT calculations.
- NNT is the reciprocal of absolute risk reduction (ARR) and represents the number of people who needed to be treated with a specific intervention in order to obtain one additional positive outcome compared to the comparator.[1]

$$NNT = \frac{1}{ARR}$$

- NNT_{RMST} is the restricted mean survival time (RMST) and represents the number of people who needed to be treated to gain the observed difference in mean survival time for a death or event.[2] The use of NNT_{RMST} may help deal with issues that occur from using the regular NNT method, this includes:
  - NNT failing to capture treatment effects over time.
  - NNT may result in misinterpretations of treatment benefits.
  - NNT_{RMST} is able to account for information between follow-up periods.

$$NNT_{RMST} = \frac{1}{\frac{RMST_I(t)}{RMST_C(t)} - 1}$$

- COPE is an additional step that may be added to a NNT analysis to include the relative treatment costs for the treatments included in the analysis. COPE analysis estimates the difference in cost between the two comparison treatment options and applies this to the NNT to provide a value for the expected additional cost required in order to prevent an event from occurring.
- COPE analysis allows for the model to evaluate the cost-effectiveness of treatments, as opposed to NNT that is only considering the relative effectiveness of the treatments.

NNT in NICE HTA submissions

- NNT was used as part of an HTA submission for dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation (TA249), and was used to determine whether the use of dabigatran etexilate would offer benefits if used and give further value to the intervention.
- No formal HTA-standard guidelines were found on the implementation of NNT analyses in the context of health economic evaluation. Furthermore, no formal, HTA standard guidelines were available on the interpretation of NNT analyses.

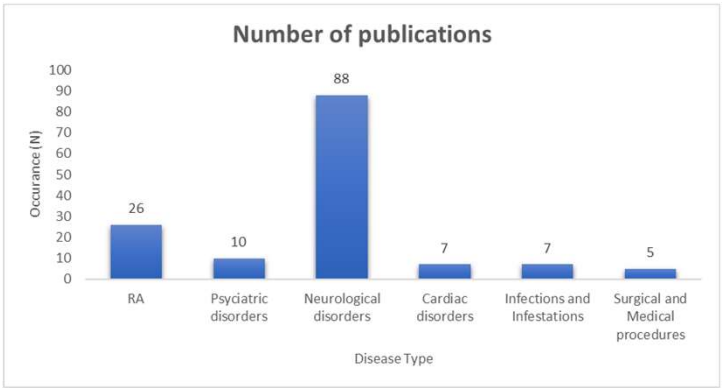

Figure 1. Occurrence of diseases from publications identified to use NNT

Discussion

- NNT and COPE analyses provide an additional approach to presenting the clinical and financial effectiveness of treatments which may be utilised alongside ICER estimations commonly used in CEAs to contextualise the outcomes of an analysis and provide more accessible evidence for non-technical audiences.
- The use of NNT analysis was identified to be mostly utilised in settings where there is a well defined endpoint, and where the dimensions used for utility measures are expected to not be sensitive to symptom effects. Neurological disorders were the most commonly identified area in which NNT evaluations were implemented, which is most likely due to the challenges in capturing the impact of conditions within the framework of a utility measure such as the EQ-5D.
- The NNT measure is reliant on the existence of a well defined binary end point given that the measure is assessing the number of patients that meet the criteria. It may therefore be necessary to run the NNT analysis across a range of endpoints in order to fully explore the value of a treatment.
- Due to the measure of NNT being based on the number of patients who have achieved the required outcome this does restrict the analysis to only assessing outcomes at a single timepoint and is therefore not well powered to test the effect of treatment over time. Additionally, when conducting analysis it is necessary to ensure that data exists for all included treatment options at the same timepoint.
- As NNT analyses are built around specific endpoints used within the disease area of interest this introduces challenges for the comparability of results across disease areas and for the development of standardised thresholds for decisions making.
- Further understanding into the use of NNT_{RMST} could allow for a more robust method of use for NNTs to be used alongside cost effectiveness analysis.
- Although NNT analyses use fewer specific health economic techniques and assumptions than CEA or BIMs, and therefore the methodology is more accessible to non-health economists, the lack of guidelines to contextualise and interpret NNT and COPE results mean that it is difficult for decision makers to determine what is an acceptable or good NNT value. This limits the usefulness of these analysis in decision making, particularly when there is a need to compare between different disease areas.
- Due to the lack of insight on an acceptable NNT value, the use of these measure currently remains limited to like-for-like comparisons, for example for comparators in the same indication, or for analyses between population subgroups.

Conclusion

- NNT measures can be used in decision making, particularly with stakeholders who are less familiar with health economic methods. Generalisability, a key strength of the QALY measure, can be of less relevance for stakeholders interested in a specific disease area, therefore NNT and COPE can be used for treatment comparisons within a specific disease area.
- The main challenge in wider adoption of these approaches is a lack of standardisation across NNT models, and development of best practice guidelines would support wider use of these methods.

References:

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