MSR22

Methodological approaches to assess cost-effectiveness using pathway models in oncology

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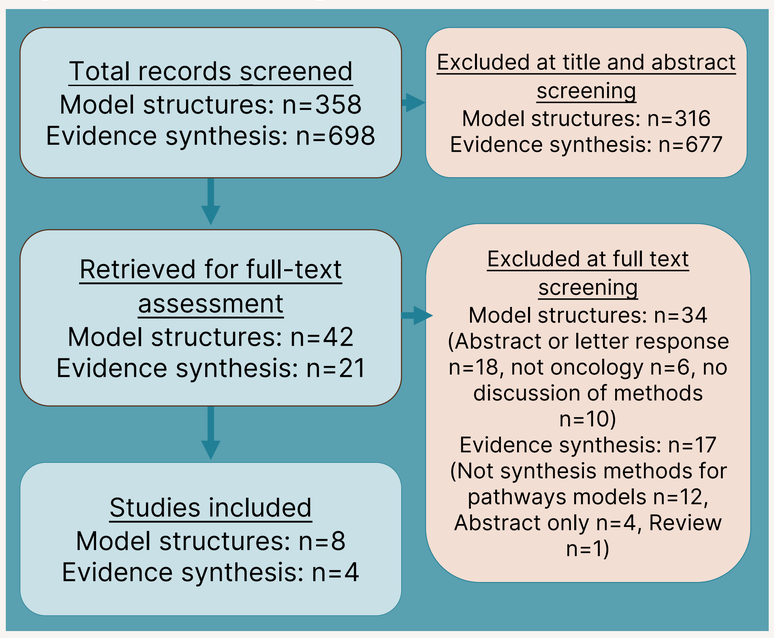
Background

The NICE technology appraisals (TA) programme conducted a pilot project to explore the potential use of 'pathway' or treatment sequence models to assess the cost-effectiveness of interventions in TA guidance. Pathway models incorporate multiple decision nodes in a treatment sequence and can be used to assess the most cost-effective sequence of treatments or the optimal point of introduction of a new technology within a pathway. TAs typically consider comparisons of interventions at a single decision point aligned to the technology's marketing authorisation, and so there has been limited use of pathway models in oncology at NICE to date.
We aimed to review methodologies used to evaluate cost-effectiveness of interventions in pathways disease models within oncology, and design a novel model structure and evidence synthesis for a pathway model for advanced NSCLC.

Review methods

A search was designed to identify papers on methodological approaches to oncology pathway modelling. The search terms included pathways models, core/core disease and whole disease models. We also ran a supplementary update review of Lewis et al. to identify studies on methods for evidence synthesis to inform pathways models.

Figure 1: PRISMA diagram



Findings

Table 1: Studies on evidence synthesis

Study	Approach
Jansen (2019)	Multi-state NMA models at each line of therapy using a mixture of Weibull and flexible fractional polynomial models to allow for time-varying HRs. A multinomial likelihood is given for the numbers of patients who are progression free, progressed, and dead at each non-overlapping interval extracted from Kaplan-Meier curves.
Schettini (2022)	Bayesian network meta-analyses assuming proportional hazards, for PFS/TTP, ORR and OS, at first-line and further lines along the treatment pathway, considered separately.
Stenner (2012)	Combined observational data comparing two different sequences
Diaby (2016)	Fit parametric models for PFS and OS, including proportional hazards and accelerated failure time models. Analysis conducted separately for each treatment and line of therapy.

Table 2: Studies on model structure

Study	Summary of recommendations
Huang (2022): Review of oncology treatment sequence models	Models should include progression, treatment-free intervals and death. Use of a single, long-term trial to estimate survival for a sequence. IPD to adjust for patient characteristics and outcomes based on position of treatment in sequence.
Tappenden (2012): Methodological framework for whole disease modelling	Implementation of model using patient-level simulation. Conceptualisation involves disease logic, service pathways modelling, structured systems design and analysis methods. Consideration of multiple frameworks for decision making.
Zheng (2017): Review of approaches used to model treatment sequences in NICE TA	Sequences should be modelled if the selection, efficacy or costs of treatment are affected by prior treatments. Patient-level modelling preferred if patient characteristics or treatment history affects subsequent treatment, or event risks change with time.
Lord (2013): Case study of two analyses using framework proposed by Tappenden	Capture the interaction between disease progression over time with the service pathway. Note inconsistencies between bodies of evidence that inform different elements of the model.
Blommestein (2016): Case study with methods discussion	Registry data used to inform a patient level simulation model. RCTs run for a limited time, limiting the ability to assess cost effectiveness of multiple treatment sequences.
Jansen (2019): Open-source sequence model	The value and feasibility of developing an open-source model.
Jin (2023): Review of whole disease models	The appropriateness of alternative modelling methods should be assessed, and the chosen method justified.

Key themes: modelling

Key themes from existing methodological papers exploring pathways model development state a preference for patient-level model structures and emphasise the need for IPD and data from a single source. These models are likely to have a large computational time which may need to be accounted for when choosing an appropriate software package.
There is value in further methods development allowing for the inclusion of multiple data sets limited to published data whilst adhering to the processes outlined in the literature.

Key themes: synthesis

Multi-state network meta-analysis with flexible survival models was most appropriate for evidence synthesis for pathways models. However, it may be necessary to conduct separate syntheses at each line of therapy due to data limitations.

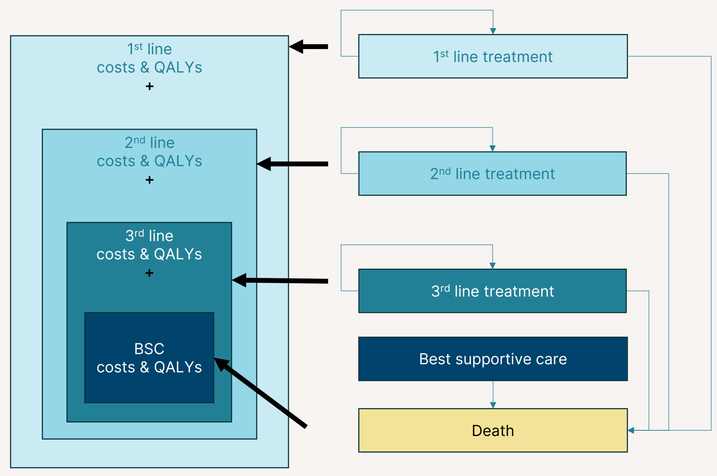
Implications for modelling

The choice of model structure to model treatment sequences in NSCLC has been informed by both methodological and operational requirements. Any model intended to be multi-use and adapted for analysis by external stakeholders requires a high level of transparency.

- This leads to a preference for a model developed in MS Excel given its familiarity amongst stakeholders, and the use of published summary data to populate model inputs.
- Due to its reliance on OS data, a conventional partitioned survival model will not be suitable for modelling decision nodes as mortality data would be confounded by subsequent treatments.
- Patient-level models capture the complexities involved in the NSCLC pathway but require access to patient level data and have a lengthy run time. Accounting of baseline level heterogeneity is unlikely to be a pivotal factor and can be accounted for by selecting appropriate sources of data.

A novel nested partition structure was developed to avoid extensive use of tunnel states required for a semi-Markov model.

Figure 2: Proposed model structure for NSCLC



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References: Available as supplementary material

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