MISS EMMA MCMANUS (Orcid ID : 0000-0002-3442-8721)

Article type : Review Article

TITLE PAGE

Title: An introduction to the methods of decision-analytic modelling used in economic evaluations for Dermatologists

Key words: Economic evaluation, decision-analytic modelling, education

Authors:

E McManus[1*], T H Sach[1], N J Levell[2]

[1] Health Economics Group, Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ.

[2] Dermatology Department, Norfolk and Norwich University Hospitals NHS Foundation Trust, Colney Lane, Norwich, NR4 7UY

***Corresponding author**

Emma McManus

Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ

Emma.mcmanus@uea.ac.uk

Funding

This paper was written whilst EM, TS and NL were being funded by Professor Tracey Sach's Career Development Fellowship (CDF award-2014-07-006) supported by the National Institute for Health Research. The views expressed in this paper are those of the authors

and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health and Social Care.

Competing Interests

The authors declare that they have no competing interests.

ABSTRACT:

Economic evaluations are used to identify which health treatments or preventions, offer the most effective use of resources, or value for money. This is achieved by identifying, measuring and valuing the inputs and outcomes of alternative interventions. These evaluations are often conducted alongside clinical trials, however these trials may end before the outcomes of economic interest have been observed and measured. An alternative to within trial economic evaluation is to use decision modelling, which can model the cost-effectiveness of interventions over an extended time period.

This paper aims to provide an overview for clinicians of the different modelling techniques used within health economic evaluations and to introduce methods for critical appraisal.

The most common modelling approaches, and their associated strengths and weaknesses, were discussed. Alongside this, practical examples specific to dermatology were given. These examples include studies where the model chosen or the methods used may not have been the most appropriate. Methods for critical appraisal were also highlighted.

Common modelling approaches include Decision Trees, Markov Cohort, extensions to the Markov model (Monte Carlo Simulation), and Discrete Event Simulation models. Items of the Philips Checklist were discussed in the context of performing critical appraisal.

Health economic decision models are multi-faceted and can often be complex. Full critical appraisal requires clinicians' unique knowledge, which is complementary to the knowledge of health economists.

MANUSCRIPT:

INTRODUCTION

Economic evaluation is a systematic approach, involving the identification, measurement and valuation of inputs and outcomes of two or more alternative healthcare interventions1, measured in terms of their costs and health benefits. Such health benefits are usually measured in terms of quality adjusted life years (QALYs) to facilitate cross comparison of interventions for different disease areas, as advocated by the National Institute for Health and Care Excellence (NICE) reference case2. The aim of an economic evaluation is to identify which treatment (or prevention strategy) represents the most effective use of resources, commonly referred to as cost-effectiveness. Due to the limited budgets available to provide health care, the need to demonstrate an intervention as being value for money is now considered the fourth hurdle of technology approval, along with quality, safety and efficacy3. Economic evaluations are often conducted alongside clinical trials (known as within trial economic evaluations), however the timeframe of these trials often focus on demonstrating clinical efficacy and thus may end before the outcomes of economic interest have been fully observed and measured. This is particularly relevant within dermatological conditions, many of which are chronic. To address this decision modelling methods can be used, defined as:

"An analytic methodology that accounts for events over time and across populations, that is based on data drawn from primary and/or secondary sources, and whose purpose is to estimate the effects of an intervention on valued health consequences and costs"4.

The benefits of using a modelling approach are that multiple sources of evidence can be used, an extended time horizon can be considered, the effect of changing parameters can be explored and perhaps most importantly, the uncertainty surrounding the long-term result can be assessed. Whilst decision models have many associated advantages, it should be acknowledged that they are not complete alternatives to within trial economic evaluations, as the economic data from these trials is often used within modelling studies.

Economic models underpin health economic assessments in medicine. Clinicians reading scientific papers incorporating such assessments require knowledge and understanding of economic modelling, to aid their critical appraisal and assess their validity. Health economics

is a recent addition to many medical school's curriculum5, 6. However, senior clinicians, responsible for making important healthcare decisions, may lack essential health economic competencies. Furthermore, clinicians are often consulted to generate parameters for modelling studies in the absence of clinical data as well as to provide guidance on potential disease and treatment pathways7, 8. It is therefore, important that clinicians have an understanding of how decision models are constructed and used, along with the associated advantages and disadvantages of each modelling approach.

This paper reviews the most common modelling approaches used within economic evaluations, using real world examples found within a systematic review of modelling studies for atopic eczema9. As it is often easier to learn through mistakes than successes, where possible, the examples cited throughout this paper, have been chosen to highlight elements that could have been improved within the modelling methodology. This paper aims to be a general overview and guide to critical evaluation of commonly used modelling techniques, accessible to dermatologists and is not a comprehensive description of every model type or methodology. Interested clinicians may wish to read or consult more comprehensive papers on modelling which are referenced in the text. Key modelling terms that are used throughout this manuscript are defined in Table 1.

MODELLING APPROACHES

Decision Tree Model

The decision tree is often the simplest modelling method available and may be used to model one-off decision processes (e.g. treat eczema with oral antibiotics or do not treat)10. To produce a decision tree model, the tree must begin with a decision node, which is a point where a choice is made. Importantly, the choice options branching from the decision node must be mutually exclusive, meaning if one is chosen then the other is not.

Along each branch there may be further nodes (referred to as event or chance nodes), which represent points at which different events can arise (for example switching to a second-line antibiotic or not). As with the decision node, the events represented by the chance node must also be mutually exclusive, as well as being collectively exhaustive, meaning that all possible patient pathways are shown.

Alongside each of these branches, probabilities are displayed which show the likelihood of the event occurring, and at the end of each patient pathway or branch, the resulting outcome measures are displayed, such as effect on utility value and cost.

A simple, hypothetical, example of a decision tree is detailed in Fig. 1. This tree models the different effects of treatments A and B, on the likelihood of a patient experiencing an eczema flare.

A decision tree is an appropriate choice of model when the time frame is short, the individuals represented in the tree can be thought of as independent from one another and the number of events spanning from the decision node are manageable. If these criteria are satisfied, then decision trees are usually simple to produce and make calculations from.

However, due to the general probabilities applied, decision trees represent an aggregate (population) level approach and therefore do not consider individual-level attributes. They may ignore characteristics of the patient that may make certain events unlikely (such as antibiotic allergy). Furthermore, decision trees do not demonstrate the passage of time, only that at some point an event will occur. This is why they may be regarded as only suitable to model events over a short time horizon. Thus, they are not appropriate to model chronic illnesses or choices that may vary greatly depending on individual attributes.

Literature review examples:

- Two decision trees used in childhood atopic eczema studies were found to use relatively long time horizons: 3 and 6 years. Given that such modelling approaches are recommended to consider primarily short-term events, the choice of model type in these studies was considered as inappropriate11, 12.
- Xu et al.13 used a decision tree to evaluate the use of seven moisturisers amongst new-borns (deemed to be high-risk of developing atopic eczema) over 6 months. As this model assumed the same clinical effectiveness across all of the moisturisers, it is not surprising that the moisturiser found to be most cost-effective was the moisturiser that was the cheapest.

Markov Cohort Model

A Markov model (also referred to as a state-transition model) comprises a finite number of mutually exclusive and collectively exhaustive disease or treatment states. These states aim to represent the consequences of treatment options under analysis14. In a simple example using disease states in elderly people with eczema, the states could be “Remission”, “Eczema flare” or “Dead” (see Fig. 2). Attributed to each disease state is a cost and associated utility value for being in that state. It is possible to transition between these disease states, which allows the Markov model to deal more succinctly with disease recurrence and flare up than the growing number of branches that would be seen within a decision tree. The likelihood of the patient moving from one state to another is defined by transition probabilities. The main advantage of using Markov models is their ability to deal easily with recurrent events10.

Time is represented in the model using unit cycles. It is assumed that only one state transition (e.g. moving from remission to eczema flare up) can be made during each cycle. The length of the cycle is chosen to represent a clinically meaningful time interval, which might be a year in a superficial basal cell carcinoma recurrence study, a month when considering plaque psoriasis severity, or week when considering infective exacerbations of eczema. The cycle length must be short enough so that events that change over time can be represented by individual, successive cycles15.

A great benefit to introducing time cycles into the model, is that the transition probabilities between states (for example the likelihood of an eczema flare up), as well as the cost and health utilities experienced can vary with time. This, for example, allows the transition probability from any state to the “Dead” state to increase over time, representing either general or disease specific mortality. During each time cycle, the various costs and utilities attributed to being in each disease state can be totalled. This gives a different cost and overall health utility output dependent on the pathway taken (representing the course of the disease) and the number of cycles spent in each state.

All of this is represented in a state transition diagram, where disease states are represented as circles, and arrows from these circles represent the possibility and direction of transition to a different disease state. It is possible to remain in the same transition state for consecutive cycles16, which is represented by circular arrows going and returning to the same state.

One fundamental restriction that must hold in a Markov model is known as the Markovian assumption17. This specifies that the probabilities that govern how an individual stays in, or moves from, any given disease state are not affected by the previous disease states or the duration spent in such states. For example, if applied to the eczema model described above, it would be assumed that the risk of an infective exacerbation of a patient with stable atopic eczema is affected by neither the number of previous infective flares nor the time that the patient has had stable eczema. In this sense, the Markovian assumption means that the process has no memory and that all individuals within any given state are treated in the same way (homogeneity).

This inherent "lack of memory" is a disadvantage of Markov Cohort models. However, the severity of this limitation can be reduced by creating additional states that take into account the history of the individual. For example in eczema, two disease states for "stable mild eczema" could be created, "stable mild eczema with no history of infective flare" and "stable mild eczema with history of infective flare," to allow for the individual's history to impact on the transition probabilities.

Furthermore, a series of "tunnel states" could be introduced. Tunnel states allow transition through one state directly into another, which might allow for an extended treatment time. An example of this could be when modelling treatments for severe hand eczema. A cycle length of 4 weeks might be used in the model to allow for short prednisolone courses to treat flares, however to also evaluate longer periods of treatment, a series of 3 tunnel states (representative of 12 weeks) could be constructed pending the 12 week efficacy assessment followed by a further 3 tunnel states to model treatment continuation. This would mean that those receiving the first month of treatment would directly transition into the state representing the second month of treatment. Despite there being potential to build in some form of memory into the Markov model, as with the decision tree, the model may quickly become complex with a cumbersome number of disease states.

Literature review examples:

- A study18 developed a model using the following Markov States: Atopic dermatitis, no atopic dermatitis, asthma, no asthma. These states were modelled as mutually exclusive, which is not actually a true reflection of the disease process and thus reduces the validity of the model.

- In contrast, the Markov model developed by Garside et al., which informed NICE guidance on managing eczema in children19, used states that more accurately reflected eczema, for example: 'Non recurrence' and 'Disease controlled' as well as a series of treatment states: low, mid and high potency topical steroids, calcineurin inhibitors and systemic treatment.

Markov Monte Carlo Simulation

Instead of assuming patients can be grouped into homogenous cohorts as is done in the Markov approach above, it is also possible to simulate patients with individual level attributes, using Monte Carlo Simulation20. In this process, each patient begins in a given starting state. At the end of each cycle, a random number generator (see section 4.4 17) produces a value, from which this and the predetermined transition probabilities determine which state the individual will move to for the beginning of the next cycle16. In a simplistic example with only two states: alive and dead, where the transition probability of staying alive over a twelve month period is 0.7 and the probability of death is 0.3, a random number can be generated between 0 and 1. If the random number is between 0 and 0.7, the individual will remain in the well state, if the number is between 0.7 and 1, the individual will move to the dead state. This process is repeated over a finite number of cycles, defined as the time horizon of the model, or until the individual has reached the dead state (which is an example of an absorbed state – see Glossary contained in Table 1). As with the Markov Cohort model, each respective state has associated utility values and costs, able to vary with time, which accumulate over the number of cycles. This process can be repeated to simulate a large number of individuals. The Markov Monte Carlo simulation gives a measure of variability that is not possible with the previously described Markov Cohort approach15.

Discrete Event Simulation

Discrete Event Simulation (DES) is a method primarily used for modelling queue systems or processes21, an example might be to look at the effects of changing a particular health service pathway22. This is achieved by allocating each individual their own attributes, which may then affect their progression through the model and the events that occur.

The DES model structure, comprises of entities, events, resources and time20. Entities are the items (usually, but not always; patients) that proceed through the simulation. Each entity can be given different attributes, such as age, sex or duration of disease, and these can be

updated as the entity progresses through the simulation. Events refer to any defined diseases or treatments that may occur during that patient's lifetime. Events may occur simultaneously (for example an eczema flare and hospital treatment) and future events (e.g. biological treatment) may be determined by previous event history (such as previous hospital treatment for an eczema flare whilst taking methotrexate). The occurrence of an event in the model does not necessarily imply that the patient has changed disease state (for example, a patient with stable disease may be started on a new treatment). This approach allows patients to experience competing probabilities of risks; in which the experience of one event (starting a biological drug), may influence subsequent risks to both the individual (reduced risk of flare) and other entities within the simulation (possible reduced access of other patients to a rationed drug).

Timing within DES is based on an events list; all events that take place are listed in the model in a way that allows them to be processed in a chronological order. In contrast to the Markov process which focuses on the probability of transitioning to another state, DES is focused on the events an entity has experienced and the decision about what the next event will be and for how long until it occurs17. By having an events list, the idea of a queue system (e.g. patients waiting for a referral to secondary care) can be introduced into the model. With DES, it is unnecessary to specify the unit of time, as patients move through the model and can experience events at any discrete point. This means that DES simulations can proceed very efficiently, as the simulation clock can advance to the time when the next event (e.g. eczema flare) will occur, without conducting the interim computations required in models that utilise unit cycles21. Resources are incorporated directly, and entities are able to consume a resource at any appropriate time, it is also possible for entities to consume more than one resource (e.g. multiple medications) at a time.

Overall, DES provides greater flexibility than a Markov process and it may also add a greater sense of realism to the model than the use of disease states and transition probabilities23. However, to achieve this, DES requires a large volume of clinical data to populate parameters, access to specific software, specialist programming knowledge as well as the need for greater computational power. As well as this, due to the complexity of DES, it is often difficult to thoroughly and transparently report the methods and data sources used within the model within the confines of a published manuscript.

Literature review example:

- Norrlid et al.24 reported using a DES model to evaluate the use of a barrier strengthening moisturising cream. In this model, entities were patients and the event of interest was an eczema relapse. A total of 10,000 patients were simulated, over a 1-year time horizon.

The associated advantages and disadvantages of each of the modelling approaches discussed above are summarised within Table 2.

Critical Appraisal

In addition to knowing when different modelling techniques may or may not be appropriate, it is also important for clinicians to review any underlying assumptions, and particularly the sources of data used to construct the model. Models are vulnerable to manipulation, and selective use of the medical literature can alter the output of analyses. Therefore, clinicians should ensure that sufficient justification has been given for the use of different assumptions and data. Details should be given as to how data were selected, with preference given to systematic identification methods, such as systematic reviews of published literature, or meta-analyses. Particularly, if the funder of the research is also the manufacturer of the product being evaluated, then there may be financial, shareholder or marketing pressure to manipulate the model to generate a favourable result.

Furthermore, clinicians should always be mindful that the primary purpose of a model is to demonstrate the uncertainty surrounding a decision, rather than produce a single estimate of cost-effectiveness. To evaluate the uncertainty around a decision, sensitivity analyses should be carried out, which may involve changing the structural assumptions of the model, varying the parameters used or looking at different population subgroups, and the results of these variations presented.

Several checklists exist that can be used as an aid to the critical appraisal process. For example, The Consolidated Health Economic Evaluation Reporting Statement (CHEERS)26 is a relatively simple, 24 point, checklist designed to ensure the thorough reporting of economic evaluations, both those conducted alongside trials and using a decision model. There is also a decision modelling specific checklist, the Philips checklist,27 which is more commonly used by health economists to critically appraise decision models. This checklist is

more comprehensive, comprising of over 50 items designed to evaluate if the decision model and any underlying assumptions have been thoroughly reported. Of these items, there are several into which clinicians may be able to give particular insight; listed in Table 3.

FURTHER READING

For interested clinicians there are multiple publications to consult for further information on modelling methodologies. Barton et al.10 provides a detailed overview of modelling approaches, although this is not specific to any clinical condition. Brennan et al.20 developed a taxonomy of modelling structures to help modellers choose which method should be used. Karnon23 provided a detailed evaluation of Markov models in comparison to DES models to evaluate the same clinical situation, discussing in what instances one method is preferred to the other. The process of constructing decision models is comprehensively detailed within the Briggs text book 28, which provides practical exercises and solutions.

CONCLUSION

It is important that clinicians are able to understand when different modelling approaches are appropriate and how to appraise such studies. Clinicians should be aware that whilst models do produce a value for the cost-effectiveness of an intervention, this should only be considered a decision aid and not as an absolute truth. Moreover, it is widely acknowledged that decision-models are only as good as the quality of their inputs, with the phrase “rubbish in, rubbish out” holding true. There is value in Dermatologists conducting critical appraisals of these models to determine the validity of any conclusions, given the specialist knowledge they possess which enables them to appraise areas which may be inaccessible to health economists.

REFERENCES

[1] Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford university press. 2015.
[2] National Institute for Health and Care Excellence. Guide to the methods of technology appraisal. 2013.
[3] Paul JE, Trueman P. ‘Fourth hurdle reviews’, NICE, and database applications. Pharmacoepidemiology and drug safety. 2001;5; 429-438.
[4] Weinstein MC, O'Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C, et al. Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices—Modeling Studies. Value in health. 2003;6; 9-17.

[5] Howe A, Campion P, Searle J, Smith H. New perspectives—approaches to medical education at four new UK medical schools. Bmj. 2004;329; 327-331.
[6] Persad GC, Elder L, Sedig L, Flores L, Emanuel EJ. The current state of medical school education in bioethics, health law, and health economics. The Journal of Law, Medicine & Ethics. 2008;36; 89-94.
[7] Leal J, Wordsworth S, Legood R, Blair E. Eliciting expert opinion for economic models: an applied example. Value in Health. 2007;10; 195-203.
[8] Bojke L, Claxton K, Bravo-Vergel Y, Sculpher M, Palmer S, Abrams K. Eliciting distributions to populate decision analytic models. Value in Health. 2010;13; 557-564.
[9] McManus E, Sach T, Levell N. The Use of Decision–Analytic Models in Atopic Eczema: A Systematic Review and Critical Appraisal. PharmacoEconomics. 2017; 1-16.
[10] Barton P, Bryan S, Robinson S. Modelling in the economic evaluation of health care: selecting the appropriate approach. Journal of health services research & policy. 2004;9; 110-118.
[11] Mertens J, Stock S, Luengen M, v. Berg A, Kraemer U, Filipiak-Pittroff B, et al. Is prevention of atopic eczema with hydrolyzed formulas cost-effective? A health economic evaluation from Germany. Pediatric Allergy and Immunology. 2012;23; 597-604.
[12] Kiencke P, Viehmann K, Rychlik R. Cost-effectiveness analysis, prevention of atopic dermatitis by oral application of bacterial lysate in newborns/small children. European Journal of Health Economics. 2013;14; 995-1002.
[13] Xu S, Immaneni S, Hazen GB, Silverberg JI, Paller AS, Lio PA. Cost-effectiveness of Prophylactic Moisturization for Atopic Dermatitis. JAMA Pediatrics. 2016; e163909.
[14] Sonnenberg FA, Beck JR. Markov Models in Medical Decision Making: A Practical Guide. Medical decision making. 1993;4; 322-338.
[15] Briggs MA, Sculpher M. An introduction to Markov modelling for economic evaluation. Pharmacoeconomics. 1998;4; 397-409.
[16] Barton P, Bryan S, Robinson S. Modelling in the economic evaluation of health care: selecting the appropriate approach. Journal of Health Services Research & Policy. 2004;2; 110-118.
[17] Briggs A, Sculpher M, Claxton. Decision modelling for health economic evaluation. Oxford university press, 2006.
[18] Lenoir-Wijnkoop I, Aalderen WMC, Boehm G, Klaassen D, Sprikkelman AB, Nuijten MJC. Cost-effectiveness model for a specific mixture of prebiotics in The Netherlands. European journal of health economics, 2012. 101-110.
[19] National Institute for Health and Care Excellence. Atopic eczema in children: Management of atopic eczema in children from birth up to the age of 12 years. 2012.
[20] Brennan A, Chick SE, Davies R. A taxonomy of model structures for economic evaluation of health technologies. Health economics. 2006;12; 1295-1310.
[21] Caro JJ. Pharmacoeconomic analyses using discrete event simulation. Pharmacoeconomics. 2005;4; 323-332.
[22] Vahdat V, Griffin JA, Stahl JE, Yang FC. Analysis of the effects of EHR implementation on timeliness of care in a dermatology clinic: a simulation study. Journal of the American Medical Informatics Association. 2018;25; 827-832.
[23] Karnon J. Alternative decision modelling techniques for the evaluation of health care technologies: Markov processes versus discrete event simulation. Health economics. 2003;10; 837-848.
[24] Norrlid H, Hjalte F, Lundqvist A, Svensson A, Tennvall GR. Cost-effectiveness of Maintenance Treatment with a Barrier-strengthening Moisturizing Cream in Patients with Atopic Dermatitis in Finland, Norway and Sweden. Acta Dermato-Venereologica. 2016;96; 173-176.
[25] Tappenden P, Chilcott J, Brennan A, Squires H, Stevenson M. Whole disease modeling to inform resource allocation decisions in cancer: a methodological framework. Value in Health. 2012;15; 1127-1136.
[26] Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. Cost Effectiveness and Resource Allocation. 2013;11; 6.
[27] Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. 2004.
[28] Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation. OUP Oxford. 2006.

Table 1: Glossary of modelling terms

Term	**Meaning** (in terms of decision modelling)
Model Technicalities	
Collectively exhaustive states	An individual must be in one of the modelling states.
Cycle length	An interval of time used in some models during which there are defined probabilities of changing to a different health state. The cycle length should be determined by the frequency of clinical events or interventions, ideally the cycle length should be sufficiently short so that only one event is likely to happen per cycle. (see Markov Cohort model)
Discounting	Not all costs and benefits of a health care intervention are incurred at the same time. To take account of these potential time differences in economic evaluations, both future costs and benefits are discounted (the NICE reference case currently uses a discount rate/year of 3.5%2). Discounting takes into account individuals preference for benefit (or cost) of an intervention now (later) rather than later (now).10
Mutually exclusive states	If an individual is in one state, it is impossible for them to be in any other, at the same point in time. For example, the states alive and dead are mutually exclusive. (see definition of State below)
Parameter	An input value into the model, used to define a characteristic (such as likelihood of disease flare, or mortality risk).
Sensitivity Analysis	Inputs of the model (such as parameters, structural assumptions) are varied in order to assess how the results are altered.
State	States represent the different health or treatment statuses of a cohort within a model. Such states each have a defined cost and health outcome associated with them. For example, in an eczema model, the different states could be based on disease progression: no eczema, mild, moderate or severe eczema. Alternatively, it could be based on treatment states: emollient, topical corticosteroids or biologics.
Tunnel States	Tunnel states allow transition through one state directly into another; they are often used to represent occurrences of a set length, which are longer than the cycle length of the model.
Absorbed State	A state where individuals can enter but not leave. The most common example would be death.
Structural Assumptions	These refer to assumptions made in the modelling type, as well as the potential treatment or disease pathways within a model. For example, assuming that following an eczema flare an individual can return to a normal skin state would be a structural assumption.
Transition probability	The probability of moving from one health state to another at the end of a cycle (see Markov Cohort model)
Health Outcomes	
EQ-5D	This is a standardised instrument used to measure health status. It comprises of 5 dimensions: pain and discomfort, anxiety and depression, usual activities, mobility and self-care.

	Depending on the version of the questionnaire 3L (or 5L), each domain can have 3 (or 5) levels for the respondent to choose from, ranging from no problems to extreme problems.
Utility	A measure of the preferences of individuals or society towards a particular set of health outcomes, 0 (death) and 1 (full health). With reference to the EQ-5D, conventionally the responses are converted to a single number (a utility) based on stated preferences of the UK population.
Quality adjusted life year (QALY)	An outcome used in economic evaluations, which takes into account both the length and the quality of life. 1 QALY is equivalent to living 1 year at perfect health or 2 years at 50% health, at any age.

Table 2: The associated advantages and disadvantages of different modelling approaches.

Modelling approach	Advantages	Disadvantages	Dermatological Examples
Decision Tree	• Easy to produce and make calculations from.	• Does not take into account individual attributes. • Can quickly become "bushy" when modelling complex scenarios. • Does not account for the time the event occurred or the passage of time.	• Applicable to curable, short term acute illnesses – such as a comparison of treatments for impetigo • Treatments for basal cell carcinoma (operation, compared to a course of radiotherapy or a course of topical treatment)
Markov Cohort	• Ability to deal with recurrent events. • Transition probabilities, as well as incurred costs and utilities can be made to change over time.	• Markov assumption prevents memory. • Patient can only be in one state at a given time.	• A Markov model could be used to model recurrent acute infections such as recurrent herpes simplex or lower limb cellulitis. • The long term treatment of psoriasis using different treatment options.
Markov Monte Carlo Simulation	• Ability to deal with recurrent events. • Transition probabilities, as well as incurred costs and utilities can be made to change over time. • Allows for different individual attributes. • Provides measures of variability.	• Markov assumption prevents memory. • Calculations can become extensive and time consuming.	
Discrete Event Simulation (DES)	• DES can be run with many entities at once, all with different individual attributes, unlike the Markov model, which would require the model to be run again for each individual with differing attributes. • Allows for individual interactions, such as competition over finite resources.	• May require specialist programming knowledge and a large amount of computational power. • A large amount of parameters may be required to reflect individual patient history.	• Modelling the change of a service pathway, for example examining the effect of varying the length of clinician-patient contact time within a dermatology clinic

Table 3: Modified Philips checklist for clinical assessment of Health Economic Decision Models.

Questions for critical appraisal	**Relevance to clinicians/Explanation**
Is the structure of the model consistent with a coherent theory of the health condition under evaluation?	The validity of a model is strongly underpinned by the structure the model takes and if it is reflective of the disease. Unless the model is particularly simplistic, clinicians are better placed than health economists to assess this checklist point.
Have all feasible and practical options been evaluated?	This requires specialist knowledge of the various treatments available to patients.
Is there justification for the exclusion of feasible options?	Unlike clinical trials, where the number of treatment arms is usually limited to two or three, decision models can model a greater number of comparators and thus all feasible options for patients with a particular disease should be evaluated.
Is the time horizon of the model sufficient to reflect all-important differences between options?	If the costs or benefits of an intervention are likely to occur at different points in time to the comparator, it is important that the time horizon of the model is long enough to capture these. For example, a biological treatment may have a risk of side effects that do not become evident until 1-2 years after, for example prion disease. The duration of treatment and the timing of its effect must be realistically modelled. Clinicians are better placed to assess the potential importance of possible long-term events.
Is the time horizon of the model, and the duration of treatment and treatment effect described and justified?	
Do the disease states (state transition model) or the pathways (decision tree model) reflect the underlying biological process of the disease in question and the impact of interventions?	All models represent a simplification of the clinical condition under evaluation. However, it is important that any simplifications are still representative of the condition. For example, it may be inappropriate to model that after a severe eczema flare that the skin returns immediately to its pre-flare state.
(If applicable) Is the cycle length defined and justified in terms of the natural history of disease?	This is applicable to Markov modelling studies. A detailed explanation of the clinical condition being evaluated is needed in order to answer this checklist point.

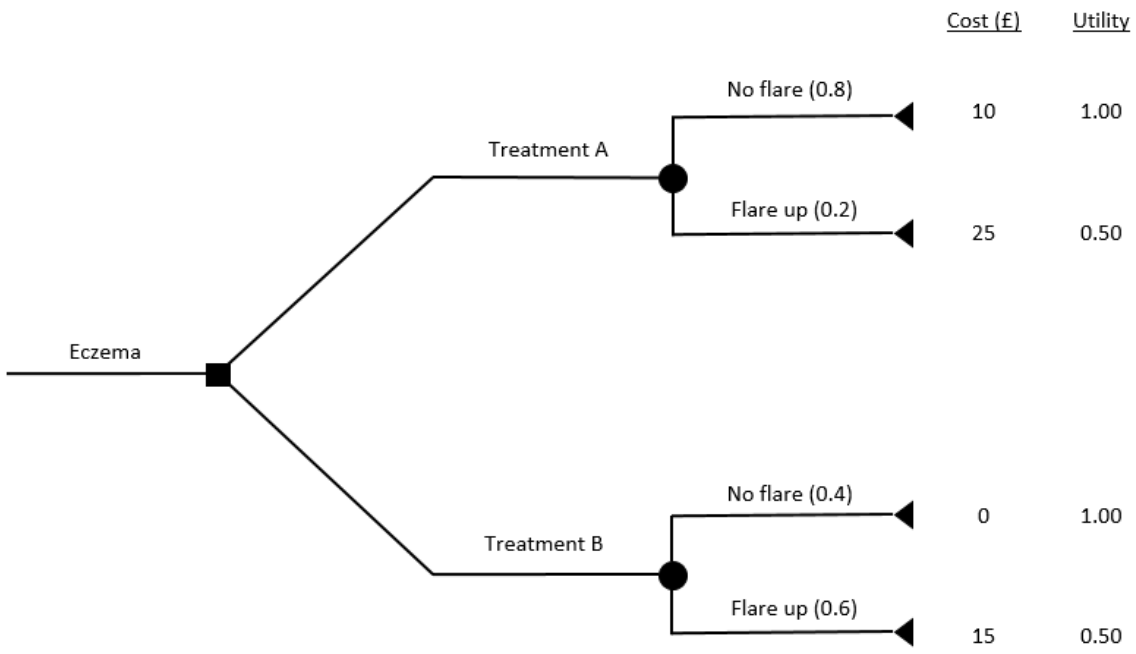

Figure 1: Example of a simple decision tree.

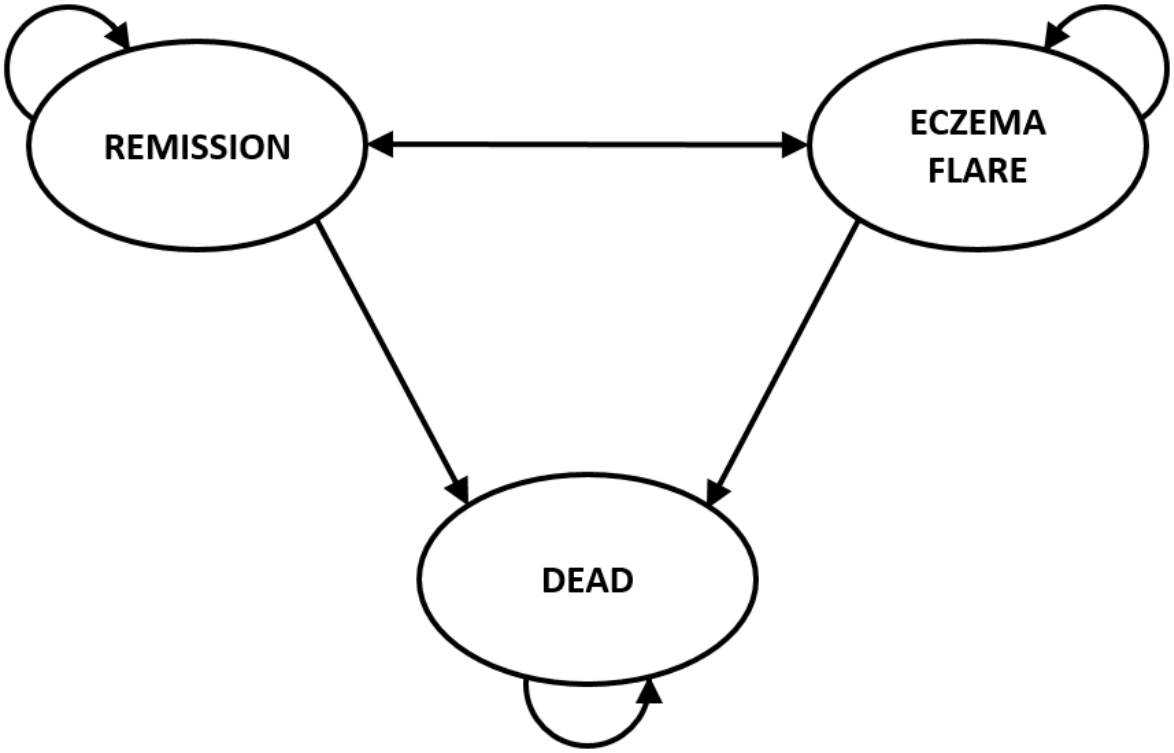

Figure 2: Example of a simple Markov model.