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DICE for NICE? Lessons from a Single Technology Appraisal

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Objectives

To assess the suitability of a Discretely Integrated Condition Event (DICE) approach to discrete event simulation (DES) modelling in Microsoft Excel for a company submission to the National Institute for Health and Care Excellence (NICE) Single Technology Appraisal (STA) process

Background

DICE

- In March 2016, DICE simulation was proposed as a unifying approach to pharmacoeconomic analysis, designed to meet the modelling requirements of such analyses.[1]
- Within a DICE simulation, the analyst structures a pharmacoeconomic decision problem as a set of conditions (aspects that persist over time) and events (aspects that occur at a point in time) within spreadsheet tables that specify condition values and event consequences.[1] Model execution involves the selected software reading the specifying tables and processing the consequences of each event when it occurs. The occurrence of events is implemented using straightforward background code that establishes an event schedule and maintains it as events happen and conditions change.
- A key advertised benefit of DICE simulation is transparency and ease of stakeholder review. The specification of a disease process and its care pathway in terms of conditions and events within a spreadsheet is argued to facilitate validation, as the reviewer needs only to be familiar with spreadsheet format and not with a particular software programme or programming language.[1]
- While a range of cohort-level and individual-level model types typical to pharmacoeconomic evaluations could be specified as a DICE simulation, and a DICE simulation could be specified within a range of software options, the transparency benefits of DICE simulation may be particularly appealing to individual-level pharmacoeconomic models, and contemporary pharmacoeconomic models are very likely to be built in Microsoft Excel®
    - An overwhelming majority of contemporary pharmacoeconomic models are built in Microsoft Excel®, as evidenced by a review of NICE STA documentation for STAs published between May 2016 and May 2017 that found 35 of the 36 company submissions *that stated model software* to have used Microsoft Excel®.[2]
    - In individual-level models versus cohort level models in Microsoft Excel®, there is a greater call to specify model logic as “back-end” Visual Basic for Applications (VBA) logic versus “front-end” spreadsheet logic
    - An overwhelming majority of contemporary pharmacoeconomic models are cohort-level models, as evidenced by the same review of STAs published between May 2016 and May 2017 finding 43 of the 48 submissions to be based on a pharmacoeconomic model specified solely at the cohort-level.[2] As such, practicing health economic modelers build and review far more cohort-level than individual-level models, and require and develop fewer practiced skills in the elements of VBA logic that are useful for individual-level models versus the subset of these required for cohort-level models (or, individual-level models specified as a DICE simulation)

NICE TA494: Naltrexone–bupropion for managing overweight and obesity

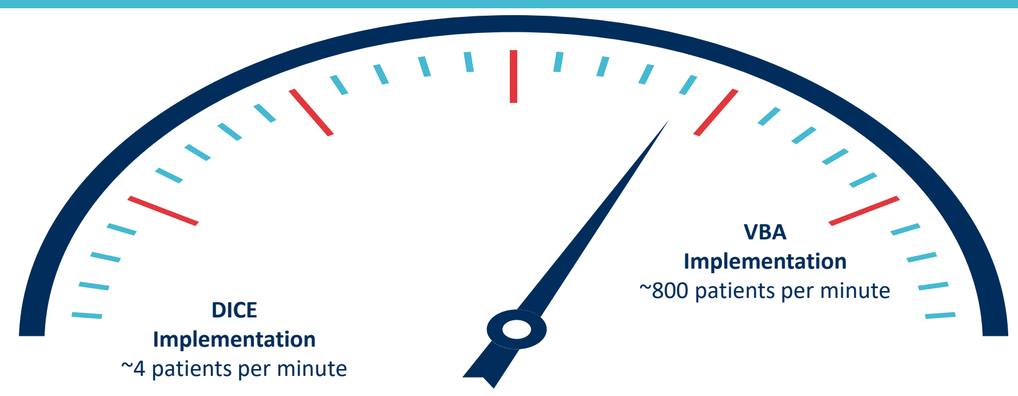
- The decision problem required the NICE appraisal committee to consider whether naltrexone-bupropion (NB), within its licensed indication and in addition to diet and physical activity, would be a clinically effective and cost-effective strategy for NHS England, for the management of people with obesity or overweight with risk factors.[3]
- The company approach to modelling built on an existing systematic review and economic evaluation of drugs to treat obese patients in primary care in the UK from Ara *et al.*,[4] produced as part of the UK National Institute for Health Research Health Technology Assessment programme.[3]
- An individual-level approach was considered better suited than a cohort-level approach to capture the chronic implications of both weight and weight-related health events in a heterogenous group of patients, by both Ara *et al.* and the company submission for TA494.[3,4]
- The key clinical effectiveness evidence for NB were from four multicenter, randomized, double-blinded, placebo-controlled studies. Data and assumptions about long-term effectiveness and natural history used in TA494 were underpinned by the work of Ara *et al.*[3,4]

Methods

- We reviewed published comment from the appraisal committee from NICE TA494 on the company’s approach to pharmacoeconomic modelling, and the use of DICE simulation in particular.

Results

- The Appraisal Consultation Document reports the Evidence Review Group (ERG) and company experiencing “extremely slow run times” and the committee concluded that “an alternative approach to implementing the DES model would be more practical for decision-making”.



- The ERG Report describes the ERG being able to “check formulae in the DICE sheet” but being “unable to examine the internal validity of the model according to its usual standards” and that this was mainly a “consequence of long model run times for one single deterministic analysis”.[5]
- The use of a DES model type was endorsed by the committee and ERG.[6]
- The Final Appraisal Determination states that a “revised model [using VBA directly] ran more efficiently”.[5] This “revised model” was similar to the originally submitted model, but implemented directly in VBA, trading off the transparency benefit of DICE spreadsheet tabulation for increased speed of model execution. Base case model execution was approximately 200 times faster in the revised version of the model.
- The revised model was deemed appropriate for decision-making.[6]

Discussion

- In TA494, the benefits of DICE simulation were clearly outweighed by its costs.
- The transparency benefits of DICE simulation, for both verification and validation, are more valuable for less typical pharmacoeconomic model types and pharmacoeconomic model types that require more underlying code logic versus spreadsheet logic, e.g. individual-level modelling approaches such as DES
- However, the cost of DICE simulation in terms of increased run time is pronounced in such modelling approaches. The difference in model execution speed between the originally submitted DICE implementation and revised implementation in TA494 is explained by the relative speed of processing calculations completely within VBA logic versus through interactions between VBA and spreadsheets in Microsoft Excel®.
- On the limitation of model execution speed, the introductory publication for DICE says only the following: “Very complex analyses requiring many profiles and scenarios may tax spreadsheet calculations but that is a limitation of the software not of DICE. Given its flexibility and transparency, DICE should be considered a good option whenever a decision-analytic model is required.”[1]
    - The pharmacoeconomic model underpinning TA494 was not very complex. That it analysed cost-effectiveness at the patient-level could be considered a complexity, but if so it is one that we would hope a unifying approach for pharmacoeconomic analysis would be able to comfortably handle.
    - The proponent of DICE may bear no responsibility for the processing speed limitations of spreadsheet calculation in Microsoft Excel®, but the model execution speed when using DICE simulation in software that is almost ubiquitous in contemporary pharmacoeconomic modelling is certainly relevant when considering DICE as an option for decision analytic modelling.
    - Our findings are consistent with conclusions from as separate study validating DICE against an equivalent code-based approach, published in July 2017.[7]

Conclusions

When considering implementing DICE methodology, the speed at which the chosen software can read specifying tables and process consequences of events, and the practical implications of this, should be carefully evaluated.

Evidence from TA494 suggests that applying DICE methodology for a DES in Microsoft Excel® may lead to impractically long run times for a NICE STA model.

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Further information is available on request. Please visit BresMed at Stand 605.

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