COMPREHENSIVE DISCRETE EVENT SIMULATION MODEL FOR THE EVALUATION OF HEALTH CARE TECHNOLOGIES IN DEPRESSION

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Background

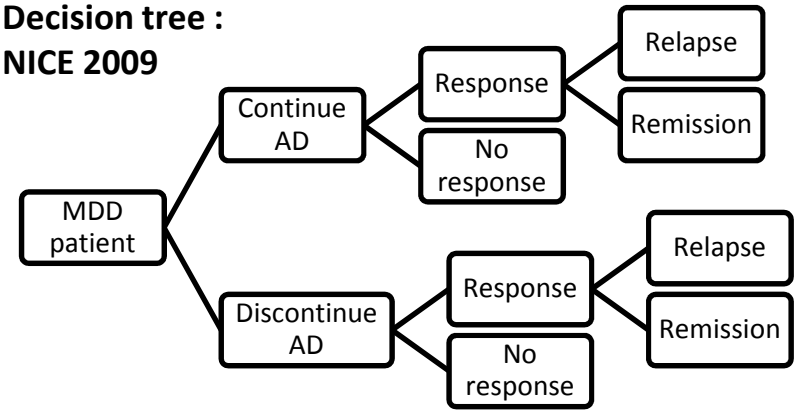
- Large number of antidepressant drugs on the market with different efficacy and tolerability profiles [1]

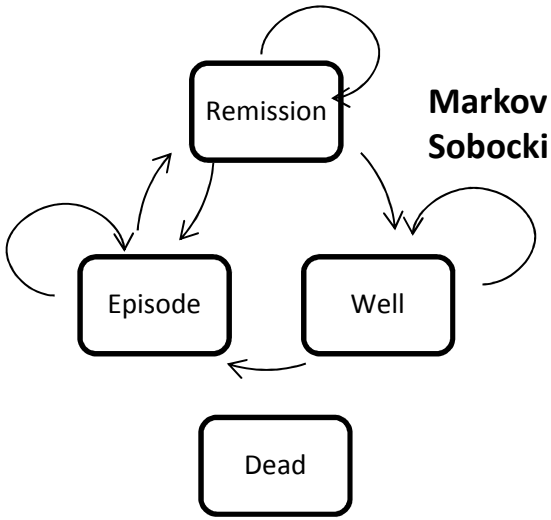
⇨ Cost-effectiveness analyses can be useful to guide the choice between alternative treatment strategies

- However, some limitations have been identified in the existing health economic models :
  - Short time horizon (i.e., 1 year)
  - Long-term clinical outcome (e.g., recurrence) and adverse events not often considered
  - Failure to account for subsequent treatments (often limited to 1st line)

⇨ *Flexibility* of decision trees and Markov models is limited:

Decision tree :
NICE 2009





Markov Model :
Sobocki et al., 2008

Cipriani et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet. 2009;373:746-758.

Objective

To develop a comprehensive Discrete Event Simulation (DES) model to reflect the clinical evolution of depressed patients over a long period and to simulate different treatment pathways in order to estimate health and cost outcomes associated with alternative treatments

Advantages of DES

- **Flexibility:**
  - Adaptable to a wide range of strategies in different countries
  - Variation in time horizon (from 1 year to lifetime)
- **Comprehensive:**
  - Taking into account relevant 'disease characteristics' and aspects of depression management (dose changes, switches, combination)
- **Accurate** predictions in the model

Attributes and events

- The model takes into account variability in MDD patient attributes at baseline:
  - Age
  - Gender
  - Number of previous depression episodes
  - Working status

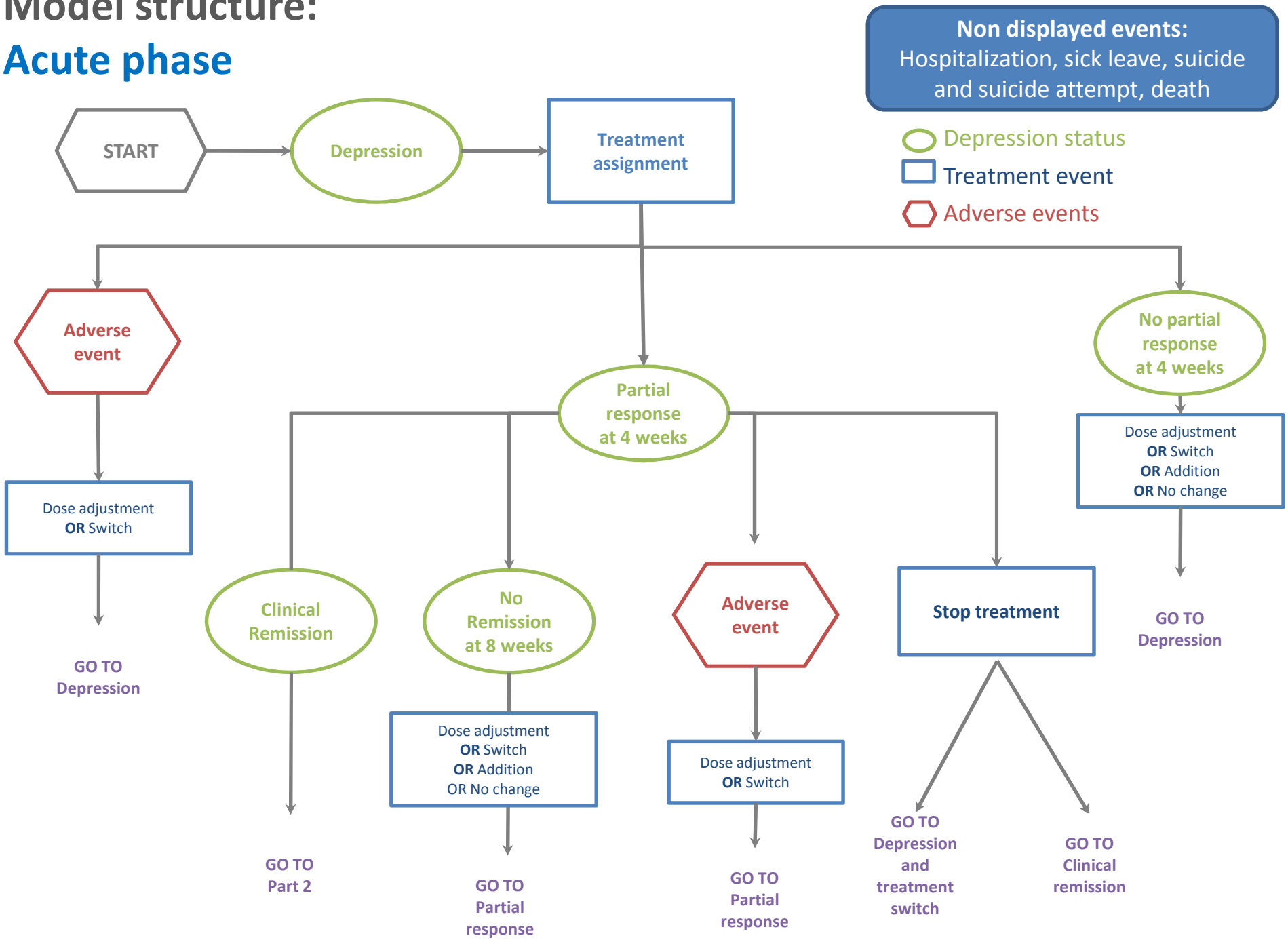
- All clinical events identified in previous models are included. In addition, consideration of:
  - 'Partial response' allowing for early switch
  - Two types of remission: 'clinical remission' based on the MADRS or HAM-D score, and 'full remission': a combination of clinical remission and normal functioning
  - Long-term events: 'relapse' and 'recurrence'

- Inclusion of relevant aspects linked to the tolerability profile of antidepressants with the consideration of the most frequent types of Adverse Events (AEs):
  - Nausea, diarrhea, headache, insomnia and others (short-term AEs)
  - Sexual dysfunction (long-term AE)

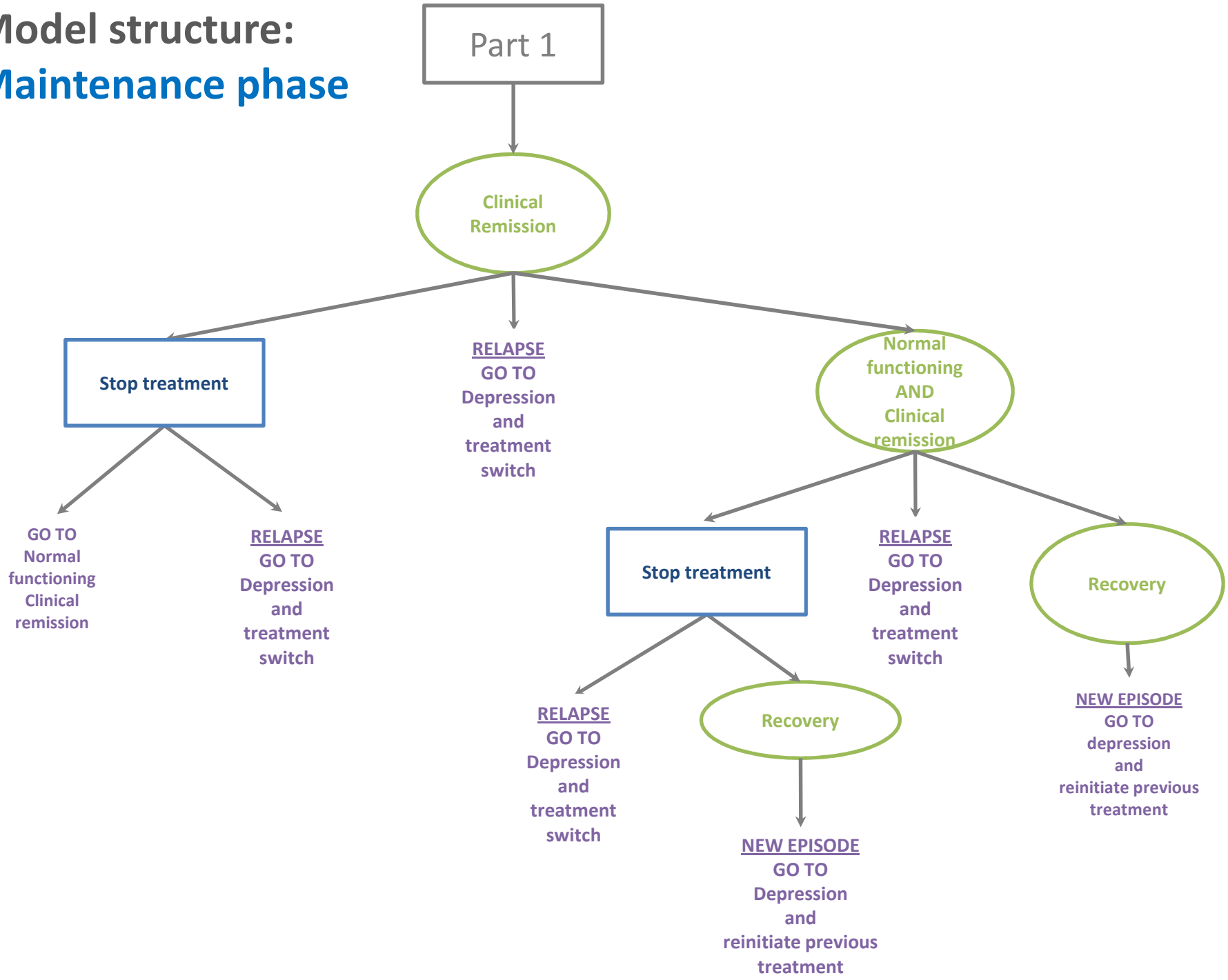
MADRS: Montgomery and Aasberg Depression Rating Scale
HAM-D: Hamilton Depression Rating Scale

Model structure:

Acute phase



Model structure:
Maintenance phase



Analyses

- Performed for testing the model and identifying parameters having the greatest influence/impact on results ('drivers')
- Inputs reflecting the UK setting:
  - Choice of the country driven by the data availability and the possible comparison of the results with those from previous models
- Model implemented using Base Case (BC) analysis:
  - Only one strategy
  - First line treatment = medium *efficacy / tolerability / treatment co*st profile
  - Choice of subsequent treatment depends on the reason for treatment change
- Software: Scilab v5.2.1

Hypothetical treatments with 3 profiles of efficacy, tolerability and treatment cost

LoE =Lack of Efficacy
AE= Adverse Event

1st-line

A
Efficacy: Medium
AE rate: Medium
Price: Medium

LoE | AE

2nd-line

B
Efficacy: High
AE rate: High
Price: High

C
Efficacy: Low
AE rate: Low
Price : Low

LoE | AE | LoE | AE

3rd-line

D
Efficacy: High
AE rate: High
Price: High

E
Efficacy: Medium
AE rate: Medium
Price: Medium

F
Efficacy: Medium
AE rate: Medium
Price : Medium

G
Efficacy: Medium
AE rate: Medium
Price: Medium

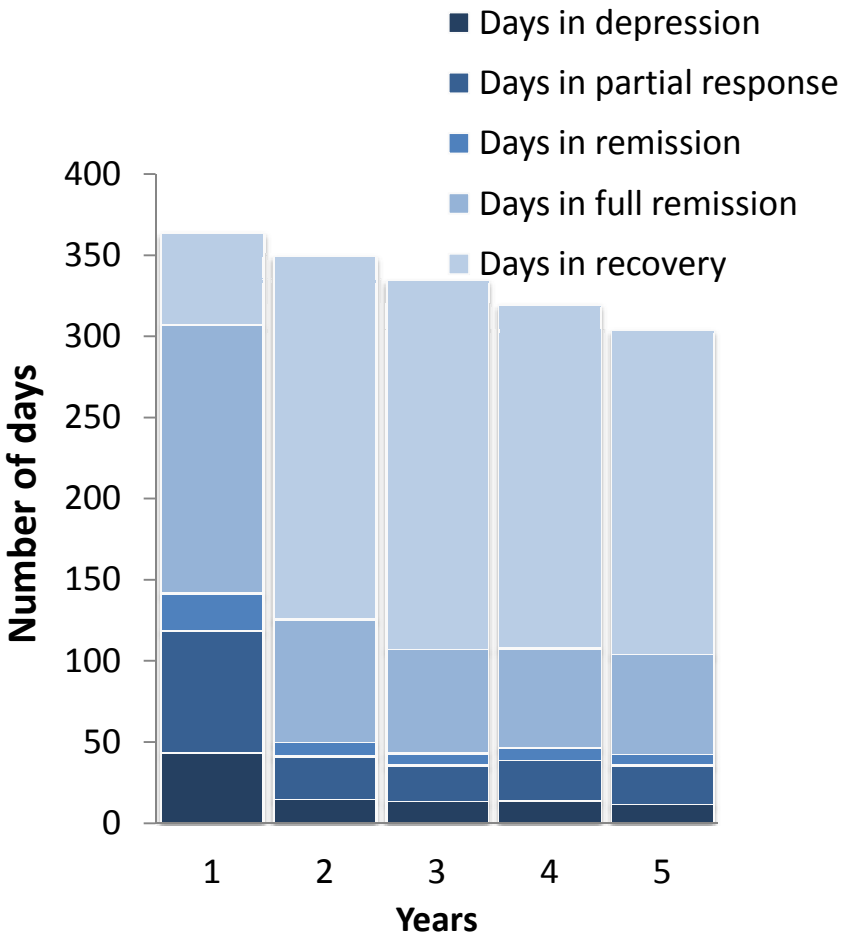
4th-line

Medium treatment | Medium treatment | Medium treatment | Medium treatment

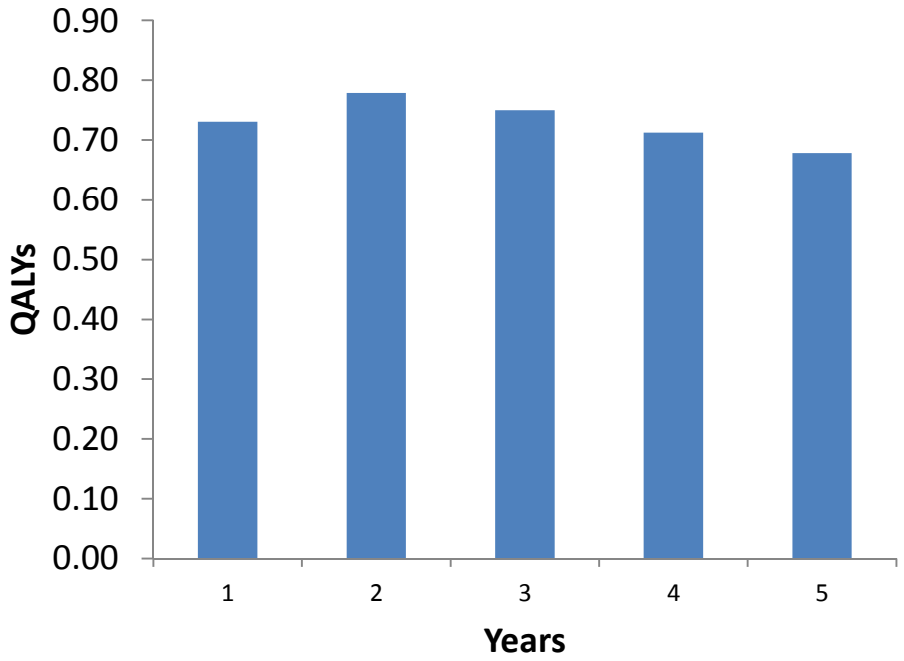
Outputs of the model

- Outputs given by strategy, by year and by full time horizon period:
  - *Quality-adjusted life years* (*QALYs*)
  - Time in depression (days), time in clinical remission (days), time in full remission (days), time in recovery (days)
  - Costs disaggregated in the following components:
    - physician costs, hospitalization costs, productivity loss costs, direct total costs and societal total costs
      - Direct total costs include all the costs with the exception of presenteeism cost and productivity lost
      - Societal total costs include all the costs
  - ICER (incremental cost-effectiveness ratio) per QALY per perspective (TPP and societal)

Average clinical status is stable after the second year

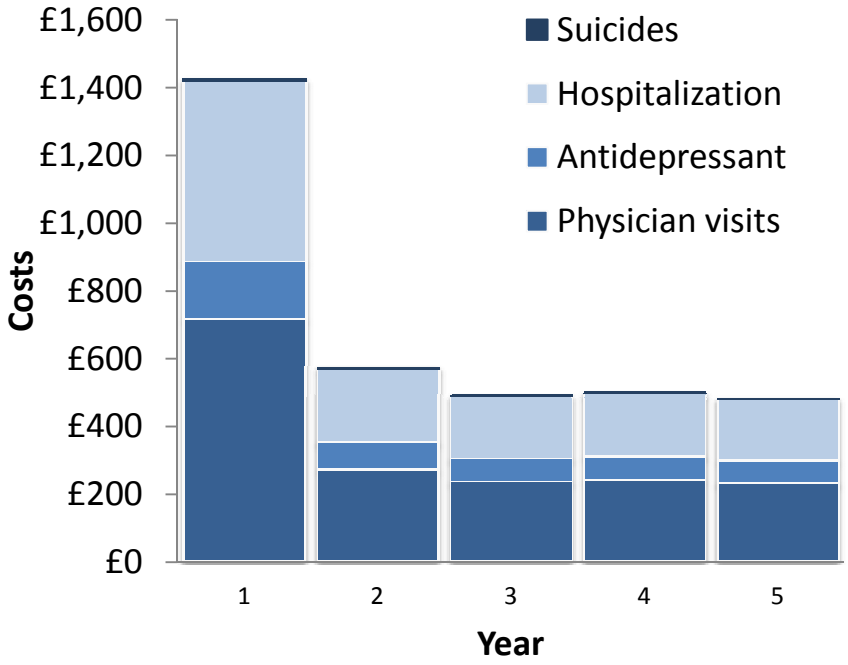


Distribution of average number of days/year by clinical status (all patients)

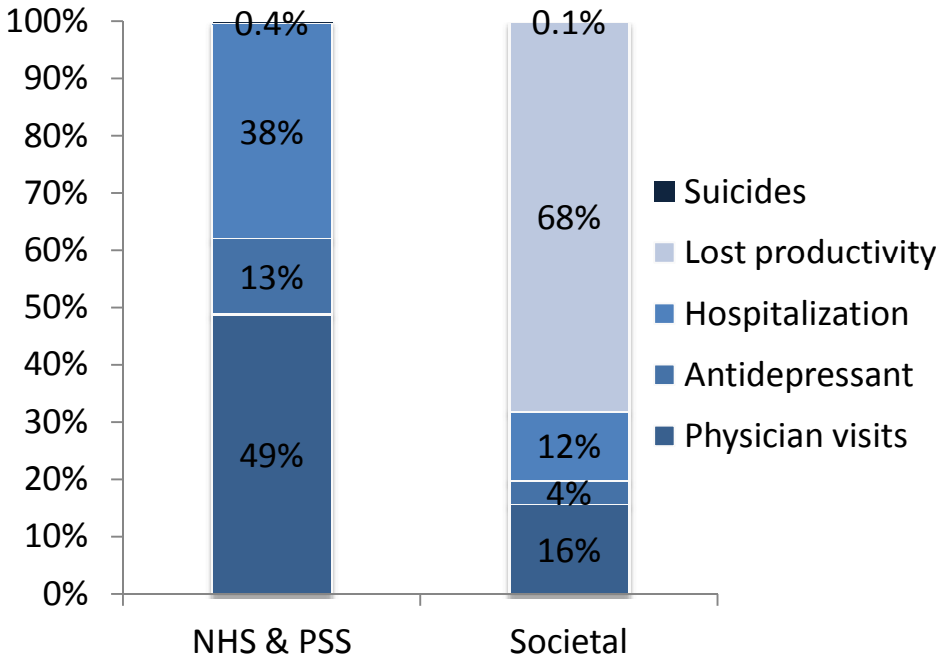


Number of QALYs by year

Hospitalisation and physician visits are the main cost drivers from the NHS & PSS perspective



Distribution of costs by component by year (in £)

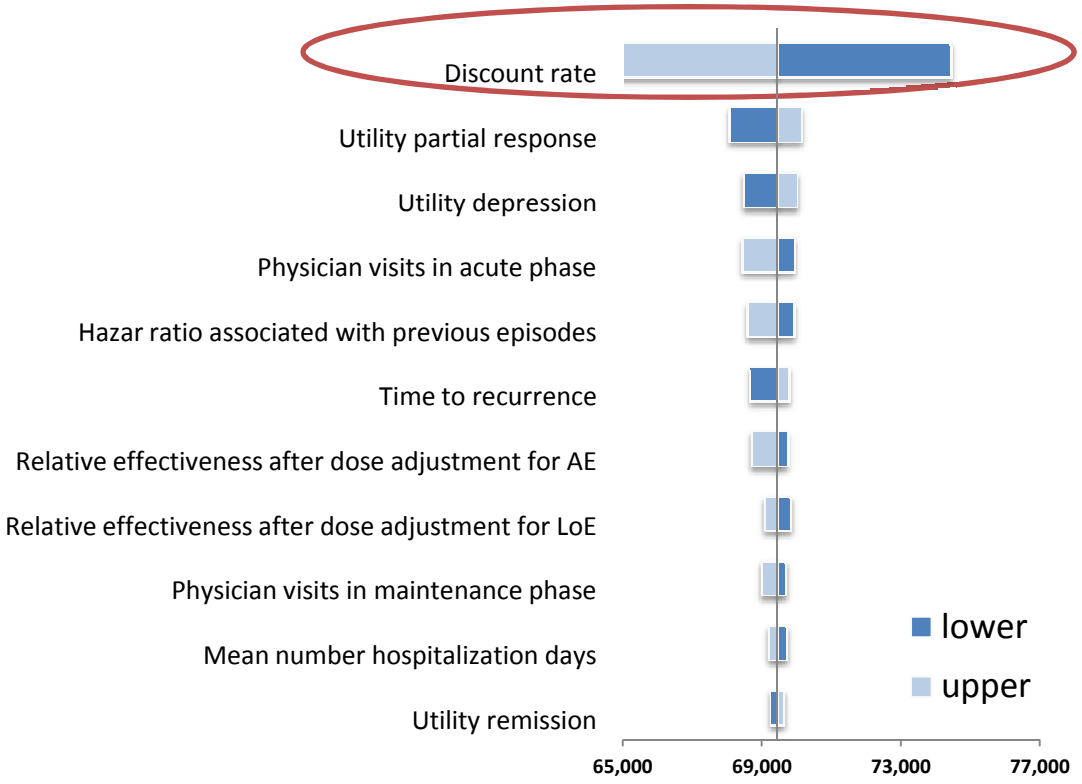


Distribution of costs by % and by perspective

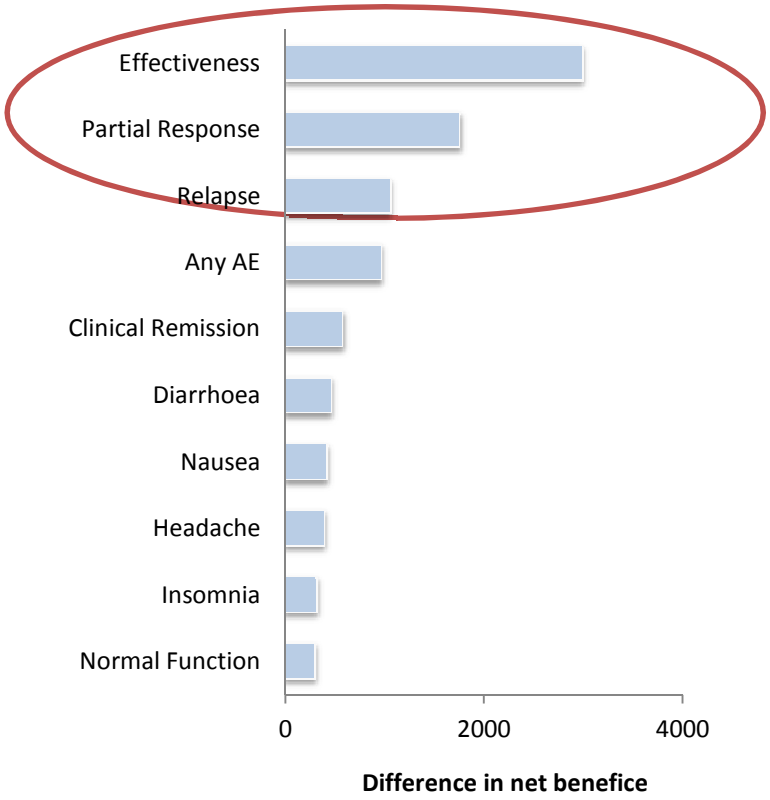
Effectiveness and discount rates are key drivers of net monetary benefit

Net monetary benefit = λ.ΔQALYs – Δcosts
λ: cost-effectiveness threshold

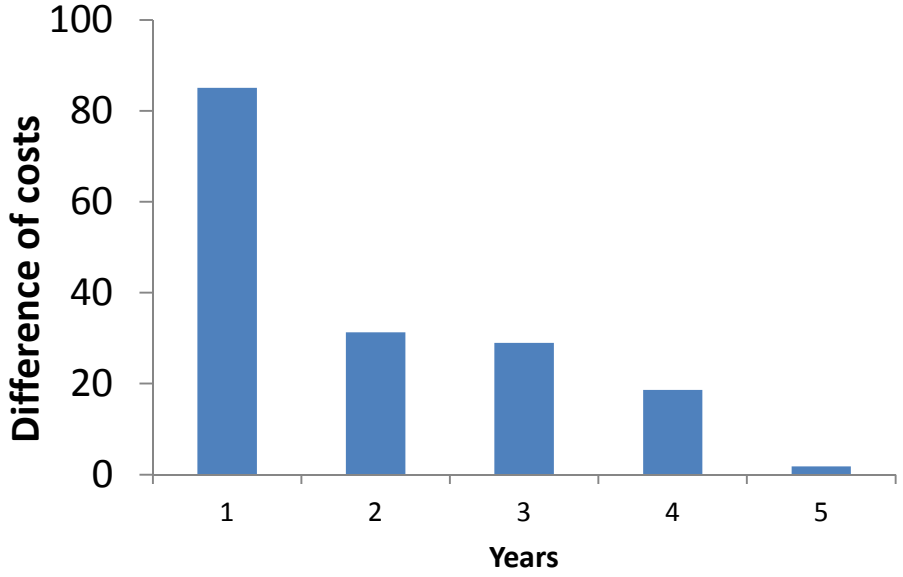
Non-treatment related parameters

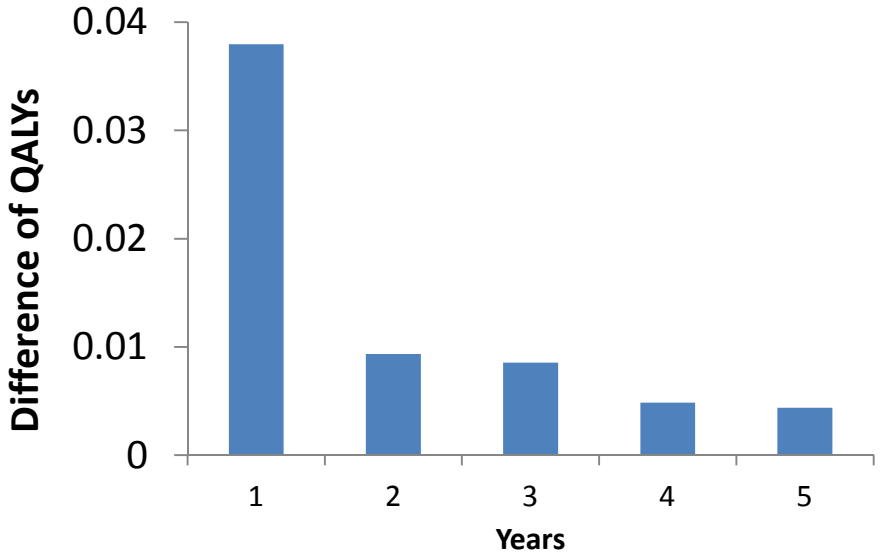


Treatment related parameters



Rationale for time horizon





Difference of NHS & PSS costs/QALYs between two profiles of treatment (high effectiveness and high price versus medium effectiveness and low price) over 5 years

- Reducing the time horizon from 5 to 3 years led to an underestimation of incremental costs by 10% and of incremental QALYs by 14%.

Sample size

- For 1,000 patients :
  - SE for incremental costs was £72.8/patient (45% of the mean)
  - SE for incremental QALYs was 0.010/patient (15 % of the mean)
  - 6500 patients are needed to detect a difference of 0.065 in QALYs (as observed) with a Standard Error (SE) of 5%

Discussion

- **QALY drivers :**
  - Effectiveness
  - Utility values associated with depression status
  - Relative effectiveness after dose adjustment for lack of efficacy.

- **Cost drivers :**
  - Effectiveness
  - Sick leave (from a societal perspective)
  - Frequency of physician visits

- DES model requires many input data ➔ several assumptions were needed at the time of this evaluation
- Overall results appear to be valid compared to those from the published literature

General conclusions

- **Comprehensive model to estimate health and cost outcomes associated with different treatments and therapeutic strategies in MDD patients**
  - The model considers both short-term and long-term clinical events
  - The model can incorporate a wide range of treatment pathways, over long-term
- **Flexible model:**
  - The model can be adapted to a wide range of treatment pathways
  - The model is designed to facilitate adaptations for different countries
- **Interactive open-source programs** http://www.open-model-mdd.org
  - Transparency
  - Facilitating use by other researchers
  - Enabling other researchers to contribute to model implementation (depending on data generation: *e.g., coming from observational studies*)

Thank you

http://www.open-model-mdd.org

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