The challenges of health economic modelling for mental health, behavioural and neurodevelopmental disorders

Sinha A, Jones C
Mtech Access, Bicester, United Kingdom

ISPOR Poster Acceptance Code: HTA4
Abstract ID: 131472

Introduction & Objectives

Mental health, behavioural and neurodevelopmental disorders affect up to 15% of the population (1). These disorders tend to be chronic, with long-term detrimental effects on quality of life. Furthermore, they pose significant burden to caregivers.

There are several challenges in economic modelling for pharmacological treatments for these disorders. For example, data from short-term clinical trials are often used to model the chronic disorders. Patients are likely to relapse and remit over the course of their disorder and are likely to present with comorbidities. Further, the subjective nature of these disorders might result in use of multiple effect-measuring scales. It can therefore be challenging to develop economic models that accurately represent the patient population and disorder history in question.

The National Institute for Health and Care Excellence (NICE) received 11 evaluations for treating disorders. This analysis summarises the model structures and assesses the methodology for sourcing base case parameter values. It examines challenges faced by manufacturers when developing models, and solutions attempted to mee these problems. Finally, it studies how Evidence Assessment Groups (EAGs) received these solutions.

Methodology

All health technology appraisals (HTAs) for mental health, behavioural and neurodevelopmental conditions were identified from NICE's website (2). Submissions that were terminated were omitted from the evaluation.

A data extraction table was developed to identify key features from each submission. The key features identified were:

- Model structure
- Patient population and comorbidities
- Time horizon and cycle length
- Clinical data values
- Resource use values
- Utility data values
- Data used to calculate societal costs and caregiver burden, if these were included in the submission

The sources used to parameterise the cost, clinical and quality of life data were also documented. Finally, comments from EAGs, although they were not presented in this poster.

Thus, an evaluation was carried out of the key modelling challenges, common solution and criticisms from EAGs.

Results

A total of 11 submissions were identified from NICE's website. Two were terminated due to insufficient evidence to develop an economic model for the chosen indication and population: TA286 and TA231. This left nine submissions for evaluation. Summary data for each of the nine remaining, non-terminated submissions were extracted and presented in Table 1.

Table 1: Summary of data extraction table for health technology appraisals approved for treatments of mental health, behavioural and neurodevelopmental disorders

Technology appraisal	Model structure	Clinical data source	Length of trial follow-up	Population & comorbidities	Measure of disease	Resource use source	Utility data source	Societal costs and caregiver burden
TA292: Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar 1 disorder[3]	Markov model, 3-year time horizon, 1-week cycle length	Treatment acute phase clinical data evaluated. Equal efficacy assumed among comparators	30-week study; 4-week acute phase and 26-week extension phase	Patients with comorbid diagnoses, including ADHD – criticised by EAG as not representative of clinical practice	Change from baseline YMRS score – 11-item instrument based on patients' subjective report of severity	Resource use intensity based on expert clinical opinion	No data found relevant to the population; data taken from a utility study for a proxy population	Not included
TA213: Aripiprazole for the treatment of schizophrenia in people aged 15 to 17[4]	Decision tree/Markov model hybrid, 3-year time horizon, 6-week cycle length	Clinical trial shows acute efficacy of intervention treatment, ITC for comparison. Long-term schizophrenia study data used	24-week follow-up; comparator efficacy from ITC; long-term data from schizophrenia study	Patients diagnosed with schizoaffective disorder, major depressive disorder, delirium, or bipolar disorder were excluded	Change in PNSS – considered gold standard in assessing antipsychotic treatments	Adult schizophrenia data applied to adolescents; validated by clinical experts	Schizophrenia values for adults presumed relevant for adolescents; experts recommend sensitivity analysis for differences	Not included
TA217: Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease[5]	Markov model, 20-year time horizon, 1-month cycle length	Data taken from clinical trials with the longest follow-up time of 6 months	4-week acute phase, 36-week extension phase	Clinical evidence not identified for patients comorbid with dementia; however, patients with Alzheimer's disease often also have dementia	Disease measured by time to institutionalisation, calculated as a composite of MMSE and ADCS-ADL scores – subjective and non-subjective tests	Taken from IPD studies, UK Dementia report	Data taken from five QoL studies, two of which were for the correct population	Caregiver utility considered in a scenario analysis Caregiver costs not found
TA854: Esketamine nasal spray for treatment-resistant depression[6]	Markov model, 5-year time horizon, 4-week cycle length	Clinical trial data and systematic review confirmed treatment efficacy and relapse/discontinuation rates for treatment-resistant depression therapies	24-week follow-up	Trial excluded patients with some psychiatric comorbidities – criticised by EAG as treatment resistant depression is correlated with psychiatric comorbidities	Depression measured using MADRS scale – subjective measure of severity of depression	Retrospective review of patients in primary and secondary care commissioned by the company	Health state utility values taken from clinical trial	Caregiver costs and disutility included as a scenario
TA114: Methadone and buprenorphine for the management of opioid dependence[7]	Decision tree with Monte Carlo simulation, 1-year time horizon, assessing outcomes at 2, 6, 13, 25 and 52 weeks	Seven clinical trials comparing intervention treatments	Initial treament for 13 weeks, open-label trial for 72 weeks	Evidence is reported for patients with no serious psychiatric or medical comorbidities	Retention on treatment, illicit use of opioids	Literature sources	Health state utilities taken from 2005 paper	Sensitivity analysis includes effects of omitting crime victims' costs; data from RWE study
TA325: Nalmefene for reducing alcohol consumption in people with alcohol dependence[8]	Markov model, Acute phase: 1-year, 1-month cycles. Maintenance phase: 5-years, 1-year cycles	Clinical trial data and subsequent literature on treatment evaluation	24 and 52-week follow-ups	Patients excluded from clinical trial with current axis 1 disorders others than GAD, SAD	POM: change from baseline in number of heavy drinking days, change in total alcohol consumed	Resource use intensity based on a clinically validated assumption	Pooled results from EQ-5D surveys in the treatment's clinical trials	Crime risk and productivity costs included in scenario analysis
TA115: Naltrexone for the management of opioid dependence[9]	Decision tree with Monte Carlo simulation, 1-year time horizon, assessing outcomes at 2, 6, 13, 25 and 52 weeks	Data from five clinical trials for the intervention treatment combined and used in Kaplan-Meier analysis	Mean length of follow-up of 29 weeks	Patients with severe comorbidities excluded from all clinical studies – criticised by EAG	Retention on treatment, illicit use of opioids	Literature sources	Health state utilities taken from 2005 paper	Not included
TA337: Rifaximin for preventing episodes of overt hepatic encephalopathy[10]	Markov model, Lifetime (42 years) time horizon, 1-month cycle length	6 and 24-month trial data extrapolated via Kaplan-Meier curves	24-week follow-up	Clinical trial excluded medical conditions that may impact study participation	Time to remission/overt episodes – committee satisfied that relevant outcomes assessed	Based on clinical trials or validated assumptions	Derived from a utility study	Not included
TA367: Vortioxetine for treating major depressive disorder[11]	Decision tree/Markov model hybrid, 12-month time horizon, 2-month cycle length	Trial interventions; comparator ITC data; clinician-validated literature inputs	12-week follow-up	Patients excluded from clinical trial with current axis 1 disorders other than GAD, SAD	Mean change from baseline MADRS scores – criticised by EAG as score made of only 10 items	Clinical trial, clinical advice RWE identified in a systematic literature review	Acute phase: trial data Maintenance phase utility values: French MDD patient study	Not included

Abbreviations: ADHD, attention deficit hyperactivity disorder; EAG, Evidence Assessment Group; GAD, general anxiety disorder; IPD, individual patient data; ITC, indirect treatment comparison; MADRS, Montgomery Asberg Depression Ratings Scale; MDD, major depressive disorder; MMSE, Mini Mental State Examination; Activities of Daily Living for Mild Cognitive Impairment; POM, primary objective measure; PNSS, Positive and Negative Syndrome Scale; QoL, quality of life; RWE, real-world evidence; SAD, social anxiety disorder; YMRS, Young Mania Rating Scale.

Conclusion

Four main challenges have been identified across models for mental health, neurological, and behavioural disorders. Firstly, the exclusion of patients with comorbid disorders resulted in criticism. Patients will often suffer with comorbid disorders. Exclusion of comorbidities in clinical trials, therefore, is unrepresentative of patients in clinical practice. This challenge may be addressed by seeking clinical opinion when determining clinical trials' inclusion and exclusion criteria.

Secondly, the use of patient-reported measures of disease drew some criticism. Clinical outcomes are often measured with scales that assess the presence of disorders according to patient surveys. The responses to these surveys are subjective, resulting in potentially inaccurate clinical efficacy data in economic models. However, these measures of disease tend to be used in clinical practice. They are therefore likely to be the best measures of clinical efficacy for economic models in mental health disorders.

Thirdly, a lack of long-term clinical data has been criticised, given the chronic nature of most mental health disorders. Using a shorter time horizon, or extrapolating from short-term data may not fairly represent the true nature of these disorders, compromising models' cost-effectiveness results. However, extrapolation of short-term data as a solution to this challenge received the most positive response from EAGs.

Lastly, submissions were criticised for excluding the caregiver burden and disutility. Disutility data for caregivers are lacking, therefore submissions included caregiver effects as a scenario, at most. The lack of data for caregiver disutility was often acknowledged by EAGs.

It should be noted that many submissions had to rely on proxy data or data identified through literature sources for health state utility and resource use data, as these values were not collected in clinical trials. These approaches were well-received by EAGs, if sources were representative of the economic model's patient population.

Mtech Access

ISPOR Europe 2023, 12–15 November 2023, Copenhagen, Denmark

(Stand No. C3-053)

References

1. CG123: Common mental health problems: identification and pathways to care. NICE 2011
2. NICE. Mental health, behavioural and neurodevelopmental conditions. Available at: https://www.nice.org.uk/guidance/conditions-and-diseases/mental-health-behavioural-and-neurodevelopmental-conditions
3. TA292: Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder. NICE 2013
4. TA213: Aripiprazole for the treatment of schizophrenia in people aged 15 to 17. NICE 2011
5. TA217: Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease. NICE 2013
6. TA854: Esketamine nasal spray for treatment-resistant depression. NICE 2022
7. TA114: Methadone and buprenorphine for the management of opioid dependence. NICE 2007
8. TA325: Nalmefene for reducing alcohol consumption in people with alcohol dependence. NICE 2014
9. TA115: Naltrexone for the management of opioid dependence. NICE 2007
10. TA337: Rifaximin for preventing episodes of overt hepatic encephalopathy. NICE 2015
11. TA367: Vortioxetine for treating major depressive disorder. NICE 2015

Abbreviations

EAG: Evidence assessment group
EQ-5D: EuroQoL 5 Dimensions
GAD: General anxiety disorder
HRQoL: Health-related quality of life
HTA: Health technology appraisal
IPD: Individual patient data
ITC: Indirect treatment comparison
MADRS: Montgomery–Åsberg Depression Rating Scale
MDD: Major depressive disorder
NICE: The National Institute for Health and Care Excellence
POM: Primary outcome measure
QoL: Quality of life
RWE: Real-world evidence
SAD: Social anxiety disorder