NOTTINGHAM CLINICAL TRIALS UNIT
at the University of Nottingham

"Put a SoC in it!"- approaches for incorporating standard of care comparisons in head-to-head within-trial economic evaluations: A case study from the BRIGHTMIND trial.

Edward Cox, Sandy Ma, Mathew Keane, Marilyn James

Background

Randomised controlled trials (RCTs) serve as valuable tools for evaluating the effectiveness, safety, and cost-effectiveness of new treatments. While RCTs typically compare experimental interventions to a standard of care (SoC) or placebo, there are many instances where this benchmark is not included as a comparator, typically due to ethical concerns, feasible issues, and/or clinical interest. Such head-to-head trials can leave decision makers responsible for local commissioning and those issuing national guidance in a difficult position, particularly if trial arms represent a significant departure from routine care. This work explores methods to help provide indirect economic comparisons of trial alternatives to SoC by using data from the BRIGHTMIND trial.

Methods

The BRIGHTMIND trial tested the effectiveness of treating moderate to severe treatment resistant depression using repetitive transcranial magnetic stimulation (rTMS) or personalised MRI connectivity guided stimulation (cgiTBS), treatments that are only available in very select areas of the UK and according to strict criteria. We seek to provide evidence of their cost-effectiveness compared to current SoC, an alternative not compared within-trial and one that markedly differs in its approach, cost and efficacy to magnetic stimulation. To help bridge this gap, we developed a SoC vignette with a plausible trajectory of outcomes and costs guided by expert opinion, data from BRIGHTMIND and the literature. The SoC vignette assumes participant health-related quality of life (HRQoL) persists at baseline values over the 6-month trial horizon; and that health care utilisation aligns with that observed sans intervention costs, see Figure 1). This scenario analysis was seen as a conservative assessment of cost-effectiveness since HRQoL gains beyond the trial time horizon, and potential health service savings from improved status, were not included. We are in the process of incorporating literature findings, a structured expert elicitation and new trial data within a decision-analytic model (DAM) framework (Figure 2).

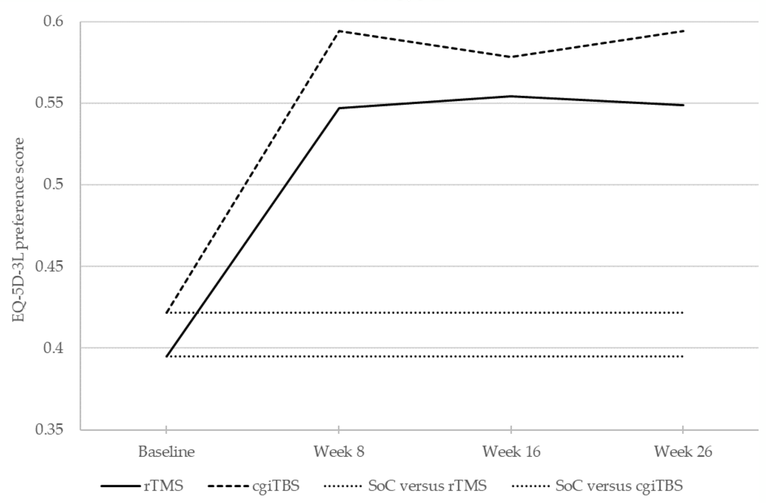
Results

Figure 1

Costs

rTMS versus SoC	
rTMS	
Intervention cost	£2,354
Health care costs	£1,067
SoC	
Intervention cost	£0
Health care costs	£1,067
rTMS versus SoC	
cgiTBS	
Intervention cost	£2,309
Health care costs	£771
SoC	
Intervention cost	£0
Health care costs	£771

HRQoL



	Costs	QALYs	ICER
SoC	£771	0.204	
cgiTBS	£3080	0.280	£30,520

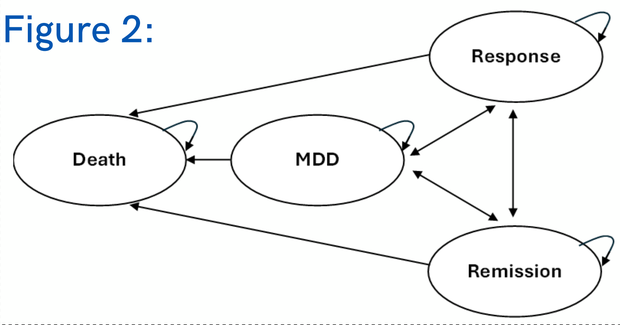
QALY: Quality-adjusted life years; ICER: Incremental cost-effectiveness ratio

	Costs	QALYs	ICER
SoC	£1067	0.197	
rTMS	£3422	0.264	£35,150

QALY: Quality-adjusted life years; ICER: Incremental cost-effectiveness ratio

In both scenario analyses, the incremental cost-effectiveness ratios for both magnetic stimulation therapies exceeded £30,000/QALY. ICER's fell below £30,000/QALY with modest extrapolations in HRQoL and when distributing equipment costs over more people than the trial average (base case analysis only 51 people). These vignettes informed by expert opinion, the literature and conservative assumptions where necessary, are fast scenario analyses to produce and can serve as a useful benchmark for commissioners and relevant stakeholders. Where researcher time and evidence permits, SoC can be better specified within a DAM:

Figure 2:



BRIGHTMIND trial data
CLAHRC trial data
Structured expert elicitation
Further literature

Ongoing work, watch this space!

Conclusion/Discussion

This study explores ways in which we can use trial data, methodological assumptions, expert opinion and modelling to help bridge an important gap between interventions in head-to-head trials and SoC when evaluating their cost-effectiveness. The results from this research are primarily designed to inform UK resource allocation decisions for the treatment of moderate to severe treatment resistant depression, however we hope the findings can serve similar head-to-head within-trial economic evaluations and aid in discussions surrounding best methodological practice.

University of Nottingham
UK | CHINA | MALAYSIA

NIHR | National Institute for Health Research

MRC Medical Research Council

This work was funded by the Efficacy and Mechanism Evaluation (EME) programme, a MRC and National Institute for Health and Care Research (NIHR) partnership.