EUnetHTA JA3 WP4 - Other technologies,
Comments by external experts on the 2nd draft rapid assessment on HF-rTMS for TRD

Comments should be submitted not later than 15:00 *17/03/2017*

The objective of this reviewer form for external reviewers is to standardise the process of reviewing rapid relative effectiveness assessments by external reviewers.

The reviewer form is organised and structured in a similar fashion to the assessment template. The form will consequently address the following:

Part I) Methods (please see Appendix 1 or chapter 2 of the assessment)
Part II) Results: Domain reports
Part III) Summary of relative effectiveness (please see summary section of the assessment)
Part IV) Other considerations

Please use this form for submitting your comments and please return to coordination team representative: judit.erdos@hta.lbg.ac.at

1. Please put each new comment in a new row.
2. Please insert the page number and section number on which your comment applies. If your comment relates to the document as a whole, please put **'general'** in this column.
3. Please provide a description of your comment as specific as possible and preferably also provide a suggestion for rewording. If you wish to draw our attention to published literature, please supply the full reference.
4. Please **DO NOT** comment on typos or wording as long as they do not affect comprehensibility/readability of the assessment – the document will undergo medical editing prior to publication.

All comments will be formally responded to in a combined document that will be published on the EUnetHTA website, individual names of the reviewers disclosed.

The 2nd version of the Rapid Assessment on HF-rTMS for TRD is open to review by external reviewer(s) between 10/03 and 17/03/2017.

Please add extra rows as needed.

[1] a "major": the comment points to a highly relevant aspect and a thorough answer is expected from the author(s)
b "minor": the comment does not necessarily have to be answered in a detailed manner
c"linguistic": grammar, wording, spelling or comprehensibility

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Comment from *Insert your name, title and affiliation*	**Page number** *Insert 'general' if your comment relates to the whole document*	**Line/ section number**	**Comment and suggestion for rewording** *Please insert each new comment in a new row.*	**Character of comment** • 'major'[a] =1 • 'minor'[b] = 2 • 'linguistic'[c] =3 *Please indicate your choice by writing the according number in this field, e.g. for major choose "1".*	**Author's reply**
EH		266	Flow chart: Why the 3 studies not available had been excluded from the systematic review of literature? Do you try to contact the investigators or authors ?		Yes, we did and received no answer.
Summary					
Description and technical characteristics of the technology					
EH	23	442	MagPro X100 is missing		MagPro X100 is a research device, we were considering only the therapeutic devices.

Please add extra rows as needed.

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EH	23	457	"nor the patient can say if the active or sham coil is being used" : In most studies, I'm sure that it's wrong.		We changed the paragraph to: "Sham stimulation is defined as comparator in the scope of this assessment. Sham stimulation is delivered either with regular TMS coil that is tilted so that an edge remains in contact with the head or with a purpose-built sham TMS coils that resemble regular TMS coils but is equipped with a magnetic shield that attenuates the magnetic field. If a tilted regular coil is used, a sham TMS pulse produces a clicking sound that is very similar to an active TMS pulse and, depending on the geometry and orientation of the TMS coil, the magnetic field can still be sufficiently strong to result in somato-sensory effects. This variant was used in many clinical studies, but the current gold standard seems to be the purpose-built coil combined with surface electrodes for skin stimulation. The critical question is still whether blinding success can be achieved with the combined coil. Several very similar sham TMS setups were developed and their blinding success was evaluated. The general finding of these studies was that electrical stimulation of the skin resulted in somato-sensory effects that were very similar to active TMS if the stimulation intensity was individually calibrated. However, the skin sensation was more electric so that experienced participants might have been able to distinguish between active and sham TMS. Indeed, naïve participants have been found to mistake sham TMS for active TMS, whereas experienced participants can tell them apart. These results indicate that sham TMS approaches might suffice for clinical applications where patients are generally naïve to differences between active and sham TMS, in which case a blind research design is achieved (operator, the patient and the investigators are blinded). Never-theless, the sham approaches require further developments and efficient blinding should be con-trolled for by systematically questioning the patients about their guess as to group allocation" https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4341423/

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EH	24	471	"There are no absolute contraindications for ECT": it's wrong; intracranial hypertension is an absolute contraindication as unstable medical condition		We corrected. "The absolute contraindication for ECT is intracranial hypertension, however, patients with myocardial ischemia, cardiac arrhythmias, space-occupying cerebral lesion, increased intracranial pressure, recent cerebral haemorrhage, unstable vascular aneurysm or malformation, abdominal aortic aneurysms, pheochromocytoma, and class 4 or 5 anaesthesia risk are also more likely to be harmed as they carry a higher morbidity and mortality risk."
EH	26	558	"558 about 60 minutes (15 minute treatment and 45 minutes …": it's not so long, approximately30 to 40 min: 5 to 10 min treatment and 20 to 30 min preparation and post-treatment routine		We corrected. "According to clinical experts, ECT treatment takes about 25-40 minutes (5-10 minute treatment and 20-30 minutes preparation and post-treatment routine)."
Health problem and current use					
EH	30	707	TRD is associated with significantly higher per-patient medical costs due to higher health care utilization (Olchanski et al, 2013)		We add this refernce and the sentence: "According to a study on the economic burden of TRD (reference), due to higher health care utilization TRD is associated with 29.3% higher per-patient medical costs than non-TRD." https://www.ncbi.nlm.nih.gov/pubmed/23490291
EH	30	717	i.e. Antidepressant Treatment History Form (1990; 1999)		We added this information with these 2 references: Sackeim et al., The impact of medication resistance and continuation pharmacotherapy on relapse following response to electroconvulsive therapy in major depression. J. Clin. Psychopharmacol. 1990, 10 (2), 96–104. Oquendoet al., Inadequacy of antidepressant treatment for patients with major depression who are at risk for suicidal behavior.Am. J. Psychiatry 1999, 156 (2), 190–194.
EH	30	718	Remission rate is about 37% with a first line of antidepressant (STAR*D)		We were referring to response rate. We added this information about remission.

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EH	31	727	The Maudsley Staging Method is more efficient in staging treatment resistance than currently available method (Fekadu et al, 2009; 2012)		We add a sentence about this staging method: "The Maudsley Staging Method is also used in staging treatment resistance. It is a points-based staging model incorporating 3 factors: treatment, severity of illness, and duration of presenting episode. The overall level of resistance estimated using this model varies from minimal to severe resistance. The rating system allows specifying categories: mild (score of 3), moderate, and severe (score of 15), based on severity of resistance." https://www.ncbi.nlm.nih.gov/pubmed/19192471
Clinical effectiveness					
Safety					
EH	45	1196	There are few data concerning patients subgroups (ie psychomotor retardation, and nicotinic consumption) (Poulet et al 2016; Brunelin et al, 2014)		They are LF-rTMS interventions, which was out of our scope, that's whya we did not include them.
Appendix					

Please add extra rows as needed.

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Depending on your expertise, you may want to comment on some of the questions provided below.

	Yes	Partly (please specify)	No (please specify)	Other (please specify)
Part I: Methods				
1. Are inclusion/exclusion criteria for selection of the studies described in appropriate detail?				
2. Are the quality appraisal tools appropriate?				
3. Is the type/presentation of evidence (e.g. Meta analysis, qualitative synthesis, GRADE) appropriate for this analysis?				
4. Is the risk of bias sufficiently assessed, both on study level and on an outcome level?				
5. Is the choice of study types appropriate to the population, intervention(s), comparison(s) and outcome(s)?				
6. Are the types of studies to be included (randomised trials, quasi-randomised trials or other designs) described?				
7. If it was relevant to include data from indirect comparisons, is this step justified and the methods of indirect comparisons sufficiently described?				
8. Are appropriate methods of measuring each outcome and appropriate time points for measurement identified?				
Comments:				

9. Are details on sources of information and literature search strategies provided?					
Search strategy	Databases	Year range	Language restriction	Primary data	Other kind of information resources
O	O	O	O	O	O
Comments:					

10. Information on basis for the assessment and interpretation of selected data and information:		
Method of data extraction described?	Critical appraisal method (for quality assessment of the literature) described?	Method of data synthesis described?
O	O	O
Comments:		

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	Yes	Partly (please specify)	No (please specify)	Other (please specify)
Part II: Results (See Domain Reports)				
Description and technical characteristics of the technology				
1. Does the section describe the intervention under review including how it works and how it may have an impact on potential recipients?				
2. Does the section describe the comparator(s) under review including how it works and how it may have an impact on potential recipients?				
3. Are the supporting references current and do they provide an international picture of the problem?				
Comments:				
Health problem and current use of the technology				
4. Does the section describe the health issue including incidence and prevalence, how it occurs, who is affected (including high-risk groups, vulnerable/disadvantaged populations, where it occurs, how it is diagnosed, symptoms and consequences)?				
5. Are the supporting references current and do they provide an international picture of the problem?				
Comments:				
Safety and effectiveness				
6. Is the risk of bias clearly reported?				
7. Is quality of data sufficiently evaluated?				
8. Are both relative and absolute effect measures presented for each dichotomous outcome?				
9. Are continuous data reported according to appropriate statistics (e.g. 'standardised mean difference' or 'weighted mean difference')?				
10. In case of time-to event analysis, are hazard ratios (HR) and ratios of medians presented?				
11. Are measures of the precision of the effect estimates presented or, in case of absence of this essential information, is this fact reported?				
12. Is frequency of adverse events, frequency of occurrence, relative risk or number needed to harm (NNH) presented for the safety data?				

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	Yes	Partly (please specify)	No (please specify)	Other (please specify)
13. In cases where adverse events are incorporated in utility values of quality of life, is the source of quantification accessible?				
14. Was the transformation of the surrogate outcomes into patient-relevant final outcomes considered (if relevant)?				
Comments:				
General				
15. Do you agree that the data extracted are relevant to the research questions formulated in the beginning and that analysed and synthesised data still answer the question?				
16. Can the results be applied to the intended population?				
17. Is the assessment sufficiently transparent and evidence ('facts') distinguished from judgements (including values and preferences)?				
Comments:				
Part III: Summary of Relative Effectiveness				
18. Does the summary present a balanced representation of the content of the report?				
19. Does the discussion of the summary clearly address the uncertainty in the available evidence, the evidence gaps and the applicability of the evidence?				
Comments:				
Part IV: Other Considerations				
20. Have all relevant ethical, organisational, social and legal aspects been considered? (See Appendix 3 of the Pilot assessment)				
Comments:				

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