

National Institute for Health and Care Excellence
IP1767 Transcranial magnetic stimulation for auditory hallucinations

IPAC date: 11 June 2020

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response
1	Consultee 1 Company Magstim	General	During the meeting a clear need was conveyed for an alternative treatment for auditory hallucinations (AHs) and the wide variety of patients groups who may experience these. The amount of published TMS research in this area was larger than initially anticipated. Some studies were likely limited by too short durations and unrefined protocols. Overall, the meeting gave hope for TMS having some potential as a future treatment option for patients suffering from AHs.	Please respond to all comments Thank you for your comment.

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2	Consultee 2 Royal College of Psychiatrists	1.2	<p>Paragraph 1.2</p> <p>As this recommendation is focused on particular type of psychopathology in psychosis i.e., auditory hallucinations, it would be appropriate to explicitly mention that studies should report details of patients selection, including specific psychopathology and nature of mental disorder.</p> <p>They should also describe methods used in localisation of stimulation site such as neuronavigation or conventional methods to identify the anatomical region for the treatment.</p>	<p>Please respond to all comments</p> <p>Thank you for your comment.</p> <p>Section 1.2 of the draft guidance has been changed to include specific psychopathology.</p>
3	Consultee 2 Royal College of Psychiatrists	1.1	<p>Line 4</p> <p>As stated in the document, auditory hallucinations are experienced in various conditions both in functional and organic illnesses. However, this review relates to psychosis (schizophrenia), it is important that this is mentioned at the end of the paragraph to avoid misinterpretation of the recommendation by patients suffering with hallucinations secondary to non-psychotic conditions.</p>	<p>Thank you for your comment.</p> <p>The indication is 'auditory hallucinations', including hallucinations secondary to non-psychotic conditions, but most of the evidence identified related to schizophrenia.</p> <p>A committee comment has been added, noting that most of the evidence was from patients with schizophrenia.</p>

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4	Consultee 2 Royal College of Psychiatrists	2.3	Paragraph 2.3 Line 19 The magnetic field is <u>localised to the region of stimulation</u> therefore this needs to be mentioned in the sentence along with <i>relatively powerful but short lived</i> .	Thank you for your comment. This section of the guidance is intended to be a brief summary of the way the procedure is typically done. 'Targeted area of the brain' has been added to the procedure description.
5	Consultee 2 Royal College of Psychiatrists	2.3	Line 21 Kindly consider adding, <i>The excitatory and inhibitory effects on cortical neurons <u>depends on frequency of the pulse stimulation.</u></i>	Thank you for your comment. This section of the guidance is intended to be a brief summary of the way the procedure is typically done. The Committee considered this comment but decided not to change the guidance.
6	Consultee 2 Royal College of Psychiatrists	2.3	Line 22 <i>The amount of stimulation and target area is adjusted for each patient, <u>based on various factors including resting motor threshold.</u></i>	Thank you for your comment. This section of the guidance is intended to be a brief summary of the way the procedure is typically done. The Committee considered this comment but decided not to change the guidance.

7	Consultee 2 Royal College of Psychiatrists	3.3	<p>Paragraph 3.3</p> <p>Over the recent past TMS has been offered to patients in both NHS and private setting. Within England there are more than 25 clinics administering TMS for multiple psychiatric conditions under research or clinical treatment pathway. It is well established that majority of patients tolerate common side effects well without considerable difficulties.</p> <p>Evidence within this review suggest headache, muscle twitching, localised discomfort at the site of stimulation are some of the common side effects and rare side effects such as exacerbation of symptoms in dropouts. However in the recommendation document this has been inferred as <i>'worsening underlying psychiatric disease.'</i></p> <p>In my opinion exacerbation of symptom is very different from worsening of psychotic disorder, therefore this needs to be reworded as there is no evidence in the review stating this claim.</p> <p>The recommendation document also mentions <i>'triggering of manic episodes'</i>, I was not able to find any evidence within the overview document. Can this be investigated, as the indication for TMS in this review relates to psychosis rather than affective disorders. It has been acknowledged in various depression studies about incidences of manic episodes, which is of less frequent occurrence.</p> <p>In conclusion this paragraph needs to differentiate common side effects such as headache, tingling sensation, local scalp discomfort and explicitly mention exacerbation of symptoms as rare side effects and to avoid mentioning worsening of underlying psychiatric disease.</p>	<p>Thank you for your comment.</p> <p>Section 3.3 of the draft guidance has been changed to include 'exacerbation of symptoms' instead of 'worsening underlying psychiatric disease'.</p> <p>The key safety outcomes are agreed by the committee and come from different sources, including published evidence and the views of professional experts.</p> <p>Professional experts considered that the following were theoretical adverse events: TMS induced psychosis, anxiety, insomnia and suicidal ideations.</p>
8	Consultee 2	3.5	Page 4 paragraph 3.5	Thank you for your comment.

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	Royal College of Psychiatrists		It would be helpful if the statement with <u>large placebo effect</u> explained in detail with quantitative figures.	Please respond to all comments Section 3.4 of the draft guidance has been changed to remove the word 'large'. The evidence for this statement is summarised in the efficacy section of the overview.
9	Consultee 2 Royal College of Psychiatrists	Overview	Points relating to Overview Document Page 5 Safety Summary <u>Aggravation of sensory symptoms</u> The findings reported in the first sentence applies to all pathological positive sensory phenomena rather than auditory hallucinations therefore this should be removed from the recommendation document. On page 7 <u>Anecdotal and theoretical adverse events</u> Last sentence does not have any reference and it would be appropriate for the author to provide evidence for this statement.	Thank you for your comment. The overview states that the first sentence relates to all patients and the second sentence is specific to patients with auditory hallucinations. The anecdotal and theoretical adverse events were described by a professional expert and the completed questionnaire is available on the NICE website, as stated on page 27 of the overview.

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