PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such High-frequency repetitive transcranial magnetic stimulation at dorsolateral prefrontal cortex for migraine prevention: A protocol for a systematic review of controlled trials
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number The International Prospective Register of Systematic Reviews (PROSPERO) registration number for this systematic review is CRD42020220636.
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author

No.	Author	E-mail address	Institutional affiliation
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Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review

Conceptualization: Nabil Izzaatie Mohamad Safiai, Wan Aliaa Wan Sulaiman, Mohd Hazmi Mohamed, Liyana Najwa Inche Mat

Data curation: Nabil Izzaatie Mohamad Safiai, Nur Afiqah Mohamad, Kai Wei Lee

Formal analysis: Nabil Izzaatie Mohamad Safiai, Mooi Ching Siew, Kai Wei Lee, Abdul Hanif Khan, Yusof Khan, Janudin Baharin, Anna Misyail Abdul Rashid, Fan Kee Hoo

Funding acquisition: Wan Aliaa Wan Sulaiman

Methodology: Nabil Izzaatie Mohamad Safiai, Wan Aliaa Wan Sulaiman, Nur Afiqah Mohamad, Patricia Pozo-Rosich, Vasudevan Ramachandran

Project administration: Mooi Ching Siew, Fan Kee Hoo, Liyana Najwa Inche Mat, Mohd Hazmi Mohamed, Intan Nureslyna

		Samsudin, Aaron Fernandez, Hamidon Basri **Supervision:** Wan Aliaa Wan Sulaiman, Intan Nureslyna Samsudin, Aaron Fernandez, Hamidon Basri **Writing – original draft preparation:** Nabil Izzaatie Mohamad Safiai, Nur Afiqah Mohamad **Writing – review & editing:** Nabil Izzaatie Mohamad Safiai, Nur Afiqah Mohamad and Vasudevan Ramachandran **Guarantor of review:** Wan Aliaa Wan Sulaiman
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments No Amendment
Support:		
Sources	5a	Indicate sources of financial or other support for the review Research Grant: Grant Number GPB/2017/9585500
Sponsor	5b	Provide name for the review funder and/or sponsor Director of Research Management Centre of Universiti Putra Malaysia Prof. Dr. Mohd Adzir Bin Mahdi 03-9769 1610 dir.rmc@upm.edu.my / mam@upm.edu.my
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol The funders had and will not have a role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known Several systematic reviews had evaluated the use of TMS in headache and migraine, but none reported the use of hf-rTMS applied at DLPFC in migraine prophylaxis. Therefore, we propose this review protocol to investigate the evidence of the efficacy

		of the treatment for migraine prophylaxis.
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) The population is participants diagnosed with migraine headache. The intervention is hf-rTMS at the DLPFC area, and the comparator is sham stimulation. The main outcome is the treatment efficacy (measured by headache days). The secondary outcomes are tolerability (measured by discontinuation rate) and safety (measured by adverse events and side effects).
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review This systematic review will include only randomised controlled clinical trials (RCTs) that study migraine treatment using hf-rTMS applied over the DLPFC area in migraine patients. Only articles written in English from inception until December 2020 will be included in this review. Only full-text articles written in English will be included. Conference and proceedings article will be excluded from this review. Studies primarily examining other comorbid conditions with migraine will also be excluded.
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage a) Electronic data sources: Scopus, Cumulative Index to Nursing and Allied Health Literature Plus, PubMed, Cochrane Central Register of Controlled Trials and Biomed Central. b) clinicaltrial.gov and the World Health Organization trial registry. c) citation searching in which the papers that have cited the included articles will be scanned. d) reference list of the included studies and other relevant papers to conduct a thorough search for this systematic review. Planned date of coverage: From inception until December 2020.
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be

repeated

No.	Search terms
1.	rTMS or “repetitive transcranial magnetic stimulation” AND migrain*
2.	rTMS or “repetitive transcranial magnetic stimulation” AND headache*
3.	rTMS or “repetitive transcranial magnetic stimulation” AND hemicran*
4.	rTMS or “repetitive transcranial magnetic stimulation” AND migraine disorders

Study records:

Data management 11a Describe the mechanism(s) that will be used to manage records and data throughout the review

All searches result will be exported to Endnote referencing software, and duplicates will be removed manually.
Data will be saved in an excel sheet. Data synthesis will be performed using Cochrane Collaboration’s software program Review Manager (RevMan) V.5.4.1 for desktop.

Selection process 11b State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)

The study screening and selection process will be performed by two independent reviewers. We will do the initial screening using titles and abstracts screening, and those match the interest and relevant to our systematic review will be included.

Data collection process 11c Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators

The process of data extraction will be performed by two independent reviewers. A pre-prepared excel datasheet will be used by the reviewers. Insufficient data will be requested from the trialist whenever possible.

Data items 12 List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications

For each study, the following information will be extracted:
Authors’ name
Publication year
Type of migraine
Preventive treatment
Group allocation of treatment

		Number of patients randomised (total and per group) Gender and mean age of participant Stimulation protocol Primary outcome and additional outcome Side effects Dropout (and reasons)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale The main outcome is the treatment efficacy (measured by headache days). The secondary outcomes are tolerability (measured by discontinuation rate) and safety (measured by adverse events and side effects).
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis For quality assessment, 3-4 independent reviewers will assess the articles using the version 2 Cochrane risk-of-bias tool for randomised trials (RoB 2) from the Cochrane Handbook for Systematic Reviews of Interventions Version 6.1. The bias that will be assessed includes bias arising from the randomisation process, bias due to deviations from intended interventions, bias due to missing outcome data, the bias in the measurement of the outcome and bias in the selection of the reported result. Disagreements will be resolved by discussion between the reviewers.
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised Data from the intervention will be compared with the data from the comparator sham group. If feasible, a meta-analysis will be performed to determine the most efficacious and tolerable hf-rTMS protocol.
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ) For dichotomous data, the outcome will be presented as relative risks (RRs) with 95% CIs. For continuous data, the effect size of the interventions will be calculated using the mean differences (MDs) with 95% CIs. If the study trials present the outcome values using different scales, the standard mean difference (SMD) with 95% CIs will be used. Meanwhile, the data for the meta-analysis will be calculated using fixed or random effects.

	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) For heterogeneity assessment, the degree of heterogeneity between the studies will be calculated using the I^2 statistic. Value >50% will be considered indicative of substantial heterogeneity. If the level of heterogeneity is high, subgroup analysis will be performed to explore the possible causes of heterogeneity. Subgroup analyses will be performed according to factors affecting the outcomes.
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned If quantitative data synthesis is not possible, a narrative analysis will be performed.
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) The bias that will be assessed includes bias arising from the randomisation process, bias due to deviations from intended interventions, bias due to missing outcome data, the bias in the measurement of the outcome and bias in the selection of the reported result.
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) The strength of the body of evidence will be assessed using GRADE.

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