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⊕ Unclear insomnia types in randomized controlled trials and systematic reviews: the protocol for a meta-epidemiological study V.3
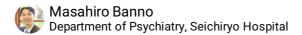
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Objectives. To examine tendencies and characteristics of randomized controlled trials (RCTs) and systematic reviews (SRs) that mention insomnia in abstracts and cannot be distinguished between insomnia disorder and insomnia symptoms (insomnia types) from the abstract and what is the intent of the unclear insomnia types described in the abstracts.

Methods. This study is a meta-epidemiological study. We will include RCT and SR articles that include the word "insomnia" in methods or results of structured abstracts, published after 2010. We will exclude RCTs and SRs, which had neither methods nor results in non-structured abstracts. We will search MEDLINE via PubMed with English language restrictions. We will extract the information about whether abstracts of RCTs and SRs describe insomnia type clearly or not, and the characteristics. We will also extract information about the diagnosis of insomnia disorder for RCT and SR articles with unclear insomnia types and which intent insomnia disorder as insomnia in abstracts. We will report the proportion of RCT and SR articles with unclear insomnia types. We will compare characteristics between RCT and SR articles with unclear insomnia types and those with clear insomnia types. We will examine the above possible characteristics associated with the unclear insomnia types using multivariable logistic regression. We will report what was the intent of the unclear insomnia types described in the abstracts. We will also report what and how much proportion of diagnostic criteria was used for insomnia disorder for RCT and SR articles with unclear insomnia types.

Ethics & Dissemination. This study does not need ethical approval. We registered this study protocol. We will publish the findings in a peer-reviewed journal and may present them at conferences.

Discussion. This study will clarify what proportions and characteristics that do not describe insomnia type clearly in abstracts of RCTs and SRs. The results will inform the researchers, reviewers, and readers of the points that need special attention.

Registration: Protocols.io

protocol20220328.pdf

DOI

We added the following sentences in the definition of two variables "Diagnostic criteria" and "Who diagnoses insomnia disorder" to clarify the definition of variables: "For RCT, we will check methods and results in abstracts and full texts. For SR, we will check the inclusion criteria described in the methods of abstracts and full texts." We changed the "unnamed criteria" option for the variable "Diagnostic criteria" to the "not reported" option to clarify the meaning of the option.

insomnia, randomized controlled trials, systematic reviews, meta-epidemiological study

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None.

None.

None.

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None.

BACKGROUND

1   Insomnia disorder is diagnosed when both nocturnal insomnia symptoms and daytime dysfunctions continued for at least 1 month in the tenth revision of the International Statistical

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Classification of Diseases and Related Health Problems (ICD-10), and for at least 3 months in the third edition of the International Classification of Sleep Disorders (ICSD-3) and Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [1-4]. Insomnia disorder is a single clinical entity, not a symptom because insomnia disorder may often have arisen before the other diseases or may continue beyond the diseases even after the diseases have been treated [5]. Criteria for insomnia disorder in DSM-5 abolished the distinction between primary insomnia and secondary insomnia, which are types of insomnia disorder [1]. The prevalence of insomnia disorder is 4.7 to 22.1% in the cross-cultural general population [6].

Insomnia symptoms are a broad concept that includes insomnia disorder. The operationalized criteria of nocturnal insomnia symptoms are often used, for example, "taking >30 minutes to fall asleep, spending >30 minutes awake after sleep onset or awakening >30 minutes before the desired time and before obtaining 6.5 hours of sleep" [1]. The nocturnal insomnia symptoms are difficulties initiating sleep at the bed, frequent or continued waking up, or early-morning waking up [1]. Populations with insomnia symptoms include people with acute sleep disturbance, temporary phenomena characterized by nocturnal insomnia symptoms for a few weeks, as well as patients with insomnia disorder[1, 7]. The prevalence of insomnia symptoms all over the world is 30 to 35% [6].

In several abstracts of randomized controlled trials (RCTs) and systematic reviews (SRs), participants have been described as "patients with insomnia", which readers cannot determine whether participants had insomnia disorder or insomnia symptoms (insomnia types) [8-16]. Clinicians have an increased burden in reading such papers to apply them to clinical practice, and researchers who do not specialize in sleep medicine may misunderstand the content of the paper. This study will examine tendencies and characteristics of RCTs and SRs that mention insomnia in abstracts and cannot be distinguished between insomnia disorder and insomnia symptoms (insomnia types) from the abstract and what is the intent of the unclear insomnia types described in the abstracts.

MATERIALS AND METHODS

2 This publication is the full study protocol. This protocol has been registered in protocols.io (https://www.protocols.io/).

2.1 Study design and aims
Using a meta-epidemiological approach, we will address the following two issues;

i) what proportion and characteristics that do not describe insomnia type clearly in abstracts of RCTs and SRs?
First, we will determine the proportion of RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms from the abstract on RCT and SR articles whose methods or results mention insomnia. Second, we will examine the characteristics of RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms with RCT and SR articles that can be distinguished from the abstract.

ii) what was the intent of the unclear insomnia types described in the

abstracts?

First, for RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms from the abstract, we will investigate the extent to which the term "insomnia" refers to insomnia disorder or insomnia symptoms in the methods or results of the abstract. Second, for RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms from the abstract and in which methods or results of full texts mention insomnia disorder, we investigate what and how much proportion of diagnostic criteria was used for insomnia disorder.

2.2   Types of studies included

The inclusion criteria for RCTs and SRs are as follows: 1) RCT and SR articles that include the word "insomnia" in methods or results of structured abstracts, 2) published in the English language, 3) years of publication after 2010. We will include articles in which the abbreviation containing the word "insomnia" is listed in the methods or results, such as Cognitive Behavioral Therapy for Insomnia (CBT-I). We will also include articles that have the word "insomnia" in the same section as methods, such as methodology, main results, or in the same section as results, such as findings. We will also include articles with the word "insomnia" in sections that are considered part of the methods, such as study eligibility criteria, participants, and interventions. We will exclude RCTs and SRs, which had neither methods nor results in non-structured abstracts. We will exclude conference abstracts and protocols.

2.3   Search methods

We will search MEDLINE via PubMed with English language restrictions. The search strategy for RCTs is insomnia[tiab] AND method*[tiab] AND Randomized Controlled Trial[pt]. The search strategy for SRs is insomnia[tiab] AND method*[tiab] AND Systematic[sb]. We will use "method*[tiab]" in the search strategy to exclude unstructured abstracts.

2.4   Study selection and data extraction

Two authors will independently review the eligibility criteria of abstracts for whether random samples (see 2.7 Sample size and statistical consideration) of RCTs and SRs included the word "insomnia" in methods or results of abstracts and meet the above exclusion criteria (for example, unstructured abstracts). MB will obtain the full text for included RCTs and SRs and exclude conference abstracts without full text. Other authors will confirm the judgment by MB. Then, two authors will independently review the description of methods or results of abstracts to classify eligible RCTs and SRs as RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms with RCT and SR articles that can be distinguished from the abstract. Disagreements will be solved through discussion. If necessary, other review authors will arbitrate disagreements. As for the data extraction, one author will extract the information described below from each of the included RCT and SR articles, and other authors validated the contents.

Disagreements will be solved through discussion. If necessary, the third reviewer will arbitrate disagreements.

2.5   Assessment of the proportion and characteristics that do not describe insomnia type clearly in abstracts of RCTs and SRs
We will extract the information about whether abstracts of RCTs and SRs describe insomnia type clearly or not, and the following characteristics: years of publication, impact factors, word counts, and word limitations about abstracts, funding, compliance with reporting guidelines, registrations or protocols.
We will assign ''clear insomnia types'' to RCT and SR articles that mention insomnia types in methods or results of abstracts and assign "unclear insomnia types" to those that did not. We will consider "clear insomnia types" if methods or results of abstracts include the phrase "insomnia disorder", "primary insomnia", "secondary insomnia" or "insomnia symptoms". We will categorize primary insomnia and secondary insomnia as "insomnia disorder". We describe the definitions of other variables the extraction methods in Table 1.
We will examine tendencies in RCT and SR articles for "unclear insomnia types" across the RCT and SR articles that mention insomnia in abstracts by the calendar year by applying the Cochran-Armitage test. We will also compare characteristics between RCT and SR articles for "unclear insomnia types" and those for "clear insomnia types" using Fisher's exact test and Mann−Whitney U test. We will examine the above possible predictors associated with the unclear insomnia types using multivariable logistic regression.

2.6   Assessment for what is the intent of the unclear insomnia types described in the abstracts
For RCT and SR articles with unclear insomnia type in abstracts, we will assess what the unclear description intends based on the full text. We will consider that RCT and SR articles mention "insomnia disorder" if the standard criteria such as DSM, ICD, ICSD for insomnia disorder (including primary insomnia) are used for diagnosis for insomnia disorder or if both subjective insomnia symptoms and daytime dysfunctions continue for 1 month or more. We will consider that RCT and SR articles mention "insomnia symptoms" if insomnia is evaluated by a patient-reported sleep diary and patient-reported rating scales (for example, Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI)) [1]. We will determine that the full texts mention "insomnia" cannot be classified if the full texts lack the definition of insomnia or non-standard criteria for insomnia (for example, objective total sleep time) are used.
We will tabulate what is the intent of the unclear insomnia types described in the abstracts. We will also summarize the variables listed in Table 2, separately for SRs and RCTs.

2.7   Sample size and statistical consideration

We will perform a random sampling of at least 100 RCTs and 100 SRs for statistical analyses from the search results for RCTs and SRs. We will continue random sampling until we have collected more than 30 of the unclear insomnia types for RCTs and SRs respectively. We will not perform sample size calculations because this study is exploratory research.

We will consider two-sided P-value less than 0.05 is statistically significant. We will not execute an adjustment of the alpha level for multiple comparisons because our study is an exploratory study [17]. We will use Stata ver. 15.1 (StataCorp LLC, College Station, Texas, United States of America) for all statistical analyses above [18].

2.8 Ethics
Ethics approval will not be essential because we only use openly available data.

DISCUSSIONS

3 This study will clarify what proportions and characteristics that do not describe insomnia type clearly in abstracts of RCTs and SRs. The results will inform the researchers, reviewers, and readers of the points that need special attention.

CONTRIBUTORS

4 MB, YT, and YK contributed to the conception and design of the research. MB is fully responsible for writing the protocol. All authors gave final approval of the protocol before submission. After the publication of the protocol, we plan for the following contributions by each author: MB, KK, ED, ST and HS will conduct screen articles, and extract data. MB will conduct the data analysis. MB, YT, and YK will write the manuscript.

FUNDING

5 This protocol was supported by no funder.

COMPETING INTERESTS

6 All authors have no competing interests.

Provenance and peer review

7 Not peer reviewed.

Patient consent for publication

8 Not required.

9 We have no additional data.

Table 1. Variable table for assessment of the proportion and characteristics that do not describe insomnia type clearly in abstracts of RCTs and SRs

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A	B
Variables (Category)	Definition
Insomnia types in abstracts (clear insomnia types, unclear insomnia types)	Clear insomnia types: the number of RCT and SR articles that can be distinguished between insomnia disorder and insomnia symptoms from the description in abstracts. Unclear insomnia types: the number of RCT and SR articles that cannot be distinguished between insomnia disorder and insomnia symptoms from the description in abstracts.
Years of publication	The years in which eligible RCTs and SRs are published. We will extract years of print publication. We will extract years of electronic publication if articles have not yet been published in the print publication.

Impact factors (0 to 4, 5 to 9, 10 or more, and no value)	Impact factors in the journal in which the review was published. We will extract Journal Impact Factor 2020 of the journal in the Journal Citation Reports 2021. We will treat the following numerical variables as categorical variables: impact factor (0 to 4, 5 to 9, 10 or more, and no value).
Word counts in abstracts	The number of words in abstracts
Word limitations about abstracts	The number of maximum words about abstracts. We will extract the information in instructions for the authors of each journal. We will record "unclear" if the instructions for the authors of each journal does not mention the number of maximum words about abstracts.
Funding (industry, nonindustry, none, or unclear)	We will extract information about funding from full texts in eligible articles and from records on the Web of Science. Industry: either industry funding only or both industry and nonindustry funding nonindustry: the funds were from governments and other academic or nonprofit organizations. None: eligible articles had no funding. Unclear: no information about funding

Compliance with reporting guidelines (yes, no)	Yes: methods in full texts mention eligible articles were referring to reporting guidelines (CONSORT for RCTs, and PRISMA for SRs) No: methods in full texts did not mention eligible articles were referring to reporting guidelines.
Registrations or protocols (yes, no)	Yes: methods in full texts mention information about clinical trials registrations or SR registrations or protocols for RCTs or SRs No: other than "Yes"

Abbreviation: CONSORT, Consolidated Standards of Reporting Trials; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCTs, randomized controlled trials; SRs, systematic reviews

The denominator is the number of RCT and SR articles that mention insomnia in methods or results of abstracts.
One author will execute web scraping from PubMed with Python 3.6 (Python Software Foundation) and picked up data for the PubMed ID (PMID) and uniform resource locator (URL) of each RCT and SR article. One author will also execute web scraping from the Web of Science with Python 3.6 (Python Software Foundation) and picked up data for impact factors and funding. We will extract the year of publication (years of print and electronic publication), word counts in abstracts, funding, compliance with reporting guidelines, registrations or protocols from the records in PubMed, and the full text of each set of RCT and SR articles.

Table 2. Variable table for assessment for what is the intent of the unclear insomnia types described in the abstracts

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A	B
Variables (Category)	Definition
Intended insomnia types (insomnia disorder, insomnia symptoms, both insomnia disorder and insomnia symptoms, cannot be classified)	A classification of whether the unclear insomnia types in abstracts are insomnia disorder or insomnia symptoms if methods or results of abstracts mention insomnia. The classification is based on the context of abstracts and full text, not merely the phrase "insomnia disorder" "primary insomnia", or "secondary insomnia" or "insomnia symptoms". Insomnia disorder: the phrase "insomnia disorder", "primary insomnia", or "secondary insomnia" will appear in methods

or results in full texts, or the standard criteria such as DSM, ICD, ICSD for insomnia disorder (including primary insomnia) are used for diagnosis for insomnia disorder or if both subjective insomnia symptoms and daytime dysfunctions continue for 1 month or more.

Insomnia symptoms: the phrase "insomnia symptoms" will appear and the phrase "insomnia disorder", "primary insomnia", or "secondary insomnia" will not appear in methods or results in full texts, or insomnia is evaluated by a patient-reported sleep diary and patient-reported rating scales (for example, Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI)).

Both insomnia disorder and insomnia symptoms: the unclear insomnia types in abstracts are both insomnia disorder and insomnia symptoms based on the context of abstracts and full text.

Cannot be classified: whether the unclear insomnia types in abstracts are insomnia disorder or insomnia symptoms are unclear based on the context of abstracts and full text.

Diagnostic criteria (DSM, ICD, ICSD, other, not reported)	The name of diagnostic criteria for insomnia disorder. Other: other criteria than DSM, ICD, ICSD Not reported: Contents of diagnostic criteria are described, but the name of criteria is not reported. For RCT, we will check methods and results in abstracts and full texts. For SR, we will check the inclusion criteria described in the methods of abstracts and full texts.
Who diagnoses insomnia disorder (clinicians, researchers, not reported)	For RCT, we will check methods and results in abstracts and full texts. For SR, we will check the inclusion criteria described in the methods of abstracts and full texts.

Abbreviation: DSM, Diagnostic and Statistical Manual of Mental Disorders; ICD, International Statistical Classification of Diseases and Related Health Problems; ICSD, International Classification of Sleep Disorders

The denominator of "Intended insomnia types" is the number of RCT and SR articles with unclear insomnia types.
The denominator of "diagnostic criteria", and " who diagnoses insomnia disorder" is the number of RCT and SR articles with unclear insomnia types and in which methods or results of full texts mention insomnia disorder.

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