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Protocol for a systematic review of interventions targeting mental health, cognition, or psychological wellbeing among individuals with long COVID

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Abstract

Introduction. For some people, COVID-19 infection leads to negative health impacts that can last into the medium or long term. The long-term sequelae of COVID-19 infection, or 'long COVID', negatively affects not only physical health, but also mental health, cognition, and psychological wellbeing. Complex, integrated interventions are recommended for long COVID, including psychological components; however, the effectiveness of such interventions has yet to be critically evaluated. This protocol describes a systematic review to be conducted of scientific literature on interventions for mental health, cognition, and psychological wellbeing among individuals with long COVID. **Methods and analysis.** Standard systematic review guidelines will be followed. A health sciences librarian will identify the relevant literature through comprehensive systematic searches Medline, Embase, APA PsycInfo, CINAHL, China National Knowledge Internet, and WANFANG Data databases. Study selection will follow the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines Data extracted will include metrics indicating intervention efficacy, effectiveness, feasibility, and acceptability. Data will be narratively synthesized; if the data allows, a meta-analysis will be conducted. Methodological appraisal of studies will be assessed by Cochrane Risk-of-Bias 2 tool. **Ethics and dissemination**. Ethical approval for systematic reviews is not required. As researchers and clinicians respond to the new clinical entity that long COVID represents, this review will synthesize a rapidly emerging evidence base describing and testing interventions for mental health, cognition, and psychological wellbeing. Results will therefore be disseminated through an open-access peer-reviewed publication and conference presentations to inform research and clinical practice.

Keywords: COVID-19, long COVID, post-COVID syndrome, systematic review, protocol, mental health, cognition, psychological wellbeing

Patient and public involvement. Patient advisors will provide feedback throughout the systematic review process.

Strengths and limitations of this study

- A systematic review will examine interventions for mental health, cognition, or psychological wellbeing in long COVID.
- With broad inclusion criteria, all relevant articles will be included.
- Data synthesis may be narrative, with meta-analytical synthesis only if the nature of the literature permits.
- Study quality and risk of bias will be assessed using multiple standardized metrics.
- Search terms and the data extraction plan will need to be refined iteratively as the literature emerges.

Word count: 2962 words

INTRODUCTION

Prolonged symptoms after COVID-19 infection constitute a considerable medical concern in the ongoing COVID-19 pandemic. Most people who acquire a COVID-19 infection experience short-term illness, with recovery within days or weeks.[1] However, some people experience symptoms months after the acute infection period.[2] This clinical entity, which was first identified by patients themselves, has been given a number of names, including long COVID, post-COVID syndrome, and COVID long haulers.[3] Symptoms commonly observed in long COVID include fatigue, headaches, difficulty concentrating, shortness of breath, dizziness, myalgia, insomnia, depression, and anxiety, as part of a mixed constellation of multi-system symptoms with an unknown duration.[4 5] A meta-analysis suggests that 43% of people who contract COVID-19 are reporting long-term symptoms consistent with long COVID.[6] By conservative estimates in the context of limited testing capacity, 500 million people worldwide had been infected by COVID-19 in mid-April 2022;[7] at a rate of 43% experiencing long-term symptoms, hundreds of millions of people around the world have experienced or will experience some degree of long COVID.

A number of risk factors for long COVID have been identified, including older age, female sex, a higher body mass index, comorbidities, and more severe COVID-19 symptoms.[8 9] However, anyone can develop long COVID, from young people with no pre-existing conditions to older adults and those with a complex health status.[10] Social isolation, decreased physical activity, changed lifestyles, and pandemic-related social and economic insecurity may contribute to developing the physical and psychological symptoms of long COVID.[8] For some people, long COVID may become a long-term, debilitating, multi-systemic disability.[11 12]

The COVID-19 pandemic has had substantial mental health repercussions[13], as the public health restrictions put into place to reduce the spread of the virus have disrupted many of the protective factors[14-16] that support mental health and wellness. In addition to these widespread mental health impacts from the pandemic, long COVID is specifically associated with mental health impacts. People with long COVID are presenting with anxiety, depression, and post-traumatic stress disorder, as well as neurocognitive issues[17] and other multi-systemic symptoms that impair functioning, wellbeing, and quality of life.[18] Indeed, individuals with long COVID can experience both the mental health symptoms specific to long COVID and those associated with the pandemic's impacts on societies at large.[19]

The National Institute for Health and Care Excellence (NICE) has issued clinical practice guidelines for the treatment for long COVID.[20] According to NICE, treatment requires integrated, multidisciplinary models of care that bring patients together with healthcare practitioners from across specialties to meet the wide range of long-term needs with which patients present. In addition to treatments for physical symptoms, NICE guidelines highlight the importance of attending to mental health, cognition, and wellbeing, including among individuals with pre-existing or newly emerging mental health problems. It is therefore important that we embed evidence-based interventions for mental and cognitive health and psychological wellbeing into long COVID care.

Integrated, multi-component interventions that are applied to heterogeneous populations in heterogeneous treatment settings can be considered 'complex' interventions according to the UK Medical Research Council complex intervention framework.[21] The recommended type of integrated care for long COVID would be expected to consist of multiple evidence-based components, yet be tailored to the individual patient to produce a range of possible outcomes, while being delivered by a variety of care providers across discliplines.[20] Such complex interventions require careful preparation, implementation, and evaluation to ensure efficacy and effectiveness.

Our team's systematic review of registered trials of interventions for mental health, cognition, and psychological wellbeing in long COVID revealed that the research on such interventions is only just beginning to emerge.[masked reference] Given that COVID-19 research has been emerging at an extremely rapid pace,[22] the associated long COVID treatment literature is expected to follow suit. Timely reviews of the literature on this topic will therefore be key to the process of developing and optimizing the recommended complex, integrated interventions for individuals with long COVID.[23]

Objectives

This paper describes the protocol for a systematic review of interventions for mental health, cognition, or psychological wellbeing among individuals with long COVID.

METHODS AND ANALYSIS

Reporting guidelines

This systematic review protocol follows follow the protocol version of the Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines (i.e., PRISMA-P).[24] The systematic review will follow the PRISMA guidelines.[25]

Research question

This systematic review will synthesize the scientific literature on interventions that have been tested for mental health, cognition, or psychological wellbeing among individuals experiencing long COVID, including their efficacy, effectiveness, feasibility, and acceptability. Specific research questions are: 1) What interventions have been tested for mental health, cognition, or psychological wellbeing among individuals with long COVID? 2) What is the design and quality of the trials? 3) What are the outcomes of the interventions?

Types of interventions

This review will include articles reporting on any intervention targeting any aspect of mental health, cognition, or psychological wellbeing among people who have long COVID, reporting quantitatively or qualitatively on any outcomes related to mental health, cognition, or psychological wellbeing. Based on our existing review of registered trials on this topic,[masked reference] the literature is expected to report on psychological interventions, pharmacological interventions, nutritional or natural supplement interventions, cognitive and neurorehabilitation interventions, and physiotherapy or physical rehabilitation. Other types of interventions will also be eligible, provided that they meet the inclusion criteria.

Eligibility criteria

To be included, articles must describe or test an intervention for mental health, cognition, or psychological wellbeing in patients with long COVID symptoms after a confirmed or suspected COVID-19 infection. Any study design will be accepted. Articles can originate from any country and can report on participants of any age group or other sociodemographic characteristic. To

capture the broadest range of studies, the article's definition of long COVID will be accepted, provided that it reports on symptoms experienced at least 4weeks after acute infection, consistent with the observed lower limit of duration observed in currently registered trials.[masked reference] Articles can be published in print, online ahead of print, or in unreviewed pre-print format; unpublished summaries of findings will also be accepted. For articles published in a language other than English or French, we will contact authors for English-language summaries; if unavailable, we will have the abstracts translated and will include the English-language abstract in the review. Excluded will be any trials of participants who did not have long COVID, trials conducted prior to 2020 (i.e., before the COVID-19 pandemic), animal trials, treatment guidelines, and opinion papers.

Information sources

A comprehensive search will be conducted in Medline, Embase, APA PsycInfo, Cumulative Index to Nursing and Allied Health Literature (CINAHL), medRxiv, PsyArXiv, China National Knowledge Internet, and WANFANG Data databases using the search strategy described below. Reference lists of relevant articles will also be examined.

Search strategy

The tentative search strategy has been developed by a health sciences librarian (Table 1). However, it cannot be thoroughly tested at this time due to the paucity of literature on this topic to date. It will therefore be tested and iteratively refined and optimized as the literature emerges. Search concepts built using database-specific subject headings, natural language keywords, and advanced search operators will focus on 1) mental health, cognition, and psychological wellbeing, 2) clinical trials, built using an established clinical trials filter[26] and 3) long COVID search components using an established and tested shared search strategy.[27] No geographical or language limits will be place on the search, but it will be given a year limit of 2020 to present. The English search strategy will be translated to Chinese for use in Chinese searches and the Chinese search strategy will be optimized to each relevant database by qualified Chinese-speaking team members. In addition, specific title and author searches will be conducted for all studies identified in our existing systematic review of registered trials;[masked reference] if

unpublished, lead researchers for each previously identified trial will be contacted to request any results that might be eligible for inclusion. Upon completion of the article selection process below, the search will be rerun to update the findings.

Table 1. Tentative search strategy for Medline

Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® <1946-Present>	
1	(exp SARS-CoV-2/ or exp COVID-19/) and sequela*.ti,ab,kf.
2	"long Covid".ti,ab,kf,hw.
3	((Covid or Covid19 or "corona virus 2019" or "coronavirus 2019" or SARS-CoV-2 or nCoV or "B.1.1.7" or "B.1.351" or "B.1.1.28" or "B.1.617") adj3 (PASC or sequela* or "post acute" or postacute or prolonged or "long haul*" or chronic or lingering or ongoing or persistent or "long term" or "more than 12 weeks" or "more than 24 weeks")).ti,ab,kf,hw.
4	or/1-3
5	Mental Health/
6	exp Mental Disorders/
7	exp Neurocognitive Disorders/
8	exp Cognition/
9	exp Quality of life/
10	exp Mental Health Services/
11	exp Psychotherapy/
12	(mental* or psychiatr* or personality disorder* or post-trauma* or posttrauma* or PTSD or complex trauma or developmental trauma or (disorder* adj2 eating) or hallucinat* or (hear* adj3 voice*) or manic or mania or depress* or anxiet* or bipolar or dysthymi* or phobia* or panic* or obsess* or compulsion* or compulsiv* or OCD or mood* or (affective adj3 disorder*) or suicid* or selfharm* or self-harm* or selfinjur* or self-injur* or psychopath* or internaliz* or externaliz* or attention deficit* or ADHD or oppositional* de* or (regulat* adj3 emotional*) or (dysregulat* adj3 emotion*) or aggress*).ti,ab,kf,hw,jn.
13	((emotion* or psycholog*) adj3 distress*).ti,ab,kf,hw.
14	(wellbeing or well-being or wellness).ti,ab,kf,hw.
15	"quality of life".ti,ab,kf,hw.
16	(cognition or cognitive* or neuro*).ti,ab,kf,hw.
17	((psychosocial or psycholog* or psychiatr*) adj3 (intervention* or program* or servic* or treatment*)).ti,ab,kf,hw.
18	(psychoeducation or psycho-education).ti,ab,kf,hw.
19	(cognitiv therap* or behavio?r* therap* or CBT or DBT).ti,ab,kf,hw.
20	psychotherap*.ti,ab,kf,hw.
21	(behav* adj3 (intervention* or program* or servic* or treatment*)).ti,ab,kf,hw.
22	((lifestyle* or life style*) adj3 (therap* or intervention*)).ti,ab,kf,hw.
23	or/5-22

24	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.
25	exp Randomized Controlled Trial/
26	exp Randomized Controlled Trials as Topic/
27	exp Controlled Clinical Trial/
28	exp Controlled Clinical Trials as Topic/
29	Random Allocation/
30	Double-Blind Method/
31	Single-Blind Method/
32	Placebos/
33	Control Groups/
34	(random* or sham or placebo*).ti,ab,kf,hw.
35	((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,kf,hw.
36	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,kf,hw.
37	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf.
38	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,kf,hw.
39	allocated.ti,ab,hw.
40	((open label or open-label) adj5 (study or studies or trial*)).ti,ab,kf,hw.
41	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,kf,hw.
42	(pragmatic study or pragmatic studies).ti,ab,kf,hw.
43	((pragmatic or practical) adj3 trial*).ti,ab,kf,hw.
44	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,kf,hw.
45	(phase adj3 (III or "3") adj3 (study or studies or trial*)).ti,kf,hw.
46	or/24-45 [CADTH Clinical Trials Filter]
47	(intervention* study or intervention* studies).ti,ab,kf,hw.
48	(("Before after" or "pre post") adj3 (study or studies)).ti,ab,kf,hw.
49	4 and 23 and (46 or 47 or 48)

Study selection

Identified records will be uploaded into Covidence systematic review software[28] for record management. Titles and abstracts will be reviewed independently by two study staff based on the inclusion and exclusion criteria; any conflicts will be resolved by consensus through discussion with the project lead. Selected documents will be reviewed at the full text level by two staff in the same manner until a final set of included articles is obtained. The record review and selection process will be illustrated using a PRISMA flow chart.[25]

Data extraction

The documents selected for inclusion will undergo data extraction and analysis. Data will be extracted as a team by the two study staff and research lead together for the first 5 documents as a pilot and training stage, to establish consensus. The remaining data will be extracted by one of the study staff and confirmed by a second team member, in discussion with the study lead for any uncertainties. Data extraction will tentatively include the elements summarized in Table 2. Additional elements may be identified over the course of the project as literature emerges, in an iterative manner.

Table 2. Data extraction plan

Category	**Variables to be extracted**
Basic descriptive information	Country, city, publication reference, trial year(s), funder, report type, peer review status
Research question(s)	Primary and secondary objectives, research questions, aims
Participant characteristics	Age, sex, gender, ethnicity
Intervention characteristics	Intervention name, intervention description, dose, delivery format, type of administering professional
Study design	Controlled trial (control group), longitudinal (number of assessments, timeline of assessments), qualitative (number of stakeholder groups, type of stakeholders)
Methodological components	Inclusion criteria, exclusion criteria, long COVID definition, randomization, masking, control group description, sample size, timing of assessments
Measures	Quantitative: Primary outcomes measures, secondary outcome measures Qualitative: Interview guide description
Outcomes	Primary outcomes: Mental health, cognition, psychological wellbeing

	Secondary outcomes: If appropriate based on the resulting literature, physical and neuropsychological outcomes may be reported on. Quantitative: Intervention and control group means, standard deviations, standard errors, *p* values, effect sizes, odds ratios, relative risk Qualitative: Themes and subthemes

Outcomes and prioritization

Given the rapidly emerging nature of this new literature base, it is intended that all efficacy, effectiveness, feasibility, and acceptability outcomes of the interventions on the mental health, cognition, and psychological wellbeing of research participants will be sought. Efficacy or effectiveness of the interventions with regard to mental health, cognition, or psychological wellbeing outcomes will be prioritized, including pre- and post- assessments, with follow-up measures where available. The feasibility and acceptability of interventions will be the secondary outcome of interest. Measures of effect will be determined by the outcome tool or instrument used and the design of the studies, given the wide range of symptoms and potential breadth of studies. It is anticipated that standardized mean difference (for continuous outcomes) and odds ratio or relative risk (for binary outcomes) will be the primary measures of effects.

The outcome prioritization plan may be expanded upon based on the scope and nature of the literature that is identified. For example, we may include additional secondary outcomes with neuropsychological relevance, such as pain, headache, and fatigue, depending on the nature of the data.

Data synthesis

Data will be summarized in narrative and table format. We will descriptively report on the

number, types, and characteristics of the interventions identified. We will also provide a descriptive summary of their efficacy, effectiveness, feasibility, and acceptability. If sufficient trials are found that provide treatment efficacy data suitable for a meta-analyses, we will conduct meta-analyses using random effects modeling. The heterogeneity between studies will be assessed using forest plot visually, as well as I^2 statistic. The meta-regression approach, if feasible, will be used to help understand the sources of heterogeneity. Subgroup analyses will depend on the nature and quantity of data retrieved, due to the variability of symptoms across individuals and the variability of the trials under way. If possible, we will consider subgroup analyses based on gender and other sociodemgraphic variables (Gender-Based Analysis Plus).[29]

Assessment of study quality and bias

We will conduct a number of activities to assess the body of research identified using the Cochrane Risk of Bias 2.0 tool.[30] A risk-of-bias assessment will be conducted with a bias assessment team of two independent study staff, supported by discussions with the study lead to resolve any disagreements. Generalizability indices will be calculated using the demographic characteristics of the identified samples, such as age and gender; this will serve to determine the degree to which the body of evidence is generalizable to the population. If meta-analyses are conducted, sensitivity analyses will be conducted to ensure that the pooled results are not unduly influenced by one study.

Patient and public involvement

From a patient-oriented research perspective,[31] patients with lived experience of long COVID and associated challenges in mental health, cognition, or psychological wellbeing will be engaged in the conduct of this review. Patient partners will help refine the search plan and data extraction tool and will help co-interpret the findings to ensure that the information obtained is relevant to their real-world experience.

Limitations

The inclusion criteria are intentionally broad due to the dearth of literature available at the time

of protocol development. However, the amount of research available for review may change rapidly, as COVID-19 research has emerged at an extremely rapid pace.[22] Therefore, it may become necessary to be more restrictive and adjust the draft search terms based on the emerging literature. Any literature released after the date of the updated database search will not be included and could be substantial. The review is further limited by the search in English and Chinese-language databases, the inclusion of English, French, and Chinese full text literature, and English-language translations of abstracts only for literature published in another language; this will limit the generalizability of the findings.

ETHICS AND DISSEMINATION

This systematic review is not subject to research ethics board approval as there will be no participant contact or direct data collection activities. Knowledge translation will include publication of a systematic review manuscript in an open access journal to reduce barriers and provide ease of access to stakeholders outside of academic structures. The findings will further be presented at national and international conferences with research and clinical audiences. We may present the findings in webinar format for ongoing online, international access by stakeholders interested from both research and clinical perspectives. Other lay knowledge translation opportunities may be identified by the patient partner team.

CONCLUSIONS

As clinicians and scientists respond to the new clinical entity that long COVID represents, complex integrated long COVID service pathways are required. These services must include evidence-based interventions that address mental health, cognition, and psychological wellbeing. It is essential that the literature examining the efficacy, effectiveness, feasibility, and acceptability of such interventions be rapidly synthesized as it emerges, to support further research, service development, and implementation initiatives. The results of this review will therefore be important interventionists, researchers, and decision-makers interested in interventions for individuals experiencing long COVID.

Author contributions:

LH conceptualized and designed the review and drafted the manuscript.

CFS contributed to the design of the review and edited and approved the manuscript.

WW contributed to the design of the review and edited and approved the manuscript.

DRT contributed to the design of the review and edited and approved the manuscript.

SLR contributed to the design of the review and edited and approved the manuscript.

GS contributed to the design of the review and edited and approved the manuscript.

EB contributed to the design of the review and edited and approved the manuscript.

TR contributed to the design of the review, designed the library database search, and edited and approved the manuscript.

DX contributed to the design of the review and edited and approved the manuscript.

DC contributed to the conceptualization and design of the review and edited and approved the manuscript.

Competing interests: David Castle has received grant monies for research from Servier, Boehringer Ingelheim; Travel Support and Honoraria for Talks and Consultancy from Servier, Seqirus, Lundbeck. He is a founder of the Optimal Health Program (OHP), and holds 50% of the IP for OHP; and is part owner of Clarity Healthcare. He does not knowingly have stocks or shares in any pharmaceutical company. Other authors have no conflict of interest to declare.

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Open access: Yes

Ethics: Not applicable. This research did not involve participants.

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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	Page	Checklist item
			ADMINISTRATIVE INFORMATION
Title:			
Identification	1a	1	Identify the report as a protocol of a systematic review
Update	1b	n/a	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	Pending	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:			
Contact	3a	2	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	2	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	n/a	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
Support:			
Sources	5a	2	Indicate sources of financial or other support for the review
Sponsor	5b	2	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	2	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
			INTRODUCTION
Rationale	6	5-6	Describe the rationale for the review in the context of what is already known
Objectives	7	6	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
			METHODS
Eligibility criteria	8	7	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
Information sources	9	8	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
Search strategy	10	9	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Study records:			
Data management	11a	10	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	10	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)
Data collection process	11c	11	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
Data items	12	11	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	12	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	13	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
Data synthesis	15a	13	Describe criteria under which study data will be quantitatively synthesised
	15b	13	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)
	15c	13	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	13	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	13	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	13	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Protocol for a systematic review of interventions targeting mental health, cognition, or psychological wellbeing among individuals with long COVID

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Abstract

Introduction. For some people, COVID-19 infection leads to negative health impacts that can last into the medium or long term. The long-term sequelae of COVID-19 infection, or 'long COVID', negatively affects not only physical health, but also mental health, cognition, and psychological wellbeing. Complex, integrated interventions are recommended for long COVID, including psychological components; however, the effectiveness of such interventions has yet to be critically evaluated. This protocol describes a systematic review to be conducted of scientific literature reporting on clinical trials of interventions to promote mental health, cognition, and psychological wellbeing among individuals with long COVID. **Methods and analysis.** The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines will be followed. A health sciences librarian will identify the relevant literature through comprehensive systematic searches of Medline, Embase, APA PsycInfo, CINAHL, medRxiv, PsyArXiv, China National Knowledge Internet, and WANFANG Data databases, as well as The Cochrane Central Register of Controlled Trials, clinicaltrials.gov, and the WHO International Clinical Trials Registry Platform. Studies will be selected through a title and abstract review, followed by a full-text review using inclusion and exclusion criteria. Data extracted will include intervention descriptions and efficacy metrics. Data will be narratively synthesized; if the data allows, a meta-analysis will be conducted. Risk of bias assessment will be conducted using the Cochrane Risk-of-Bias 2.0 tool. **Ethics and dissemination**. Ethical approval for systematic reviews is not required. As researchers and clinicians respond to the new clinical entity that long COVID represents, this review will synthesize a rapidly emerging evidence base describing and testing interventions to promote mental health, cognition, and psychological wellbeing. Results will therefore be disseminated through an open-access peer-reviewed publication and conference presentations to inform research and clinical practice.

Keywords: COVID-19, long COVID, post-COVID syndrome, systematic review, protocol, mental health, cognition, psychological wellbeing

Strengths and limitations of this study

- .
- With broad inclusion criteria, all relevant clinical trials will be included.
- Data synthesis may be narrative, as meta-analytical synthesis will only be possible if the nature of the literature permits.
- Study quality and risk of bias will be assessed using multiple standardized metrics.
- Search terms and the data extraction plan will need to be refined iteratively as the literature emerges.

Word count: 3184 words

INTRODUCTION

Prolonged symptoms after COVID-19 infection constitute a considerable medical concern in the ongoing COVID-19 pandemic. Most people who acquire a COVID-19 infection experience short-term illness, with recovery within days or weeks.[1] However, some people experience symptoms months after the acute infection period.[2] This clinical entity, which was first identified by patients themselves, has been given a number of names, including long COVID, post-COVID syndrome, and COVID long haulers.[3] Symptoms commonly observed in long COVID include fatigue, headaches, difficulty concentrating, shortness of breath, dizziness, myalgia, insomnia, depression, and anxiety, as part of a mixed constellation of multi-system symptoms with an unknown duration.[4 5] A meta-analysis suggests that 43% of people who contract COVID-19 are reporting long-term symptoms consistent with long COVID.[6] By conservative estimates in the context of limited testing capacity, 500 million people worldwide had been infected by COVID-19 in mid-April 2022;[7] at a rate of 43% experiencing long-term symptoms, hundreds of millions of people around the world have experienced or will experience some degree of long COVID.

A number of risk factors for long COVID have been identified, including older age, female sex, a higher body mass index, comorbidities, and more severe COVID-19 symptoms.[8 9] However, anyone can develop long COVID, from young people with no pre-existing conditions to older adults and those with a complex health status.[10] Social isolation, decreased physical activity, changed lifestyles, and pandemic-related social and economic insecurity may contribute to developing the physical and psychological symptoms of long COVID.[8] For some people, long COVID may become a long-term, debilitating, multi-systemic disability.[11 12]

The COVID-19 pandemic has had substantial mental health repercussions[13], as the public health restrictions put into place to reduce the spread of the virus have disrupted many of the protective factors[14-16] that support mental health and wellness. In addition to these widespread mental health impacts from the pandemic, long COVID is specifically associated with mental health impacts. People with long COVID are presenting with anxiety, depression, and post-traumatic stress disorder, as well as neurocognitive issues[17] and other multi-systemic symptoms that impair functioning, wellbeing, and quality of life.[18] Indeed, individuals with long COVID can experience both the mental health symptoms specific to long COVID and those associated with the pandemic's impacts on societies at large.[19]

The National Institute for Health and Care Excellence (NICE) has issued clinical practice guidelines for the treatment for long COVID.[20] According to NICE, treatment requires integrated, multidisciplinary models of care that bring patients together with healthcare practitioners from across specialties to meet the wide range of long-term needs with which patients present. In addition to treatments for physical symptoms, NICE guidelines highlight the importance of attending to mental health, cognition, and wellbeing, including among individuals with pre-existing or newly emerging mental health problems. It is therefore important that we embed evidence-based interventions to promote mental and cognitive health and psychological wellbeing into long COVID care.

Integrated, multi-component interventions that are applied to heterogeneous populations in heterogeneous treatment settings can be considered 'complex' interventions according to the UK Medical Research Council complex intervention framework.[21] The recommended type of integrated care for long COVID would be expected to consist of multiple evidence-based components, yet be tailored to the individual patient to produce a range of possible outcomes, while being delivered by a variety of care providers across discliplines.[20] Such complex interventions require careful preparation, implementation, and evaluation to ensure efficacy and effectiveness.

Our team's systematic review of registered trials of interventions for mental health, cognition, and psychological wellbeing in long COVID revealed that the research on such interventions is only just beginning to emerge.[22] Given that COVID-19 research has been emerging at an extremely rapid pace,[23] the associated long COVID treatment literature is expected to follow suit. Timely reviews of the literature on this topic will therefore be key to the process of developing and optimizing the recommended complex, integrated interventions for individuals with long COVID.[24]

Objectives

This paper describes the protocol for a systematic review of clinical trials testing interventions to promote mental health, cognition, or psychological wellbeing among individuals with long COVID.

METHODS AND ANALYSIS

Reporting guidelines

This systematic review protocol follows the protocol version of the Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines (i.e., PRISMA-P).[25] The systematic review will follow the PRISMA guidelines.[26]

Research question

This systematic review will synthesize the scientific literature on interventions that have been tested for mental health, cognition, or psychological wellbeing among individuals experiencing long COVID. Specific research questions are: 1) What are the outcomes of interventions that have been tested for mental health, cognition, or psychological wellbeing among individuals with long COVID? 2) What is the design and quality of the trials?

Eligibility criteria

This review will include articles reporting the results of clinical trials of any intervention aiming to promote mental health, cognition, or psychological wellbeing among people who have long COVID, as described in Table 1. Based on our existing review of registered trials on this topic,[22] the literature is expected to report on psychological interventions, pharmacological interventions, nutritional or natural supplement interventions, cognitive and neurorehabilitation interventions, and physiotherapy or physical rehabilitation. Applying the inclusion criteria, we will include these types of interventions in the review, as well as any other types of interventions that may emerge..

To be included, articles must report on the outcomes of an intervention aiming to promote mental health, cognition, or psychological wellbeing in patients with long COVID symptoms after a confirmed or suspected COVID-19 infection. Controlled and uncontrolled clinical trials will be included. Articles can originate from any country and can report on participants of any age group or other sociodemographic characteristic. To capture the broadest range of studies, the article's definition of long COVID will be accepted, provided that it reports on symptoms experienced at

least 4 weeks after acute infection, consistent with the observed lower limit of duration observed in currently registered trials.[22] Articles can be published in print, online ahead of print, or in unreviewed pre-print format; unpublished summaries of findings will also be accepted. For articles published in a language other than English or French, we will contact authors for English-language summaries; if unavailable, we will have the abstracts translated and will include the English-language abstract in the review. Excluded will be any trials of participants who did not have long COVID, trials conducted prior to 2020 (i.e., before the COVID-19 pandemic), animal trials, treatment guidelines, and opinion papers.

Table 1. Trials to be included in the review

Eligible studies	
Populations	Patients with long COVID symptoms at least 4 weeks after confirmed or suspected COVID-19 infection Any country, any sociodemographic characteristics
Interventions	Interventions aiming to promote mental health, cognition, or psychological wellbeing
Comparators	With any comparison group Without a comparison group
Outcomes	Impact on variables specific to mental health, cognition, or psychological wellbeing

Information sources

A comprehensive search will be conducted in Medline, Embase, APA PsycInfo, Cumulative Index to Nursing and Allied Health Literature (CINAHL), medRxiv, PsyArXiv, China National Knowledge Internet, and WANFANG Data databases, as well as The Cochrane Central Register of Controlled Trials, clinicaltrials.gov, and the WHO International Clinical Trials Registry Platform using the search strategy described below. Reference lists of included articles and any identified review articles will also be examined.

Search strategy

The tentative search strategy has been developed by a health sciences librarian (Table 2). Given the paucity of literature on this topic to date, the search strategy may be refined by the librarian at the time of the review when literature is available. It will therefore be tested and iteratively refined and optimized as the literature emerges. Search concepts built using database-specific subject headings, natural language keywords, and advanced search operators will focus on 1) mental health, cognition, and psychological wellbeing, 2) clinical trials, built using an established clinical trials filter[27] and 3) long COVID search components using an established and tested shared search strategy.[28] No geographical or language limits will be placed on the search, but it will be limited to a timeline of 2020 to present. The English search strategy will be translated to Chinese for use in Chinese searches and the Chinese search strategy will be optimized to each relevant database by qualified Chinese-speaking team members. In addition, specific title and author searches will be conducted for all studies identified in our existing systematic review of registered trials;[22] if unpublished, lead researchers for each previously identified trial will be contacted to request any results that might be eligible for inclusion. Upon completion of the article selection process below, the search will be rerun to update the findings.

Table 2. Tentative search strategy for Medline

Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® <1946-Present>	
1	(exp SARS-CoV-2/ or exp COVID-19/) and sequela*.ti,ab,kf.
2	"long Covid".ti,ab,kf,hw.
3	((Covid or Covid19 or "corona virus 2019" or "coronavirus 2019" or SARS-CoV-2 or nCoV or "B.1.1.7" or "B.1.351" or "B.1.1.28" or "B.1.617") adj3 (PASC or sequela* or "post acute" or postacute or prolonged or "long haul*" or chronic or lingering or ongoing or persistent or "long term" or "more than 12 weeks" or "more than 24 weeks")).ti,ab,kf,hw.
4	or/1-3
5	Mental Health/
6	exp Mental Disorders/
7	exp Neurocognitive Disorders/
8	exp Cognition/
9	exp Quality of life/
10	exp Mental Health Services/
11	exp Psychotherapy/

12	(mental* or psychiatr* or personality disorder* or post-trauma* or posttrauma* or PTSD or complex trauma or developmental trauma or (disorder* adj2 eating) or hallucinat* or (hear* adj3 voice*) or manic or mania or depress* or anxiet* or bipolar or dysthymi* or phobia* or panic* or obsess* or compulsion* or compulsiv* or OCD or mood* or (affective adj3 disorder*) or suicid* or selfharm* or self-harm* or selfinjur* or self-injur* or psychopath* or internaliz* or externaliz* or attention deficit* or ADHD or oppositional* de* or (regulat* adj3 emotional*) or (dysregulat* adj3 emotion*) or aggress*).ti,ab,kf,hw,jn.
13	((emotion* or psycholog*) adj3 distress*).ti,ab,kf,hw.
14	(wellbeing or well-being or wellness).ti,ab,kf,hw.
15	"quality of life".ti,ab,kf,hw.
16	(cognition or cognitive* or neuro*).ti,ab,kf,hw.
17	((psychosocial or psycholog* or psychiatr*) adj3 (intervention* or program* or servic* or treatment*)).ti,ab,kf,hw.
18	(psychoeducation or psycho-education).ti,ab,kf,hw.
19	(cognitiv therap* or behavio?r* therap* or CBT or DBT).ti,ab,kf,hw.
20	psychotherap*.ti,ab,kf,hw.
21	(behav* adj3 (intervention* or program* or servic* or treatment*)).ti,ab,kf,hw.
22	((lifestyle* or life style*) adj3 (therap* or intervention*)).ti,ab,kf,hw.
23	or/5-22
24	(Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt.
25	exp Randomized Controlled Trial/
26	exp Randomized Controlled Trials as Topic/
27	exp Controlled Clinical Trial/
28	exp Controlled Clinical Trials as Topic/
29	Random Allocation/
30	Double-Blind Method/
31	Single-Blind Method/
32	Placebos/
33	Control Groups/
34	(random* or sham or placebo*).ti,ab,kf,hw.
35	((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,kf,hw.
36	((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,kf,hw.
37	(control* adj3 (study or studies or trial* or group*)).ti,ab,kf.
38	(Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,kf,hw.
39	allocated.ti,ab,hw.
40	((open label or open-label) adj5 (study or studies or trial*)).ti,ab,kf,hw.
41	((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,kf,hw.
42	(pragmatic study or pragmatic studies).ti,ab,kf,hw.
43	((pragmatic or practical) adj3 trial*).ti,ab,kf,hw.
44	((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*)).ti,ab,kf,hw.
45	(phase adj3 (III or "3") adj3 (study or studies or trial*)).ti,kf,hw.
46	or/24-45 [CADTH Clinical Trials Filter]
47	(intervention* study or intervention* studies).ti,ab,kf,hw.

48	(("Before after" or "pre post") adj3 (study or studies)).ti,ab,kf,hw.
49	4 and 23 and (46 or 47 or 48)
50	limit 49 to yr="2020 -Current"

Study selection

Identified records will be uploaded into Covidence systematic review software[29] for record management. Titles and abstracts will be reviewed independently by two study staff based on the inclusion and exclusion criteria; any conflicts will be resolved by consensus through discussion with the project lead. Selected documents will be reviewed at the full text level by two staff in the same manner until a final set of included articles is obtained. The record review and selection process will be illustrated using a PRISMA flow chart.[26]

Data extraction

The documents selected for inclusion will undergo data extraction and analysis. Data will be extracted as a team by the two study staff and research lead together for the first 5 documents as a pilot and training stage, to establish consensus. The remaining data will be extracted by one of the study staff and confirmed by a second team member, in discussion with the study lead for any uncertainties. Data extraction will tentatively include the elements summarized in Table 3. Additional elements may be identified over the course of the project as literature emerges, in an iterative manner.

Table 3. Data extraction plan

Category	**Variables to be extracted**
Basic descriptive information	Country, city, publication reference, trial year(s), funder, report type, peer review status
Research question(s)	Primary and secondary objectives, research questions, aims
Participant characteristics	Age, sex, gender, ethnicity
Intervention characteristics	Intervention name, intervention description, dose, delivery

	format, type of administering professional
Study design	Controlled trial (control group), longitudinal (number of assessments, timeline of assessments)
Methodological components	Inclusion criteria, exclusion criteria, long COVID definition, randomization, masking, control group description, sample size, timing of assessments
Measures	Primary outcomes measures, secondary outcome measures
Outcomes	Primary outcomes: Mental health (e.g., depression, anxiety, other mental health variables), cognition, psychological wellbeing (e.g., general wellbeing, quality of life) Secondary outcomes: If appropriate based on the resulting literature, physical and neuropsychological outcomes may be reported on. Intervention and control group means, standard deviations, standard errors, *p* values, effect sizes, odds ratios, relative risk

Outcomes and prioritization

Given the rapidly emerging nature of this new literature base, it is intended that all intervention outcomes specific to the mental health, cognition, and psychological wellbeing of research participants will be sought, including pre- and post- assessments, with follow-up measures where available. Measures of effect will be determined by the outcome tool or instrument used and the design of the studies, given the wide range of symptoms and potential breadth of studies. It is anticipated that standardized mean difference (for continuous outcomes) and odds ratio or relative risk (for binary outcomes) will be the primary measures of effects. The outcome prioritization plan may be expanded upon based on the scope and nature of the literature that is identified. For example, we may include additional secondary outcomes with neuropsychological relevance, such as pain, headache, and fatigue, depending on the nature of

the data.

Data synthesis

Data will be summarized in narrative and table format. We will descriptively report on the number, types, and characteristics of the interventions identified. We will also provide a narrative summary of their efficacy following the Synthesis Without Meta-Analysis (SWiM) guidelines[30] if a meta-analytical stage is not warranted.. If sufficient trials are found that provide treatment efficacy data suitable for a meta-analyses, we will conduct meta-analyses using random effects modeling with RevMan 5.4[31]. We hypothesize that the trials will have different underlying true effects; with that assumption, random-effects models are more appropriate than fixed-effects models.[32] For the standardized mean difference, we will use group mean difference and pooled standard deviation. We will also look at odds ratios and risk ratios as effect sizes for dichotomous outcomes. The heterogeneity between studies will be assessed using forest plot visually, as well as with the I^2 statistic, as recommended by the Cochrane Handbook for Systematic Reviews of Interventions[33]. The meta-regression approach, if feasible, will be used to help understand the sources of heterogeneity. Subgroup analyses will depend on the nature and quantity of data retrieved, due to the variability of symptoms across individuals and the variability of the trials under way. If possible, we will consider subgroup analyses based on gender and other sociodemgraphic variables (Gender-Based Analysis Plus).[34] The decision of perform subgroup analysis/meta-regression will be first driven by the research questions (e.g. gender effect). The number of studies that contains information about the subgroup in question will determine whether the subgroup analyses is feasible.

Assessment of study quality and bias

We will conduct a number of activities to assess the body of research identified using the Cochrane Risk of Bias 2.0 tool for randomized studies.[35] For non-randomized studies, we will use the ROBINS-I tool.[36] A risk-of-bias assessment will be conducted with a bias assessment team of two independent study staff, supported by discussions with the study lead to resolve any disagreements. Generalizability indices, including C-statistics, SMD and Tipton's index[37], will be calculated using the demographic characteristics of the identified samples, such as age and gender; this will serve to determine the degree to which the body of evidence is generalizable to

the population. If meta-analyses are conducted, sensitivity analyses will be conducted to ensure that the pooled results are not unduly influenced by one study; this will entail repeated analyses of the primary analysis, with each study deleted from the pool one at a time. The resulting pooled effects of these sensitivity analyses will then be compared with that of the primary analysis. This process may identify studies that have had a high influence on the overall findings. The certainty of the evidence[38] and the publication bias[35] will also be assessed if the nature of the data permit.

Patient and public involvement

From a patient-oriented research perspective,[39] patients with lived experience of long COVID and associated challenges in mental health, cognition, or psychological wellbeing (i.e., 'patient partners') will be engaged in the conduct of this review. Patient partners will help refine the search plan and data extraction tool and will help co-interpret the findings to ensure that the information obtained is relevant to their real-world experience.

Strengths and limitations

This study will provide a time-sensitive synthesis of the literature examining the efficacy interventions aiming to promote mental health, cognition and psychological wellbeing among individuals with long COVID, to support further research, service development, and implementation initiatives. The inclusion criteria are intentionally broad due to the dearth of literature available at the time of protocol development. However, the amount of research available for review may change rapidly, as COVID-19 research has emerged at an extremely rapid pace.[23] Therefore, it may become necessary to be more restrictive and adjust the draft search terms based on the emerging literature. Any literature released after the date of the updated database search will not be included and could be substantial. The review is further limited by the search in English and Chinese-language databases, the inclusion of English, French, and Chinese full text literature, and English-language translations of abstracts only for literature published in another language; this will limit the generalizability of the findings.

ETHICS AND DISSEMINATION

This systematic review is not subject to research ethics board approval as there will be no participant contact or direct data collection activities. Knowledge translation will include publication of a systematic review manuscript in an open access journal to reduce barriers and provide ease of access to stakeholders outside of academic structures. The findings will further be presented at national and international conferences with research and clinical audiences. We may present the findings in webinar format for ongoing online, international access by stakeholders interested from both research and clinical perspectives. Other lay knowledge translation opportunities may be identified by the patient partner team.

Author contributions:

LH conceptualized and designed the review and drafted the manuscript.

CFS contributed to the design of the review and edited and approved the manuscript.

WW contributed to the design of the review and edited and approved the manuscript.

DRT contributed to the design of the review and edited and approved the manuscript.

SLR contributed to the design of the review and edited and approved the manuscript.

GS contributed to the design of the review and edited and approved the manuscript.

EB contributed to the design of the review and edited and approved the manuscript.

TR contributed to the design of the review, designed the library database search, and edited and approved the manuscript.

DX contributed to the design of the review and edited and approved the manuscript.

DC contributed to the conceptualization and design of the review and edited and approved the manuscript.

Competing interests: David Castle has received grant monies for research from Servier, Boehringer Ingelheim; Travel Support and Honoraria for Talks and Consultancy from Servier, Seqirus, Lundbeck. He is a founder of the Optimal Health Program (OHP), and holds 50% of the IP for OHP; and is part owner of Clarity Healthcare. He does not knowingly have stocks or shares in any pharmaceutical company. Other authors have no conflict of interest to declare.

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Open access: Yes

Ethics: Not applicable. This research did not involve participants.

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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	Page	Checklist item
			ADMINISTRATIVE INFORMATION
Title:			
Identification	1a	1	Identify the report as a protocol of a systematic review
Update	1b	n/a	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	Pending	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:			
Contact	3a	1-2	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	16	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	n/a	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
Support:			
Sources	5a	16	Indicate sources of financial or other support for the review
Sponsor	5b	16	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	16	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
			INTRODUCTION
Rationale	6	5-6	Describe the rationale for the review in the context of what is already known
Objectives	7	6	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
			METHODS
Eligibility criteria	8	7-8	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
Information sources	9	8	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
Search strategy	10	9-11	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

Study records:			
Data management	11a	11	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	11	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)
Data collection process	11c	11	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
Data items	12	11-12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	12	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	13	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
Data synthesis	15a	13	Describe criteria under which study data will be quantitatively synthesised
	15b	13	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)
	15c	13	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	13	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	13-14	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	13	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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