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An exploration of the definitions and measures used when investigating fatigue in adults with long COVID: a scoping review protocol

Abstract

Objective: The aim of this scoping review is to investigate how fatigue is defined and measured in adults with long COVID.

Introduction: Following COVID-19 infection, 10% to 20% of individuals go on to experience persisting symptoms for a minimum of 3 months; this is commonly known as long COVID. Fatigue is one of the most prevalent symptoms of long COVID, but there is currently no consistently applied definition of long COVID fatigue. To advance our understanding of long COVID fatigue, we must first identify the current definitions and measures being used to describe and quantify this condition.

Inclusion criteria: This review will consider published and unpublished studies from January 2020 onwards involving adults (≥ 18 years) that define and/or measure long COVID fatigue. There will be no initial language restrictions, and papers using both quantitative and qualitative designs will be included. Conference abstracts, editorials, and opinion papers will be excluded.

Methods: Published studies will be searched for across MEDLINE (Ovid), CINAHL (EBSCOhost), Embase (Ovid), Scopus, PsycINFO (Ovid), Web of Science, Epistemonikos, and Cochrane Central Register of Controlled Trials (CENTRAL). Dimensions, Overton, and ProQuest Dissertation and Theses will be searched for unpublished literature. Eligible records will be de-duplicated, and 2 independent reviewers will carry out title, abstract, and full-text screening. A data extraction tool will be pilot tested on a small number of papers, then modified as necessary (any modifications will be detailed in the scoping review). Findings will be presented in tables and charts, supported by a narrative summary.

Review registration: The protocol has been registered on open science framework (OSF) <https://doi.org/10.17605/OSF.IO/HNF8Z>

Keywords: definition; fatigue; long COVID; measurement; post-exertional malaise

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Introduction

Coronavirus disease (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ COVID-19 can impact individuals in various ways, ranging from asymptomatic or mild respiratory illness to a severe life-threatening syndrome.¹ The infection can result in a condition commonly referred to as long COVID, also known as post-COVID-19.^{1,2} The World Health Organization (WHO) defines long COVID as the development or persistence of symptoms 3 months after initial infection, with symptoms lasting for at least 2 months.³ The National Institute for Health and Care Excellence (NICE) defines long COVID as symptoms lasting over 12 weeks that develop during or after SARS-CoV-2 infection that cannot be explained by another diagnosis.⁴ While these 2 definitions are quite similar, differences lie in how they define the specific duration of symptoms. It is important that we acknowledge these distinctions as they could result in variations in the criteria used for participant inclusion in research and interventions, subsequently shaping the definitions and understanding of long COVID fatigue. This review adheres to the NICE definition of long COVID as it is the broadest.

Long COVID can involve the continuation or development of new symptoms following initial COVID-19 infection. These symptoms can occur regardless of the severity of initial symptoms. It can impact multiple body systems, including respiratory, gastrointestinal, neurological, cardiovascular, and musculoskeletal.¹ The most common long COVID symptoms include fatigue, cognitive impairment, shortness of breath, insomnia, muscle weakness, and joint stiffness.¹ These symptoms can significantly impact physical and cognitive function; quality of life; and the ability to perform daily activities, such as work or household chores.⁵

Of those infected with SARS-CoV-2, 10% to 20% go on to experience long-lasting symptoms.³ While the precise global prevalence of long COVID remains uncertain at present, data from the WHO suggests that within the first 2 years of the pandemic (2020/21), more than 17 million individuals in the WHO European Region may have experienced long COVID.³ As of March 2023, an estimated 1.9 million people in the UK were experiencing long COVID symptoms.⁶

Fatigue is one of the most commonly reported symptoms of long COVID and can significantly affect functioning,^{2,5,7} including an individual's quality of life,⁸ making it challenging to initiate and maintain physical activity as well as perform cognitively demanding tasks.⁹ This has economic and societal impacts due to decreased productivity and ability to work.⁸ The presence of fatigue can increase the risk of prolonged disability, leading to ongoing medical support, subsequently increasing health care utilization.¹⁰ The impact of long COVID fatigue is clear at both an individual and a societal level. It is essential

to increase our understanding of this construct for the development of management strategies necessary for this population.

Fatigue is considered a multidimensional construct. Several dimensions of long COVID fatigue have been distinguished in the literature, which has led to it being inconsistently defined.¹¹ For example, several studies investigating long COVID fatigue lack a precise definition,¹² and others display variability in how fatigue is defined, encompassing dimensions of physical fatigue,^{13,14} cognitive fatigue,^{5,15} post-exertional malaise,^{7,16} sleep-related fatigue,¹⁷ or general fatigue.¹⁸

As well as the different dimensions of fatigue, further distinction can be made between fatigue that occurs in the context of a specific activity or task and fatigue that is experienced over weeks or months. The former can be operationalized as work capacity, which represents an individual's ability to complete or sustain a task or activity.¹⁹ Fatigue has also been discussed in terms of a measurable decrease in performance and/or an increased perception of fatigue.²⁰ Different dimensions and timescales of fatigue may have different underlying mechanisms, impact on daily activities, and require different interventions or management. The lack of consistency in definitions of fatigue across the literature limits our understanding and treatment of this phenomenon.⁸

There is currently no gold standard for the measurement of long COVID fatigue.²¹ Measures of fatigue can be task-specific or may involve reflecting on fatigue over a longer time period, but these will provide different insights.¹¹ Physical fatigue can be measured using a variety of physiological measures, such as those obtained from heart rate, nerve conduction studies, and electrophysiological examinations.¹³ Cognitive fatigue, also called brain fog,⁵ is typically measured by self-report or by a decline in performance of a cognitively demanding task.²²

A wide variety of psychometric scales exist to evaluate different aspects of fatigue, including both physical and cognitive dimensions. Examples include the Fatigue Severity Scale (FSS),²³ Fatigue Assessment Scale (FAS),²⁴ Multidimensional Fatigue Inventory (MFI),²⁵ Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F),²⁶ and the Chalder Fatigue Questionnaire.²⁷ A clearly defined construct of interest is a prerequisite for developing and validating psychometric scales²⁸; the difficulties with the definition of long COVID fatigue impede efforts to validly and reliably measure this construct.

The extent to which the measures of fatigue used in a study align with the definition of fatigue adopted in that study is currently unclear. For example, does a study that defines long COVID fatigue in terms of cognitive decline, incorporate a physical measure of fatigue?

This leads to inconsistencies in our understanding of long COVID fatigue. Establishing coherence between measures and definitions is crucial to enable results to be compared across studies, aiding both researchers and clinicians in understanding and addressing long COVID fatigue.

A preliminary search of MEDLINE, the Cochrane Database of Systematic Reviews, and *JB/Evidence Synthesis* was conducted. These databases were chosen as they are reputable health databases containing a wide range of literature that is relevant to this review. They contain a number of studies that quantify the proportion of individuals with long COVID that experience fatigue, and a number that investigate the potential mechanisms and risk factors for long COVID fatigue.¹ However, we found no current or in-progress systematic or scoping reviews that investigated how fatigue is defined and measured in long COVID.

Definitions and measures of any construct are important, and become even more so when the topic is complex, multidimensional, and studied across disciplines. This review will explore the definitions and measures of long COVID fatigue that have been used in the literature to date. A scoping review will allow the exploration of these aspects in a broad manner, with the aim of providing an overview of the current definitions and measures of long COVID fatigue.

This review will go on to inform the next stage of our research where we aim to develop a definition of long COVID fatigue, consider the most effective measures of long COVID fatigue to implement in our research, and identify the current inconsistencies between long COVID fatigue definitions and measures.

Review questions

- i) How has long COVID fatigue been defined and contextualized in the literature?
- ii) What tools have been used to assess or measure long COVID fatigue?

Eligibility criteria

Participants

Only studies that involve adults (aged ≥ 18 years) who are described by the primary research authors as having long COVID will be considered, as including studies of minors might introduce unique considerations, requiring age-appropriate measures. There will be no limitations on gender or ethnicity.

Concept

This review will include any quantitative or qualitative study that investigates the concept of long COVID fatigue. All definitions of long COVID fatigue (for example, physical fatigue, cognitive fatigue, post-exertional malaise, brain fog, and sleep-related fatigue) and any form

of assessment or measurement tool that purports to quantify either the impact, severity, or symptoms of long COVID fatigue will be considered.

Context

This review will not be limited by any context, setting, discipline, or field.

Types of sources

This scoping review will include quantitative, qualitative, mixed methods, or systematic reviews. As this scoping review aims to explore how fatigue is defined in a research context, we will only include research papers conducted in an academic/research context and we will only include studies conducted by government and health organizations if they align with the primary focus of academic and research-driven investigations.

Methods

This review will be conducted in accordance with the JBI methodology for scoping reviews.²⁹

Search strategy

The search strategy aims to identify both published and unpublished studies. An initial limited search of MEDLINE and CINAHL was undertaken to identify articles on the topic. The text words contained in the title and abstracts of these articles, as well as the index terms in relevant articles, were analyzed. Keywords were identified and used to develop a comprehensive search strategy to include long COVID fatigue definitions and measures. The process of developing a search strategy was supported by a subject specialist librarian who advised on suitable terminology, databases, and review strategy. The full search strategy for MEDLINE (Ovid) is detailed in Appendix I. The structure of the search strategy will remain the same but will be adapted to align with the unique features (eg, controlled vocabulary, truncation) of each database and/or information source.

We will search MEDLINE (Ovid), CINAHL (EBSCOhost), Embase (Ovid), Scopus, PsycINFO (Ovid), Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases for published literature. We will search Dimensions, Overton, and ProQuest Dissertation and Theses for unpublished literature. Specific, established, health-related databases were chosen to ensure comprehensive coverage of relevant literature surrounding long COVID. Each database has its own unique focus and scope, which enables us to capture a broad range of studies.

There will be no initial language restrictions. Studies published since January 2020 will be included, as this is the earliest point from which long COVID was reported.³

Study selection

Following the search, all identified citations will be collated and uploaded into EndNote v.20 (Clarivate Analytics, PA, USA) and duplicates removed. The web-tool Rayyan (Qatar Computing Research Institute, Doha, Qatar) will be used to facilitate the screening process.

To ensure effectiveness in accurately identifying relevant articles, 2 independent reviewers will pilot test the title and abstract screening processes in Rayyan using the following criteria: publication on or after 2020; discusses long COVID or long COVID fatigue; studied adults (>18 years); not a conference abstract, editorial or opinion paper; not studying lockdown fatigue, fatigue from working during COVID-19 or fatigue from working on a COVID-19 ward; includes a definition and/or measure of long COVID fatigue; uses a quantitative, qualitative, experimental, observational or mixed methods design. Following this, 2 or more independent reviewers will conduct a screening of the remaining titles and abstracts, assessing them using the criteria listed here.

All potentially relevant sources will be retrieved in full and assessed in detail by 2 independent reviewers using the eligibility criteria described. Reasons for exclusion of full text papers will be recorded and reported (all non-English language papers will be excluded at this stage, this decision is influenced by the fact that all members of the research team are English speakers only, and there are no resources available for translation within the timeframe of the review). Any disagreements between reviewers at each stage of the selection process will be resolved through discussion or with a third reviewer. The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.³⁰

Data extraction

Data will be extracted from eligible articles by 2 or more independent reviewers using a data extraction tool developed by the reviewers (Appendix II).²⁹ To ensure effectiveness in accurately extracting the data, 2 independent reviewers will pilot test the data extraction tool. The data to be extracted will include author(s), year of publication, origin/country of origin, study objective, study population (including severity of initial COVID-19 infection, if patients were hospitalized during initial infection, long COVID severity and duration), sample size, methodology/methods, definition(s) of fatigue (if provided), measure(s) of fatigue (including if the measures have been validated, construct of measurement and type of measurement), and key findings that relate to the scoping review questions.

The data extraction tool will be modified as necessary during the process for each included evidence source. Modifications will be detailed in the scoping review. Any disagreements between the reviewers will be resolved through discussion, or with an additional reviewer. Authors of papers will be contacted once to request missing or additional data, where required.

Data analysis and presentation

The extracted data will be presented in tabular format, to present the concepts that are being explored in this review. Tables will be used to present general characteristics of the included studies, the definitions of fatigue, measures and assessment tools (including the name of the measure, the construct measured, whether the measure is validated and how it is scored or quantified). The tables will be accompanied by a narrative summary to uncover patterns of definitions and measures, allowing us to derive new insights and understanding from the data.

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This scoping review will contribute toward a doctor of philosophy (PhD) for BT.

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Author contributions

BT contributed to the conceptualization, methods, original material development, writing (original draft and editing). JD, CB, RP contributed to the conceptualization, methods, writing (review and editing), and supervision. DE contributed to the conceptualization, methods, search strategy input, writing (review and editing). All authors read and approved the final draft.

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Appendix I: Search strategy

OVID MEDLINE ALL <1946 to May 02,2023><level 2 heading>

Date searched: May 3, 2023

	Search	Records retrieved
1	exp Post-Acute COVID-19 Syndrome/	1942
2	((covid* or coronavirus* or sars-cov*) adj3 (Long* or chronic or sequela* or post* or survivor* or on going* or on-going*)).tw.	15,491
3	(post-covid* or post covid* or Long Covid* or Long-covid* or Long-haul-covid or Post-Acute-Covid* or post covid* or after covid* or Chronic-Covid*).tw.	13,861
4	1 or 2 or 3	20,079
5	exp Muscle Fatigue/ or exp Fatigue/ or exp Mental Fatigue/ or exp Fatigue Syndrome, Chronic/	51,546
6	(Fatig* or Brain-fog or Post-exertional malaise or Chronic-fatigue).tw.	125,207
7	5 or 6	137,503
8	4 and 7	1773
9	Limit 8 to yr="2020 – Current")	1721

325 **Appendix II: Draft extraction tool <level 1 heading>**

Draft charting table	
Item	Page number/comments
Title	
Author(s)	
Year of publication	
Origin/country of origin	
Aims/purpose	
Methodology/methods	
Sample size	

326

Study population	
Severity of initial COVID-19 infection	
Hospitalized/not hospitalized during initial infection	
Long COVID severity	
Long COVID duration	

327

Definition (s) of fatigue (if provided)	
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328

Measures of fatigue	
Type of measurement	
Construct of measurement	
If measures have been validated	

329

Key findings	
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330