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Using the ICF framework to explore a multidisciplinary approach to fatigue following traumatic brain injury

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ABSTRACT

Background. Fatigue following a traumatic brain injury (TBI) is a complex, chronic symptom, which can significantly impact quality of life. Investigation into the types of fatigue addressed by the multidisciplinary team and consequent outcomes may assist clinicians to target their care. The use of health frameworks to explore such phenomena may increase a teams' ability to incorporate multifaceted interventions. The objective of this paper is to profile and map the available evidence for fatigue management used for the TBI population onto the International Classification of Functioning, Disability, and Health framework. **Methods.** A scoping review was conducted and included papers that described an intervention focussing on post-TBI fatigue and used fatigue-specific outcome measures with an adult population. Studies were collated and summarised, and key findings are presented. **Results.** Forty-seven articles met the inclusion criteria. The results indicate that post-traumatic fatigue interventions in the literature are conducted by singular professions, that there is a strong focus on a body functions approach, and that there is a discrepancy between intervention intent and measurement. **Conclusion.** Although there is variety in multidisciplinary fatigue treatment, further opportunities to develop interventions that target other health and function components, including activities and participation, environment, and personal factors, may enable a greater impact of fatigue management approaches.

Keywords: activity-based, disease management, head injury, participation, pharmacological, psychological, rehabilitation, scoping review, therapy.

Background

Traumatic brain injury (TBI) is a worldwide contributor to death and disability, with 69 million individuals estimated to experience a TBI each year (Dewan *et al.* 2018). A common and often chronic symptom following a TBI is fatigue. Also referred to as post-traumatic fatigue, this disabling and distressing symptom impacts participation and quality of life for many individuals (Cantor *et al.* 2008; Schiehser *et al.* 2017). As such, it is of great interest to researchers and clinicians to understand best practice approaches to managing post-traumatic fatigue for patients.

Researchers have had great difficulty in both defining and assessing fatigue, despite it being one of the most common symptoms across neurologic disorders. One early definition describes fatigue as 'the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilisation, and/or restoration of resources needed to perform activity' (Aaronson *et al.* 1999). Fatigue may be the result of physiological factors, such as disease or nervous system injury, or exacerbated by psychological factors, such as stress, pain, or sleep disturbance (Malley 2006). Ponsford *et al.* (2015) explored the interrelationships of such internal and external factors and post-traumatic fatigue using a structural equation modelling approach. The results confirmed the complexity of the fatigue experience being determined by several interacting factors, including sleepiness, attentional factors, depression, and anxiety. This gives researchers and clinicians pause to consider such factors when choosing and implementing fatigue interventions for patients.

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Current literature has begun to explore effective fatigue interventions in the TBI population. Cantor *et al.* (2008) first investigated the impact of fatigue on participation and quality of life and found articles evaluating pharmacological, cognitive/behavioural, and physical activity interventions. With a high risk of bias and mixed outcome measures, the authors were unable to recommend specific interventions for practice. Other reviews targeted randomised control trials (RCTs) and highlighted several complementary and alternative interventions yet noted similar issues, such as the need for clearer outcome measures and larger sample sizes (Shuman-Paretsky *et al.* 2017; Xu *et al.* 2017). The most recent systematic review by Ali *et al.* (2022) cast a broader net to cover 30 years of research of fatigue interventions. They concluded that post-traumatic fatigue is multifaceted and that multimodal clinical treatment approaches that include sustainable levels of exercise, judicious medication prescription, and/or behavioural therapy provided by a multidisciplinary rehabilitation team are required. However, due to variability in study methodologies, including in primary interventional outcomes and measures, the way to implement such a complex treatment approach is not clear.

Considering the complex nature of fatigue, further investigation into the types of fatigue addressed by the multidisciplinary team and consequent outcomes would be useful to assist clinicians to target their care. The use of health frameworks in scientific research can help to provide structure to enable the comparison of research results. The International Classification of Functioning, Disability, and Health (ICF) is widely used as a conceptual basis for definition, measurement, and policy formulations in health and disability research. The ICF offers a logical view of different perspectives of health (biological, individual and social) comprising the following components: Body Structure, Body Function, Activities and Participation, Environmental Factors, and Personal Factors (World Health Organization 2002). Meirte *et al.* (2014) used the ICF framework to investigate the depth and breadth of burns outcome measures when examining function and quality of life. Others have also gone further to use the framework as a basis for multifaceted assessments when developing a rehabilitation management plan and targeting interventions (Steiner *et al.* 2002; Goljar *et al.* 2011). Exploring post-traumatic fatigue management through an ICF lens would support enhanced understanding of the phenomena and how to incorporate multifaceted interventions to address various levels of functioning and disability. Therefore, the objective of this scoping review was to profile and map the available evidence for fatigue management used for the TBI population onto the ICF framework.

Methods

This scoping review was conducted based on the framework designed by Levac *et al.* (2010) with no protocol previously published. The framework consists of six stages: identifying the research question; identifying relevant studies; study selection; charting the data; collating, summarising, and reporting, specifically in relation to the ICF framework; and consultation. The six stages of the scoping review process are described below.

Identifying the research question

Five research questions were established by the research team to guide the scoping review. It was important to identify key concepts to provide clarity and direction when establishing these research questions and support the overall search process. See Table 1 for full details.

(1) What type of fatigue is reported and how is it measured?
(2) What fatigue management interventions are reported, and do they address specific types of fatigue?
(3) Are the reported interventions delivered by a singular or multi-profession approach?
(4) What are the reported outcomes for fatigue management?
(5) How are measurements, interventions and outcomes mapped onto the ICF framework?

Identifying relevant studies

The research team conducted the original search strategy in February 2022 and updated it in January 2023. The first author completed the search across PubMed Central, EMBASE, CINAHL, OT Seeker, Cochrane Database, Ovid Medline, and Web of Science using Medical Subject Headings, key terms, and words such as TBI, acquired brain injury, fatigue, management, intervention, and strategies. All sources of information were considered, including published and unpublished primary studies, conference abstracts, and reviews. Additionally, the first author

Table 1. Guiding key concepts for research questions.

Traumatic brian injury (TBI)	A form of acquired brain injury, occurring when a sudden trauma causes damage to the brain. TBI can result when the head suddenly and violently hits an object or when an object pierces the skull and enters brain tissue. Symptoms and therefore classification of a TBI can be mild, moderate, or severe, depending on the extent of the damage to the brain (NINDS 2019).
Fatigue	'The awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilisation, and/or restoration of resources needed to perform activity' (Aaronson *et al.* 1999).
Multidisciplinary	The cooperation between different specialised professionals with the overarching goal of improving treatment efficiency and patient care (Taberna *et al.* 2020).

completed a manual search of identified articles' reference lists for additional studies. See the full search strategy in the supplemental material.

Study selection

Studies of quantitative, qualitative, and mixed methodologies were reviewed. Eligibility criteria incorporated studies published between 1980 and January 2023. Further inclusion criteria included studies where (1) post-traumatic fatigue, in-line with the key concept definition (Table 1), was an outcome measure; (2) fatigue was the focus of the intervention; and (3) the population of adults (18 years or older) included any percentage of individuals with a TBI. To capture the aspects of a multidisciplinary approach, the authors allowed the inclusion of any clinical setting, including inpatient, outpatient, or community-based; any discipline; and any format of intervention. Reasons for exclusion were if the journal article was a literature review, not published in English, had a paediatric population included, or if it was a dissertation paper. The scoping review methodology was enhanced using the Covidence system to systematically streamline the review process (Veritas Health Innovation 2017). All studies identified in the literature searching phase were independently screened by the first and second author according to the above criteria, with the authors meeting to resolve any conflicts to progress to the next stage. A double-blind full text review was completed with consensus required for final study inclusion.

Charting the data

Using a data-charting form developed by the research team, data were extracted from the selected studies. Extracted information included year of publication and location, study design and objectives, fatigue definition, characteristics of the sample, description of the intervention, fatigue outcomes measures, results, and whether interventions used a single profession or multi-profession approach. It was important to review the methodological quality of the literature, critically and systematically considering and identifying quality components of a reported study. This was done using the Critical Appraisal Skills Program checklist for RCTs, cohort studies, and qualitative research. This tool has a foundational approach, and therefore, no specific scoring was calculated (Critical appraisal skills programme 2018). Both authors checked and reviewed the charted data, and consensus was reached before moving onto the next step.

Collating, summarising, and reporting

Data were collated in table format to describe key characteristics pertaining to the research questions. As suggested by Levac *et al.* (2010), a qualitative content analysis was completed to complement the objective of this study, namely gathering, considering, and mapping the evidence in relation to the ICF framework. ICF linking rules were used as a foundation to the content analysis (Cieza *et al.* 2005). This was completed by first reading through the full texts of articles to identify segments of text relating to fatigue-related measurements, interventions, and outcomes. As recommended by Cieza *et al.* (2005) meaningful concepts were identified and coded to these segments. Meaningful 'concepts' are those that describe a health condition, functional activity, person, or any environmental factors (Patel *et al.* 2020). These coded segments were transferred to a spreadsheet where both authors independently reviewed and linked the data to the most precise ICF category of each ICF component. For example, the Fatigue Severity Scale (FSS) has two items: 'My motivation is lower when I'm fatigued' and 'Exercise brings on fatigue,' with concepts extracted from these as 'motivation', 'physical function' and 'fatigue'. Motivation was linked to second-level ICF category, 'b130 energy and functions', and physical function was linked to the second-level ICF category, 'b455 exercise tolerance functions', both items falling under the ICF component of 'Body Functions'. Fatigue can be coded under two third-level headings depending on type: physical fatigue 'b4552 fatiguability' or mental fatigue 'b1300 energy level'. The coded segments and associated ICF category were discussed by both authors and agreed upon before moving to the next step. The meanings of the findings as they relate to the overall study purpose as well as implications for future research, practice, and policy were also considered and reported.

Consultation

The research team included an experienced occupational therapy academic and an experienced rehabilitation occupational therapist currently practicing in the field of brain injury rehabilitation. Consultation between the researchers enabled knowledge exchange and helped refine the context of the scoping review results, including consideration of the definition of fatigue and interpretation of preliminary results and the ICF framework components, which helped shape the discussion of the study findings (Levac *et al.* 2010).

Results

Study selection and characteristics

From an initial search strategy yielding 2020 articles, 258 met inclusion criteria by blind consensus review, with 81 articles undergoing a full text review. Thirty-two articles were excluded, as they did not meet eligibility criteria or were a dissertation paper. A total of 49 articles met the criteria for inclusion. A summary of the results of the search and study selection are outlined in Fig. 1. Of the included articles, 27 reported results from a RCT, 15 were observational designs, with three of these including qualitative data, three were case reports and four were conference abstracts.

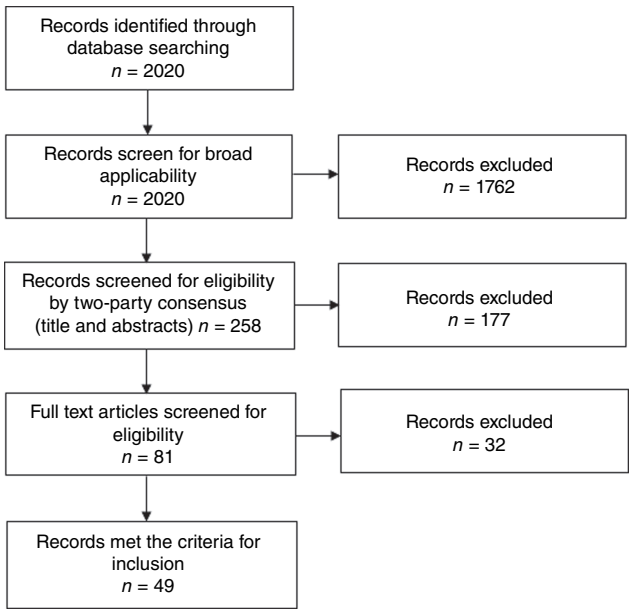

Fig. 1. Study selection flow diagram.

The characteristics of these studies are summarised in Tables 2, 3 and 4.

Methodological quality

The critical appraisal of the studies demonstrated variability in the level of evidence, and therefore, generalisable conclusions are difficult to make. All the RCTs reported satisfactory internal validity with random allocation, blinded observers, and low attrition rates. The majority of these studies were pharmacological, where clear methodologies presented a generally lower risk of bias. For the 16 observational designs, validity was impacted by small sample sizes of less than 50 and minimal follow up (less than 6–8 months). Outcome measure variation also made result comparison difficult, with a variety of standardised and non-standardised measures used. Lastly, although all studies focused on brain injury, there was heterogeneity in type, as stroke or post-surgical injuries were included alongside TBI in some populations. This coupled with variation of age, gender, and study location influenced the generalisability of the results.

Defining and measuring fatigue

To answer the first research question, the authors summarised how post-traumatic fatigue was considered and defined in the included studies, highlighting the type of fatigue and the outcome measures used (see Table 2).

Fifteen articles provided a clear definition of post-traumatic fatigue in relation to their study objectives. A significant focus on mental fatigue was found, with descriptions of cognitive symptoms including irritability, emotional instability, lack of motivation, poor concentration, and poor attention (Johansson *et al.* 2012*a*, 2012*b*, 2015*a*, 2015*b*, 2017; Dobryakova *et al.* 2020; Nilsson *et al.* 2020). Johansson *et al.* (2012*b*), and Nilsson *et al.* (2020) described the experiences of an inability to hold large amounts of information at the same time or over an extended period. Physical fatigue definitions appeared to focus on the impact of excessive energy consumption resulting in symptoms of headaches, weariness, tiredness, weakness, and sleepiness (Jha *et al.* 2008; Driver and Ede 2009; Mossberg *et al.* 2017). All made some reference to the notion of fatigue being a depletion of energy resources with a decreased capacity for work or effort. Cooper *et al.* (2009) specifically referenced the impact of this decreased capacity on functional abilities, 'exhaustion develops rapidly during both mental and physical activity, affecting all aspects of participation in everyday activities'. Twenty-six articles did not clearly define fatigue. The majority of articles simply referenced the impact of post-traumatic brain fatigue, 'fatigue is a truly disabling symptom, affecting activities in daily life and occupational ability' (Berginström *et al.* 2017) or its prevalence, 'fatigue was found to be the most frequent somatic complaint for TBI' (Quera Salva *et al.* 2020). Eight articles did not present any post-traumatic fatigue definition.

All articles used at least one fatigue outcome measure, with the FSS and Mental Fatigue Scale the most prevalent with 18 and 15 references respectively. Altogether, 20 different fatigue outcome measures were used across the reviewed articles. The majority of measures were standardised assessments; however, six articles used subjective ratings of fatigue on a visual analogue scale, four used qualitative interviews to explore experiences, and four used non-standardised satisfaction questionnaires.

The focus of fatigue management interventions

To answer the second and third research questions, the authors summarised the focus and description of fatigue management interventions, participant characteristics, delivery setting, and discipline approach (see Table 3).

There was variety in the types of fatigue management interventions reported. Fifteen articles focussed on pharmacological interventions, including Methylphenidate (Johansson *et al.* 2014, 2015*c*, 2017, 2018, 2020; Zhang and Wang 2017), (-)-OSU6162 (Carlsson 2012; Johansson *et al.* 2012*b*; Berginström *et al.* 2017; Nilsson *et al.* 2020), Modafinil (Jha *et al.* 2008; Kaiser *et al.* 2010), and Melatonin (Grima *et al.* 2018). These appeared to focus on addressing mental fatigue. Recombinant human growth hormone (rhGH) was also explored to address the impact of physical fatigue (Mossberg *et al.* 2017; Wright *et al.* 2020). Psychological interventions were described in 17 articles. Cognitive Behavioural Therapy (CBT), individual sessions focussing on mental fatigue, was used in six articles (Ouellet and Morin 2007; Lu *et al.* 2016; Potter *et al.* 2016; Nguyen *et al.* 2017; Ymer *et al.* 2021*a*, 2021*b*). Mindfulness Based Stress Reduction (MBSR), also focussing on mental fatigue, was explored in three articles

Table 2. Fatigue definitions and outcome measures.

Study, year, and location	Fatigue definition	Fatigue focus	Fatigue outcomes measures
Audrit *et al.* (2021) Canada	Not defined	Not stated	Multidimensional Fatigue Inventory
Berginström *et al.* (2017) Sweden	No clear definition – reference to impact only 'Fatigue is a truly disabling symptom, affecting activities in daily life and occupational ability, as well as physical and social functioning'	Mental/cognitive fatigue	Fatigue Severity Scale Mental Fatigue Scale
Carlsson (2012) Sweden	Not defined	Mental/cognitive fatigue	Mental Fatigue Scale
Chin *et al.* (2015) USA	No clear definition – reference to impact only 'Individuals with TBI may become fatigued while participating in physical activities that are of relatively low-energy demands. A vicious cycle may thereby be created in which these individuals avoid engaging in physical activity, further reducing their cardiorespiratory fitness, and increasing their fatigability'	Physical fatigue	Fatigue Severity Scale
Connolly *et al.* (2021*a*) Australia	No clear definition – reference to impact only 'Fatigue is the most common and persistent complaint following TBI…and imposes significant limitations on physical and social/leisure activities and participation in work and/or study, resulting in poorer quality of life'	Not stated	Brief Fatigue Inventory Fatigue Severity Scale Intervention satisfaction questionnaires
Connolly *et al.* (2021*b*) Australia	No clear definition – reference to impact only 'Fatigue and sleep disturbance are common and debilitating problems for individuals with TBI and stroke'	Not stated	Brief Fatigue Inventory Fatigue Severity Scale Intervention satisfaction questionnaires
Connolly *et al.* (2021*c*) Australia	No clear definition – reference to impact only 'Fatigue and sleep disturbance are debilitating sequelae of TBI and stroke across the spectrum of severity'	Not stated	Brief Fatigue Inventory
Cooper *et al.* (2009) UK	'Defining and measuring fatigue is notoriously difficult because of the complexity of interacting factors in this symptom. Exhaustion develops rapidly during both mental and physical activity, affecting all aspects of participation in everyday activities'	Physical and mental	The Brain Injury Fatigue Scale (an unpublished PhD thesis questionnaire) Qualitative interviews
Dobryakova *et al.* (2020) USA	'A subjective feeling of difficulty in initiating or sustaining voluntary mental tasks'	Mental/cognitive fatigue	Visual analogue scale of fatigue measured throughout task. Modified Fatigue Impact Scale
Dornonville de la Cour *et al.* (2022) Denmark	No clear definition – reference to impact only 'Fatigue is a common, debilitating, and often persistent sequela of acquired brain injury'	Not stated	Multidimensional Fatigue Inventory
Driver and Ede (2009) USA	'Tired, worn out'	Physical fatigue	Fatigue subscale of Profile of Mood States
Grima *et al.* (2018) Australia	Not defined	Not stated	Fatigue Severity Scale
Howe *et al.* (2019) Norway	Not defined	Not stated	Fatigue Severity Scale Rivermead Post Concussive Symptoms Questionnaire Intervention feedback form
Humphries (2017) UK	No clear definition – reference to impact only 'Fatigue following brain injury is a common symptom in neurological practice and can impact recovery'	Not stated	Fatigue Severity Scale Qualitative questions
Jha *et al.* (2008) USA	'An overwhelming sense of exhaustion and decreased capacity for physical and mental work regardless of adequate sleep. It has been construed both as a single discrete experience and as a multicausal phenomenon that exists along a continuum of severity. Moreover, there appears to be two types or dimensions of fatigue; physical fatigue has been defined as the end result of excessive energy consumption, depleted hormones or neurotransmitters, or diminished ability of muscle cells to contract. Psychological or mental fatigue, on the other hand, is defined as a subjective state of weariness related to reduced motivation, prolonged mental activity, or boredom'	Physical and mental	Fatigue Severity Scale Modified Fatigue Impact Scale

(*Continued on next page*)

Table 2. (*Continued*)

Study, year, and location	Fatigue definition	Fatigue focus	Fatigue outcomes measures
Johansson *et al.* (2012*b*) Sweden	'The person suffering from mental fatigue is able to exert mental effort for short periods only, and notably, it takes longer than normal to regain energy after reaching the level of exhaustion. The afflicted person is also unable to handle large quantities of information at the same time or during longer time periods. Accompanying symptoms are irritability, emotional instability, and headache'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2014) Sweden	No clear definition – reference to impact only 'Fatigue and concentration deficits are acknowledged as being one of the most distressing and long-lasting symptoms following mild TBI'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2015*a*) Sweden	'Fatigue is one of the most important long-lasting symptoms interfering with the ability to return to work. Mental activities are reported to be more energy demanding. The person is able to perform mental effort for short periods. A considerable tiredness can appear suddenly, and in that situation the affected person is not able to continue the activity'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2017) Sweden	'Mental fatigue after TBI is that mental exhaustion becomes pronounced during sensory stimulation or when cognitive tasks are performed for extended periods without breaks. There is a drain of mental energy in situations in which there is an invasion of senses with an overload of impressions, particularly in noisy and hectic environments. Another typical feature is a disproportionally long recovery time needed to restore the mental energy levels after being mentally exhausted. Mental fatigue often fluctuates during the day depending on activities. Thus, this fatigue is a dynamic process with variations in the mental energy level'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2018) Sweden	No clear definition – reference to impact only 'This symptom [mental fatigue] has a substantial impact on the ability to resume work or studies and also interferes considerably with social life.'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2020) Sweden	No clear definition – reference to impact only 'Persistent or long-term mental fatigue and cognitive impairments are common among people who have suffered from a traumatic brain injury (TBI). Fatigue is endorsed as being one of the most distressing and long-lasting symptoms after mild TBI'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2012*a*) Sweden	'The person who suffers from this mental fatigue is able to perform activities involving mental effort for short periods only and, notably, it will take longer than normal to restore energy levels after being exhausted. This mental fatigue will make it more difficult for the person to return to work and participate in social activities. Accompanying symptoms, such as irritability, sensitivity to stress, concentration difficulties, emotional instability and headache may further impair social interactions'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2015*b*) Sweden	'Mental fatigue is characterised by pronounced and rapid mental exhaustion even after moderate mental activity which involves a demand on the person's concentration and attention. The ability to manage multiple, simultaneous stimuli has been disrupted'	Mental/cognitive fatigue	Mental Fatigue Scale
Johansson *et al.* (2015*c*) Sweden	'Mental fatigue is characterised by limited energy reserves for accomplishing ordinary everyday activities, in addition to increased irritability, sensitivity to stress, difficulty concentrating, and emotional instability'	Mental/cognitive fatigue	Mental Fatigue Scale
Kaiser *et al.* (2010) Switzerland	No clear definition – reference to impact only 'Fatigue is a frequent symptom of TBI, can significantly impact quality of life and daytime functioning, including professional performances and social activities'	Not stated	Fatigue Severity Scale

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Table 2. (*Continued*)

Study, year, and location	Fatigue definition	Fatigue focus	Fatigue outcomes measures
Kolakowsky-Hayner *et al.* (2017) USA	No clear definition – reference to impact only 'Fatigue is one of the most commonly reported sequelae comprising the acute and chronic phases of TBI'	Not stated	Global Fatigue Index Barrow Neurological Institute Fatigue Scale Overall Severity Index Score Multidimensional Fatigue Inventory
Killington *et al.* (2021) Australia	'The most compelling aspect of fatigue described by patients relates to a central fatigue, with reports of increased susceptibility to effort and reduced endurance to sustain both physical and mental activities. In particular, mental fatigue affects work capacity and the ability to socialise, as related symptoms can include decreased information processing speed and divided attention'	Mental/cognitive fatigue	Barrow Neurological Institute Fatigue Scale. Patient self-evaluation of perceptions of fatigue and fatigue management principles. Qualitative interview (for perspectives of group usefulness)
Lilliecreutz *et al.* (2017) Sweden	No clear definition – reference to prevalence only 'Mental fatigue is commonly reported in individuals with ABI [aquired brain injury]'	Mental/cognitive fatigue	Mental Fatigue Scale
Lu *et al.* (2016) USA	No clear definition – reference to impact only 'Post-TBI fatigue can lead to daytime napping, which dysregulates the circadian rhythm and makes falling asleep at night more difficult'	Not stated	Multidimensional Assessment of Fatigue
Meek *et al.* (2021) Canada	Not defined	Not stated	Post-Concussion Symptom Scale – Fatigue subscaleFatigue Severity Scale
Mossberg *et al.* (2017) USA	'Central fatigue, not to be confused with apathy or depression, is typically viewed as a subjective phenomenon that can be expressed, for instance, as experiencing a lack of energy or motivation, weakness, and/or sleepiness and has been reported to greatly impact patients' lifestyles by limiting participation in therapeutic, social, and/or leisure activities'	Physical fatigue	Muscle fatigue measured through isokinetic contractions Perceived fatigue scale (self-rated) Fatigue Severity Scale
Nelson and Esty (2010) USA	Not defined	Not stated	Self-report of symptoms on a 0–10 visual analogue scale (10 being worst)
Nelson and Esty (2015) USA	No clear definition – reference to impact only 'Fatigue, a severe symptom of TBI'	Not stated	Self-report of symptoms on a 0–10 visual analogue scale (10 being worst)
Nguyen *et al.* (2017) Australia	No clear definition – reference to impact only 'Fatigue complaints may persist many years postinjury and adversely affect physical, cognitive, and emotional functioning, leading to poorer long-term quality of life'	Not stated	The Brief Fatigue Inventory Fatigue Severity Scale
Nilsson *et al.* (2020) Sweden	'Persons with mental fatigue can exert mental effort only for short periods, and they need longer time than normal to regain energy. It is also difficult for persons with mental fatigue to handle large quantities of information at the same time. Accompanying symptoms are irritability, emotional instability, and headache'	Mental/cognitive fatigue	Mental Fatigue Scale
Ouellet and Morin (2007) Canada	No clear definition – reference to prevalence only 'Fatigue is a very important, widespread, and debilitating sequela of TBI'	Not stated	Multidimensional Fatigue Inventory
Potter *et al.* (2016) UK	Not defined	Not stated	Checklist of Individual Strength
Quera Salva *et al.* (2020) France	No clear definition – reference to prevalence only 'Fatigue was found to be the most frequent somatic complaint for TBI, causes of the fatigue may be of multiple origins'	Not stated	Fatigue Severity Scale
Raina *et al.* (2016) USA	'The self-recognised state in which the person experiences an overwhelming sustained sense of exhaustion and decreased capacity for physical and mental work that is not relieved by rest'	Physical and mental	Modified Fatigue Impact Scale Patient-Reported Outcomes Measurement Information System Fatigue Scale Fatigue Severity Scale
Raina *et al.* (2022) USA	No clear definition – reference to impact only 'Fatigue, a devastating sequela of traumatic brain injury with a prevalence of 43% to 73%, persists for years after the injury. Fatigue negatively affects a person's physical, cognitive, social, and emotional functioning'	Physical and mental	Modified Fatigue Impact Scale

(*Continued on next page*)

Table 2. (*Continued*)

Study, year, and location	Fatigue definition	Fatigue focus	Fatigue outcomes measures
Schoenberger *et al.* (2001) USA	Not defined	Not stated	Multidimensional Fatigue Inventory
Shirvani *et al.* (2021) Iran	No clear definition – reference to impact only 'Mental fatigue, a severe symptom of mTBI [mild TBI]'	Mental/cognitive fatigue	Mental Fatigue Scale
Sinclair *et al.* (2014) Australia	No clear definition – reference to impact only 'Fatigue is a common, persistent, and disabling consequence of TBI, reported by more than 60% of patients with TBI. Its etiology is not well understood, although both primary (i.e. brain pathology) and secondary factors (depression, anxiety, and sleep disturbances) are implicated'	Not stated	Fatigue Severity Scale
Stubberud *et al.* (2019) Norway	'The awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilisation and/or restoration of resources needed to perform an activity'	Physical and mental	Fatigue Severity Scale Subjective fatigue questionnaire
Whyte *et al.* (2015) USA	No clear definition – reference to impact only 'Chronic pathological fatigue remains one of the most common and distressing symptoms following TBI'	Not stated	Fatigue Impact Scale Patient Reported Outcomes Measurement Information System
Wright *et al.* (2020) USA	No clear definition – reference to impact only 'The level of fatigue that patients report following TBI appears correlated with other quality-of-life-related symptoms including anxiety, sleep disturbance, and cognitive impairment'	Not stated	Modified Fatigue Impact Scale Brief Fatigue Inventory
Ymer *et al.* (2021) Australia	No clear definition – reference to impact only 'Fatigue is a common consequence, reported by 50–70% of ABI survivors, has been associated with poor functioning in activities of daily living and may contribute to decreased employment status and delayed return to study'	Not stated	Fatigue Severity Scale Brief Fatigue Inventory
Ymer *et al.* (2022) Australia	No clear definition – reference to impact only 'Fatigue is a prevalent and debilitating sequela of acquired brain injury (ABI)'	Not stated	Fatigue Severity Scale
Zhang and Wang (2017) China	No clear definition – reference to prevalence only 'Patients with TBI may present with various neuropsychiatric and mental sequelae including fatigue'	Mental/cognitive fatigue	Mental Fatigue Scale

through group face-to-face sessions (Johansson *et al.* 2012*a*, 2015*b*) or delivered live online (Johansson *et al.* 2015*a*). Physical and mental fatigue was the focus of multifaceted psychosocial education groups described in eight articles, implementing sessions on health education, symptom control and behavioural change (Cooper *et al.* 2009; Howe *et al.* 2019; Stubberud *et al.* 2019; Audrit *et al.* 2021; Killington *et al.* 2021). The Maximising Energy (MAX) intervention also utilised in problem-solving therapy for managing fatigue-related problems (Whyte *et al.* 2015; Raina *et al.* 2016, 2022). Activity-based interventions were described in five articles. Three utilised aerobic exercise (either indoor or outdoor walking) (Chin *et al.* 2015; Kolakowsky-Hayner *et al.* 2017; Lilliecreutz *et al.* 2017), one explored aquatic activity alongside a vocational education class (Driver and Ede 2009), one involved high intensity interval training (Dornonville de la Cour *et al.* 2022), and one article explored a task stimulation headset game (Dobryakova *et al.* 2020). These interventions focused on both physical and mental fatigue. Complementary and alternative medicine (CAM) interventions were described in 10 articles. These included light therapy (Sinclair *et al.* 2014; Quera Salva *et al.* 2020; Connolly *et al.* 2021*a*, 2021*b*, 2021*c*), the Flexyx Neurotherapy System (FNS) (Schoenberger *et al.* 2001; Nelson and Esty 2010, 2015), and transcranial stimulation interventions (Meek *et al.* 2021; Shirvani *et al.* 2021). None of these articles described a type of fatigue focus. Interventions mainly occurred in either community (22) or outpatient (22) settings with only three articles describing an inpatient hospital intervention.

Despite a variety in interventional modalities, all articles reported a singular discipline approach: physician/medical (17), neuropsychology (13), occupational therapy (6), psychology (3), neurotherapy (3), or physiotherapy (3). Four articles were researcher-led and did not state a specific discipline.

Fatigue management outcomes

To answer the fourth research question, the authors summarised fatigue management outcomes according to four main interventional areas: pharmacological, psychological, activity-based, and CAM interventions (see Table 4)

Table 3. Fatigue management interventions.

Study, year, and location	Setting	N = TBI sample	Intervention description	Fatigue focus	Discipline approach
Audrit *et al.* (2021) Canada	Outpatient	10	Sleep and fatigue, Attention and concentration, Anxiety and mood, Memory and organisation (SAAM intervention) – psychoeducation, group model, 1 h/week for 4 weeks. Content based on biopsychosocial model addresses misconception and perception of mild TBI recovery and symptoms and provides reassurance and counselling about recovery.	Not stated	Single profession – neuropsychology
Berginström *et al.* (2017) Sweden	Outpatient	64	(−)-OSU6162 15 mg dose given orally twice a day during a 4 week treatment period, compared with placebo.	Mental/cognitive fatigue	Single profession – physician
Carlsson (2012) Sweden	Community/ home	6	OSU6162 was given orally for 4 weeks in doses increasing from 15 to 45 mg twice a day.	Mental/cognitive fatigue	Single profession – physician
Chin *et al.* (2015) USA	Outpatient	10	Supervised independent aerobic exercise training program for 12 weeks.	Physical fatigue	Single profession – not stated
Connolly *et al.* (2021*a*) Australia	Community/ home	2	Exposure to a home-based dynamic light therapy, in which treatment consisted of ambient exposure to blue-enriched white light during the daytime and blue-depleted white light for 3 h prior to sleep. Compared with control lighting usual lighting (3000–4000 K during the day and evening). Two month intervention condition (treatment and control conditions) with 1-month follow up.	Not stated	Single profession – neuropsychology
Connolly *et al.* (2021*b*) Australia	Community/ home	23	Home-based dynamic light therapy as described in Connolly *et al.* (2021*a*).	Not stated	Single profession – neuropsychology
Connolly *et al.* (2021*c*) Australia	Community/ Home	23	Home-based dynamic light therapy as described in Connolly *et al.* (2021*a*).	Not stated	Single profession – neuropsychology
Cooper *et al.* (2009) UK	Outpatient	3	Weekly fatigue education group, lasting for 8 weeks.	Physical and mental	Single profession – occupational therapy
Dobryakova *et al.* (2020) USA	Outpatient	45	Task stimulation headset game 'E-Prime' with monetary incentive, completed whilst participants received an magnetic resonance imaging scan.	Mental/cognitive fatigue	Single profession – not stated
Dornonville de la Cour *et al.* (2022) Denmark	Outpatient	3	Six-week (18 sessions) high intensity interval training program.	Not stated	Single profession – physiotherapy
Driver and Ede (2009) USA	Outpatient	16	Intervention: Individualised physical activity aquatic and aerobic sessions, 1 h/week for 8 weeks. Control: voc rehab class aimed at improving reading and writing skills post-injury, 1 h/week for 8 weeks.	Physical fatigue	Single profession – not stated
Grima *et al.* (2018) Australia	Community/ Home	33	Prolonged-release Melatonin formulation (2 mg; Circadin®) and placebo capsules for 4 weeks each in a counterbalanced fashion separated by a 48 h washout period.	Not stated	Single profession – physician
Howe *et al.* (2019) Norway	Outpatient	6	Compensatory Cognitive Training is a manualised intervention targeting post-concussive symptom management and cognitive symptoms. A group-based treatment program delivered in 10 × 2 h sessions of psychoeducation and compensatory cognitive training strategies. One session focuses on fatigue.	Not stated	Single profession – psychology

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Table 3. (*Continued*)

Study, year, and location	Setting	N = TBI sample	Intervention description	Fatigue focus	Discipline approach
Humphries (2017) UK	Inpatient	22	Six sessions of group education, recording energy levels and analysing diary sheets to identify personal energy budgets. Sheets give a visual overview of patterns of energy. Activity and pacing plans are developed based on the diary sheets. Between sessions, clients practice strategies and develop plans.	Not stated	Single profession – occupational therapy
Jha *et al.* (2008) USA	Community/ home	51	Modafinil up to 400 mg dose compared to control of equal number of inactive placebo tablets over 10 weeks.	Physical and mental	Single profession – physician
Johansson *et al.* (2012*a*) Sweden	Community/ home	6	(−)-OSU6162 15 mg dose with option to increase pending therapeutic effect.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2014) Sweden	Community/ home	29	Methylphenidate with three treatment periods: no medication, low dose (5 mg × 3), and normal dose (20 mg × 3) for 4 weeks each.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2015*a*) Sweden	Community/ home	51	Methylphenidate 5 mg – 60 mg weekly for 12 weeks.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2017) Sweden	Community/ home	32	Methylphenidate dose individually adjusted to reach an optimal balance between positive symptomatic effects and side effects.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2018) Sweden	Community/ home	18	Two year follow up of Methylphenidate dose from above study, including evaluation of effects of a 4 week break of medication.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2020) Sweden	Community/ home	17	Follow up review 5.5 years post initial start of Methylphenidate treatment (Johansson *et al.* 2015*a*) + after a 4 week break of medication.	Mental/cognitive fatigue	Single profession – physician
Johansson *et al.* (2012*a*) Sweden	Outpatient	10	Mindfulness Based Stress Reduction (MBSR) is a structured health intervention that cultivates mindfulness in medicine, healthcare, and society; it includes gentle Hatha yoga, body scan and sitting meditation. Participants underwent 2.5 h/week group sessions for 8 weeks, 1 day-long silent led retreat, and home practice of 45 min. Waitlist control.	Mental/cognitive fatigue	Single profession – neuropsychology
Johansson *et al.* (2015*b*) Sweden	Outpatient	6	Follow on from above study (Johansson *et al.* 2012*a*). Advanced MBSR program: an 8 month program with monthly group meetings (2.5 h), and the program concluded with an all-day retreat. Program inspired from the book, 'Buddhas Brain: The Practical Neuroscience of Happiness, Love, and Wisdom'.	Mental/cognitive fatigue	Single profession – neuropsychology
Johansson *et al.* (2015*c*) Sweden	Community/ home	16	Intervention MBSR face-to-face: weekly 2.5 h sessions and one full-day session. Educational and experiential aspects of mindfulness and meditation. Intervention MBSR live internet: same session as above but delivered over the internet in patient's own home. Had opportunity to interact with each other via online platform. Control: peaceful walking group 1.5 h/week for 8 weeks.	Mental/cognitive fatigue	Single profession – neuropsychology
Kaiser *et al.* (2010) Switzerland	Community/ home	20	Modafinil 100–200 mg dose each morning compared to placebo control for 6 weeks.	Not stated	Single profession – physician

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Table 3. (*Continued*)

Study, year, and location	Setting	N = TBI sample	Intervention description	Fatigue focus	Discipline approach
Kolakowsky-Hayner *et al.* (2017) USA	Community/ home	123	Intervention: the walking module, a home-based program where each participant utilised a pedometer to track daily number of steps and frequent coaching calls. Control: nutrition module, to assist participants with learning healthy eating habits. Was created to provide coaching contact frequency and intensity equivalent to the coaching calls during the walking phase of the study. Both arms of the study were 12 weeks in duration, with participants switching groups after 12 weeks.	Not stated	Single profession – physiotherapy
Killington *et al.* (2021) Australia	Inpatient	78	Fatigue management group: twice a week for 2 weeks until the four modules had been completed. Purpose of educating clients about the common effects of fatigue after brain injury. Usual care group: received therapy from their occupational therapist in one-to-one sessions: one session on fatigue education, goal setting and encouragement using fatigue strategies, but this was not always consistent.	Mental/cognitive fatigue	Single profession – occupational therapy
Lilliecreutz *et al.* (2017) Sweden	Outpatient	6	Combination of three sessions of aerobic exercise (outdoor walking) and six sessions of mindfulness exercises (3× group setting and 3× individually guided by audio file) every week for 12 weeks.	Mental/cognitive fatigue	Single profession – physiotherapy
Lu *et al.* (2016) USA	Outpatient	3	Cognitive Behaviour Therapy for Insomnia (CBT-I) delivered four one-to-one sessions, 1 h each, generally at a pace of one session per week. The clinician followed the guidelines found in the Edinger and Carney manual 'Overcoming Insomnia'.	Not stated	Single profession – neuropsychology
Meek *et al.* (2021) Canada	Outpatient	15	Two treatment sessions of repetitive transcranial magnetic stimulation administered each day, except weekends and holidays, with a 15 min break between sessions. Participants received a total of 30 treatment sessions over the course of 3 weeks.	Not stated	Single profession – physician
Mossberg *et al.* (2017) USA	Community/ home	15	Daily subcutaneous injection of recombinant human growth hormone (rhGH) for 12 months.	Physical fatigue	Single profession – physician
Nelson and Esty (2010) USA	Outpatient	35	Flexyx Neurotherapy System (FNS) involves minute pulses of electromagnetic energy to stimulate changes in brainwave patterns, delivered via specially designed headset equipment. Number of treatment sessions ranged from 3 to 38.	Not stated	Single profession – neurotherapy
Nelson and Esty (2015) USA	Outpatient	2	FNS as described above. Participants attended 25 sessions (2–3 sessions per week).	Not stated	Single profession – neurotherapy

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Table 3. (*Continued*)

Study, year, and location	Setting	N = TBI sample	Intervention description	Fatigue focus	Discipline approach
Nguyen *et al.* (2017) Australia	Outpatient	24	Intervention: CBT of six standardised modules addressing sleep and fatigue, delivered across eight sessions and treatment as usual. Control: treatment as usual (i.e. occupational therapy, physiotherapy, pharmacotherapy, and psychotherapy for mood).	Not stated	Single profession – neuropsychology
Nilsson *et al.* (2020) Sweden	Community/ home	15	(−)-OSU6162 up to 30 mg × 2 dosages, with control of equal number of inactive placebo tablets over 4 weeks	Mental/cognitive fatigue	Single profession – physician
Ouellet and Morin (2007) Canada	Outpatient	11	CBT individual therapy with five components – one component focused on fatigue management skills training, recognising and managing fatigue more effectively, and at revising dysfunctional attitudes about fatigue and rest. Delivered 1h sessions over 8 weeks.	Not stated	Single profession – psychology
Potter *et al.* (2016) UK	Outpatient	46	12weekly, 1 h sessions of individual CBT with varying time of treatment intervals. Used an individualised, formulation-driven approach within a semi-structured protocol. Agenda-based sessions, collaborative target setting, and homework tasks were central features of treatment.	Not stated	Single profession – neuropsychology
Quera Salva *et al.* (2020) France	Community/ home	20	Bright light therapy was delivered via a face-mounted device resembling glasses. Treatment was administered every day at awakening for 30 min for 4 weeks.	Not stated	Single profession – physician
Raina *et al.* (2016) USA	Community/ home	41	Maximising Energy (MAX intervention), an 8 week program (two 30 min one-to-one sessions delivered live via the internet using web-camera technology) that combined education and problem-solving therapy to teach individuals to manage fatigue-related problems. Control group received health education (HE) via web-camera.	Physical and mental	Single profession – occupational therapy
Raina *et al.* (2022) USA	Community/ home	41	MAX intervention, an 8 week program (two 30 min one-to-one sessions delivered live via the internet using web-camera technology) that combined education and problem-solving therapy to teach individuals to manage fatigue-related problems. Control group received HE via web-camera.	Physical and mental	Single profession – occupational therapy
Schoenberger *et al.* (2001) USA	Outpatient	12	FNS therapy, 25 sessions of treatment administered over a 5–8 week period.	Not stated	Single profession – neurotherapy
Shirvani *et al.* (2021) Iran	Outpatient	48	Three transcranial direct current stimulations delivered each week for 8 weeks compared to MBSR 8-week group program delivered face-to-face.	Mental/cognitive fatigue	Single profession – psychology
Sinclair *et al.* (2014) Australia	Community/ home	30	4 week, 45min/morning, home-based treatment with short wavelength (blue) light therapy compared with yellow light therapy (containing less photons in the short wavelength range) and a no treatment control group.	Not stated	Single profession – not stated
Stubberud *et al.* (2019) Norway	Inpatient	3	Multifaceted program included three modules covering lifestyle factors and adaptive coping strategies (5 days), goal management training (5 days), and emotional regulation (2 days). Delivered 3 h of intervention each day, totalling 36 h of inpatient intervention over the course of 1 month.	Physical and mental	Single profession – neuropsychology

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Table 3. (*Continued*)

Study, year, and location	Setting	N = TBI sample	Intervention description	Fatigue focus	Discipline approach
Whyte *et al.* (2015) USA	Community/ home	34	MAX intervention compared to control group of HE. Both groups received two one-to-one sessions per week for 8 weeks via web cameras.	Not stated	Single profession – occupational therapy
Wright *et al.* (2020) USA	Community/ home	20	Dose volume equivalent of 0.4 mg of rhGH or placebo daily, increasing to volume equivalent dose of 0.6 mg of rhGH for the remainder of the treatment period.	Not stated	Single profession – physician
Ymer *et al.* (2021) Australia	Outpatient	22	Intervention: CBT for Sleep and fatigue comprised seven modules delivered across 8weekly, 1 h sessions, focused on modification of unhelpful beliefs and behaviours contributing to sleep disturbance and fatigue and addressing maladaptive responses to symptoms. Control: HE aimed to control for non-specific effects of therapy (i.e. therapeutic relationships).	Not stated	Single profession – neuropsychology
Ymer *et al.* (2021) Australia	Outpatient	22	CBT for Sleep and fatigue as described above.	Not stated	Single profession – neuropsychology
Zhang and Wang (2017) China	Outpatient	36	Methylphenidate flexibly titrated from 5 to 20 mg/day (2.5 mg/day) compared to placebo given at same dose. Completed for 30 weeks.	Mental/cognitive fatigue	Single profession – physician

Table 4. Fatigue management outcomes.

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Pharmacological					
Berginström *et al.* (2017) Sweden	RCT	To examine the effects of the monoaminergic stabiliser (−)-OSU6162 on mental fatigue in patients with traumatic brain injury (TBI).	(−)-OSU6162 15 mg dose given orally twice a day during a 4 week treatment period, compared with placebo.	Fatigue Severity Scale (FSS) Mental Fatigue Scale	Intervention showed no effect compared with placebo on both measures of mental fatigue
Carlsson (2012) Sweden	Abstract: RCT	To examine effect of (−)-OSU6162 in patients with mental fatigue of long duration following stroke or TBI.	OSU6162 was given orally for 4 weeks in doses increasing from 15 to 45 mg twice a day.	Mental Fatigue Scale	Statistically significant improvement was reached for intervention group
Grima *et al.* (2018) Australia	RCT	To determine the efficacy of Melatonin supplementation for sleep disturbances in patients with TBI.	Prolonged-release Melatonin formulation (2 mg; Circadin®) and placebo capsules for 4 weeks each in a counterbalanced fashion separated by a 48 h washout period.	FSS	Intervention significantly reduced the self-reported impact of fatigue during daily activities
Jha *et al.* (2008) USA	RCT	To evaluate the efficacy of Modafinil in treating fatigue and excessive daytime sleepiness in individuals with TBI.	Modafinil up to 400 mg dose compared to control of equal number of inactive placebo tablets over 10 weeks.	FSS Modified Fatigue Impact Scale	There were no statistically significant differences between improvements seen with intervention and placebo on either outcome measure at 4 or 10 weeks
Johansson *et al.* (2012*b*) Sweden	RCT	To evaluate the effect of (−)-OSU6162 on long-term mental fatigue after TBI or stroke.	(−)-OSU6162 15 mg dose with option to increase pending therapeutic effect.	Mental Fatigue Scale	A significant difference of improvement in scores was detected between the intervention and placebo at the primary endpoint. There was a significant effect of sex, with more females being responders, but no difference with age or diagnosis
Johansson *et al.* (2014) Sweden	Prospective cohort study	To evaluate the effect and safety of Methylphenidate treatment for mental fatigue after a mild TBI. A comparison was made between those who had continued and those who had discontinued the treatment. The effect was also evaluated after a 4 week treatment break.	Methylphenidate with three treatment periods: no medication, low dose (5 mg × 3), and normal dose (20 mg × 3) for 4 weeks each.	Mental Fatigue Scale	Significant interactions with large effect sizes over time were found between the group with Methylphenidate and the group without Methylphenidate on the fatigue outcome measure. There was a clear deterioration in mental fatigue when Methylphenidate was withdrawn
Johansson *et al.* (2015*a*) Sweden	RCT (phase A)	To investigate dosage, safety, and effects of Methylphenidate on mental fatigue and pain.	Methylphenidate 5–60 mg weekly for 12 weeks.	Mental Fatigue Scale	Methylphenidate significantly decreased mental fatigue, as evaluated by the Mental Fatigue Scale, and the effects on mental fatigue were dose dependent. No effect on pain was detected

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Johansson *et al.* (2017) Sweden	Prospective cohort study (phase B)	To evaluate the effects of individually adjusted dosages of Methylphenidate during a 6 month follow-up period.	Methylphenidate dose individually adjusted to reach an optimal balance between positive symptomatic effects and side effects.	Mental Fatigue Scale	Methylphenidate significantly improved the rating on the Mental Fatigue Scale. There was also a significant difference due to dosage (the higher the dose the better the outcome measure score). When analysing single items from the outcome measure, eight items improved significantly: mental fatigue, fatigue in general, mental recovery, memory and concentration difficulties, slowness of thinking, sensitivity to stress, and lack of initiative
Johansson *et al.* (2018) Sweden	Prospective cohort study (phase C)	To evaluate long-term use of Methylphenidate after a TBI andthe effects of a 4 week treatment break to compare effects both with and without use of Methylphenidate.	Two year follow up of Methylphenidate dose from above study, including evaluation of effects of a 4week break of medication.	Mental Fatigue Scale	Mental fatigue was significantly improved with medication compared to baseline. No difference detected between normal dose data of this study (phase B) and previous study (phase A), indicating stable effect with long-term treatment of medication
Johansson *et al.* (2020) Sweden	Prospective cohort study (phase D)	To evaluate the long-term effect and safety of Methylphenidate treatment.	Follow-up review 5.5 years post initial start of Methylphenidate treatment (Johansson *et al.* 2015) + after a 4-week break of medication.	Mental Fatigue Scale	Significant decrease in mental fatigue at start of assessments compared to baseline from previous study (phase C). Significantly increased mental fatigue was found when Methylphenidate was withdrawn for 4 weeks. Reintroduction showed significant improvement
Kaiser *et al.* (2010) Switzerland	RCT	To study the effect of daily Modafinil on post-traumatic excessive daytime sleepiness and fatigue for people with TBI.	Modafinil 100–200 mg dose each morning, compared to placebo control for 6 weeks.	FSS	After 6 weeks of treatment, the decrease in fatigue outcome scores was higher in the Modafinil group than in the placebo group, but this finding was not significant after correction for the independent variables
Mossberg *et al.* (2017) USA	Cohort study	To assess the effects of recombinant human growth hormone (rhGH) on physical and neuropsychological functioning in individuals who sustained a moderate-to-severe TBI.	Daily subcutaneous injection of rhGH for 12 months.	Muscle fatigue measured through isokinetic contractions Perceptual Fatigue Scale (self-rated) FSS	Skeletal muscle fatigue during repetitive maximal isokinetic contractions did not change in response to the year of treatment with rhGH. However, the change in perceptual fatigue rating induced by the fatiguing contractions was reduced by 25% after 1 year of rhGH therapy. Statistically significant improvements were found for total scores of the FSS

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Nilsson *et al.* (2020) Sweden	RCT	To evaluate the efficacy and safety of (−)-OSU6162 in doses up to 30 mg b.i.d. in patients suffering from mental fatigue following stroke or (TBI).	(−)-OSU6162 up to 30 mg × 2 dosages, with control of equal number of inactive placebo tablets over 4 weeks.	Mental Fatigue Scale	Positive treatment effect in 10 of 28 patients; those who responded best to treatment had their greatest improvements on the Mental Fatigue Scale
Wright *et al.* (2020) USA	RCT	To characterise the fatigue relief experienced by TBI patients with growth hormone (GH) replacement.	Dose volume equivalent of 0.4 mg of rhGH or placebo daily, increasing to volume equivalent dose of 0.6 mg of rhGH for the remainder of the treatment period.	Modified Fatigue Impact Scale Brief Fatigue Inventory (BFI)	GH treatment was associated with significant improvements in subject-rated fatigue. Over the course of 1year, total Modified Fatigue Impact Scale fatigue score decreased significantly with GH treatment as did individual subtest scores for general, physical, emotional, and mental fatigue. BFI total score also improved
Zhang and Wang (2017) China	RCT	To compare the effect of Methylphenidate with that of placebo in patients with TBI in China.	Methylphenidate flexibly titrated from 5 to 20 mg/day (2.5 mg/day) compared to placebo given at same dose. Completed for 30 weeks.	Mental Fatigue Scale	Mental Fatigue Scale score was significantly lower in the intervention group than the placebo group, indicating improvement in fatigue
Psychological					
Johansson *et al.* (2012*a*) Sweden	RCT	To implement and evaluate a novel, non-pharmacological strategy, Mindfulness Based Stress Reduction (MBSR), to improve mental fatigue after stroke or TBI.	MBSR is a structured health intervention to cultivate mindfulness in medicine, healthcare, and society; it includes gentle Hatha yoga, body scan, and sitting meditation. Participants underwent 2.5 h/week group sessions for 8 weeks, 1 day-long silent led retreat and home practice of 45 min. Waitlist control.	Mental Fatigue Scale	A significant difference in fatigue between the two groups after 8 weeks, with MBSR group showing an improvement in symptoms
Johansson *et al.* (2015*b*) Sweden	Prospective cohort study	To evaluate the effect of an advanced mindfulness program following a MBSR program, designed for subjects suffering from long-term mental fatigue after a brain injury.	Follow on from above study (Johansson *et al.* 2012*a*). Advanced MBSR program: an 8 month program with monthly group meetings (2.5 h), and the program concluded with an all-day retreat. Program inspired from the book, 'Buddhas Brain: The Practical Neuroscience of Happiness, Love, and Wisdom'.	Mental Fatigue Scale	The advanced program showed a sustained positive effect on a similar level as after the original MBSR program

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Johansson *et al.* (2015*b*) Sweden	Controlled clinical trial	To evaluate whether a MBSR program could be successfully delivered live online.	Intervention MBSR face-to-face: weekly 2.5 h sessions and one full-day session. Educational and experiential aspects of mindfulness and meditation. Intervention MBSR live internet: same session as above but delivered over the internet in patient's own home. Had opportunity to interact with each other via online platform. Control: peaceful walking group 1.5 h/week for 8 weeks.	Mental Fatigue Scale	Mental Fatigue Scale score was the only factor found to have an interaction effect, indicating that the groups differed in their response. There was greater improvement in terms of mental fatigue and cognitive function in the Internet group compared with the face-to-face MBSR group
Lu *et al.* (2016) USA	Case report	To evaluate the efficacy of Cognitive Behaviour Therapy for Insomnia (CBT-I) for the treatment of fatigue, pain, and depressed or anxious mood in addition to insomnia for individuals with TBI.	CBT-I delivered four one-to-one sessions, 1 h each, generally at a pace of one session per week. The clinician followed the guidelines found in the Edinger and Carney manual 'Overcoming Insomnia'.	Multidimensional Assessment of Fatigue	Case 1 reported clinically significant improvement in fatigue post-treatment but not at follow up. Case 2 reported clinically significant improvement in fatigue at follow up but not post-treatment. Case 3 reported improvement in fatigue but not clinically significant
Nguyen *et al.* (2017) Australia	RCT	To evaluate the efficacy of adapted CBT for sleep disturbance and fatigue in individuals with TBI.	Intervention: CBT of six standardised modules addressing sleep and fatigue, delivered across 8 sessions + treatment as usual. Control: treatment as usual (TAU) (i.e. occupational therapy, physiotherapy, pharmacotherapy, and psychotherapy for mood).	BFI FSS	The CBT group achieved clinically important improvement in fatigue whereas TAU remained above the cut-off score. Group differences in clinical improvement were not significant between CBT and TAU participants for fatigue
Ouellet and Morin (2007) Canada	Single case experimental design	1. To evaluate the efficacy of a cognitive-behavioural intervention to treat insomnia complaints in a group of people having sustained TBI. 2. To determine whether improvements in sleep were paralleled by a decrease in the level of fatigue.	CBT individual therapy with five components – one component focused on fatigue management skills training, recognising and managing fatigue more effectively, and at revising dysfunctional attitudes about fatigue and rest. Delivered 1 h sessions over 8 weeks.	Multidimensional Fatigue Inventory (MFI)	Fatigue score was significantly reduced from pre- to post-treatment, and from pre- to 3 month follow up; but, when looking at score subscales,differences were only significant for general and physical fatigue, not mental fatigue contrary to authors assumptions

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Potter *et al.* (2016) UK	RCT	To evaluate the effectiveness of a 12-session, individualised, formulation-based CBT program.	12 weekly, 1 h sessions of individual CBT with varying time of treatment intervals. An individualised, formulation-driven approach within a semi-structured protocol was used. Agenda-based sessions, collaborative target setting, and homework tasks were central features of treatment.	Checklist of Individual Strength	Examination of the data indicated that shorter intervals were associated with better outcomes. Within-group analysis showed that the intervention group showed significant improvements
Ymer *et al.* (2021) Australia	RCT	To compare the efficacy of Cognitive Behaviour Therapy for Sleep and Fatigue (CBT-SF) to an active control condition (health education [HE]) delivered in-person or via telehealth in individuals with an ABI.	Intervention: CBT-SF comprised seven modules delivered across 8 weekly, 1 h sessions, focused on modification of unhelpful beliefs and behaviours contributing to sleep disturbance and fatigue and addressing maladaptive responses to symptoms. Control: HE aimed to control for non-specific effects of therapy (i.e. therapeutic relationships).	FSS BFI	On the FSS, both groups showed a significant effect of time. When examining within-group change using simple contrasts, fatigue was significantly reduced after CBT-SF, which was maintained at all time points. No significant change in the HE group at any time point. Fatigue severity (BFI) was reduced only in CBT-SF group and was maintained until 2 months post-treatment
Ymer *et al.* (2021) Australia	RCT	To identify factors associated with treatment response to CBT-SF (secondary analysis of Ymer *et al.* 2021).	CBT-SF as described above.	FSS	The greater the severity of fatigue at baseline predicted a positive CBT-SF response, and participants with TBI and stroke differed in their response on the FSS (TBI had statistically significant reductions in fatigue immediately post- and 2-month follow-up but not 4 month, stroke had gains 2 and 4 month post. The mode of delivery (face-to-face or telehealth) did not significantly predict treatment outcome after CBT-SF. A higher estimated premorbid intelligence was associated with lower fatigue severity at baseline
Audrit *et al.* (2021) Canada	RCT	To estimate feasibility and explore the treatment effect of a psychoeducative and counselling intervention program targeting four post-concussion symptoms (SAAM: Sleep/fatigue, Attention, Anxiety/mood, Memory).	SAAM intervention – psychoeducation, group model, 1 h/week for 4 weeks. Content based on biopsychosocial model addresses misconception and perception of mild TBI (mTBI) recovery, symptoms, and provides reassurance and counselling about recovery and motivation.	MFI	There was a significant improvement of fatigue complaints for the experimental group but not for the control group

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Howe *et al.* (2019) Norway	Feasibility cohort study	To assess the feasibility of recruitment procedures and delivery of a Norwegian adaptation of a manualised cognitive intervention to a civilian sample with mild-to-moderate TBI in the south-eastern region of Norway.	Compensatory Cognitive Training (CCT) is a manualised intervention targeting post-concussive symptom management and cognitive symptoms. A group-based treatment program delivered in 10 × 2 h sessions of psychoeducation and compensatory cognitive training strategies. One session focuses on fatigue.	FSS Rivermead Post Concussive Symptoms Questionnaire (RPQ) Intervention feedback form	FSS (Fatigue Severity Scale) only used at baseline, no follow-up data reported. RPQ – fatigue subscale median score 2.5–1 at 3 months post-treatment follow up but no significance reporting. Fatigue information sessions received one of the highest ratings on CCT feedback form
Cooper *et al.* (2009) UK	Cohort study	1. To investigate the effects of an 8 week fatigue education group on fatigue intensity scores in people with an acquired brain injury (ABI). 2. To identify whether the fatigue management program resulted in changes in measures of quality of life, sleepiness, and mood. 3. To examine participants' perceptions of their fatigue and the subjective value of the education group.	Weekly fatigue education group, lasting for 8 weeks. Variety of topics, including understanding fatigue and TBI, energy conservation, sleep hygiene, exercise, healthy eating, and stress impact on fatigue.	The Brain Injury Fatigue Scale (an unpublished PhD thesis questionnaire) Qualitative interviews	There was a reduction in mean fatigue scores post-intervention; however, it did not reach statistical significance. During qualitative interviews, participants reported better self-management of fatigue at the end of the 8 week intervention
Humphries (2017) UK	Conference abstract: longitudinal cohort study	To evaluate a six-session fatigue management occupational therapy program.	Six sessions of group education, recording energy levels, and analysing diary sheets to identify personal energy budgets. Sheets give a visual overview of patterns of energy. Activity and pacing plans are developed based on the diary sheets. Between sessions, clients practice strategies and develop plans.	FSS Qualitative questions	Out of 22 clients, 14 recorded a lower fatigue score, 3 remained unchanged and 5 recorded a higher score. In the qualitative questions, all clients reported that they understood their own fatigue patterns – their energy levels remained similar, they felt able to increase their participation in structured activity. Six clients were followed up at 6 month – four maintained their post-treatment fatigue score, and two recorded pre-fatigue scores.

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Killington *et al.* (2021) Australia	RCT	To determine whether therapy supporting fatigue management can be provided economically in groups to inpatients undertaking rehabilitation.	Fatigue management group: twice a week for 2 weeks until the four modules had been completed with the purpose of educating clients about the common effects of fatigue after brain injury. Usual care group: received therapy from their occupational therapist in one-to-one sessions: one session on fatigue education, goal setting, and encouragement using fatigue strategies, but this was not always consistent.	Barrow Neurological Institute Fatigue Scale Patient self-evaluation of perceptions of fatigue and fatigue management principles Qualitative interview (for perspectives of group usefulness)	There was no interaction effect of group × time for fatigue, quality of life, or acquisition of knowledge; however, knowledge improved over time irrespective of group allocation. Qualitative interview themes: fatigue affects who I am; Fatigue after ABI is confusing – is it related to my brain injury?; Developing fatigue management strategies supports wellbeing of individuals; Preferences for individual therapy or group therapy varied. Individual therapy sessions appear to be required still for those patients who are unable to tolerate a group setting or wanted to discuss their unique issues
Raina *et al.* (2016) USA	RCT	To evaluate the feasibility of conducting a randomised clinical trial of an internet-based manualised intervention to teach individuals with a TBI to manage their fatigue.	Maximising Energy (MAX intervention) an 8-week program (two 30 min, one-to-one sessions delivered live via the internet using web-camera technology) that combined education and problem-solving therapy to teach individuals to manage fatigue-related problems. Control group received HE via web-camera.	Modified Fatigue Impact Scale Patient-Reported Outcomes Measurement Information System Fatigue Scale FSS	Independent-samples *t* tests indicated no significant difference between the two groups for all measures. Effect sizes for all measures ranged from small to medium in the favour of the MAX intervention group
Raina *et al.* (2022) USA	RCT	To evaluate the preliminary efficacy of a self-management intervention (MAX) for reducing the impact (primary outcome) and severity of fatigue on daily life, improving fatigue experience, and increasing participation compared with a HE intervention.	MAX intervention, an 8-week program (two 30 min, one-to-one sessions delivered live via the internet using web-camera technology) that combined education and problem-solving therapy to teach individuals to manage fatigue-related problems. Control group received HE via web-camera.	Modified Fatigue Impact Scale (mFIS)	Linear mixed-effects models indicated significant group × time interaction for: • fatigue impact, with MAX participants reporting lower mFIS scores at time 4. • experience of fatigue, with MAX participants reporting lower fatigue at time 2 and 4. • fatigue severity, with MAX participants reporting lower scores at time 2 and 4.

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Stubberud *et al.* (2019) Norway	Longitudinal cohort study	To describe and explore a group-based multifaceted intervention for patients with post-ABI fatigue.	Multifaceted program included three modules covering lifestyle factors and adaptive coping strategies (5 days), goal management training (5 days), and emotional regulation (2 days). Delivered 3 h of intervention each day, totalling 36 h of inpatient intervention over the course of 1 month.	FSS Subjective fatigue questionnaire	Ratings on the FSS showed a significant reduction in fatigue symptoms post-intervention and at 3 months follow up, with large effect-size estimates. Compared to baseline, there was also a tendency towards fatigue reduction at 9 months follow up, with a medium effect size, but this failed to reach significance
Whyte *et al.* (2015) USA	Conference abstract: RCT	To test the efficacy of a novel intervention (MAX intervention) compared to a HE attention control intervention for decreasing the impact of post-TBI fatigue.	MAX intervention compared to control group of HE. Both groups received two one-to-one sessions per week for 8 weeks via web cameras.	Fatigue Impact Scale Patient Reported Outcomes Measurement Information System	There was a significant difference for improvement in fatigue over time for the experimental group and no differences for the control
Activity-based					
Chin *et al.* (2015) USA	Clinical trial, pre- and post-study	To examine the effects of a supervised, 12 week, vigorous aerobic exercise training program on cardiorespiratory fitness and fatigue severity in individuals with TBI.	Supervised independent aerobic exercise training program for 12 weeks.	FSS	A significantly lower fatigue score was observed following aerobic exercise training
Dobryakova *et al.* (2020) USA	Prospective cohort study	To examine whether cognitive fatigue experienced during task performance (on-task fatigue that is experienced in the moment) can be reduced through the presentation of monetary rewards.	Task stimulation headset game 'E-Prime' with monetary incentive, completed whilst participants received an magnetic resonance imaging scan.	Visual analogue scale of fatigue (VAS-F) measured throughout task Modified Fatigue Impact Scale	A significant group ×condition interaction demonstrated that attaining a rewarding outcome resulted in on-task fatigue reduction in individuals with TBI. The interaction was driven by a significant difference in VAS-F scores in the TBI group, with lower scores being reported after the outcome vs no outcome condition
Dornonville de la Cour *et al.* (2022) Denmark	Mixed methods	To explore short- and long-term changes in self-reported fatigue, cardiorespiratory fitness, cognitive performance, and exercise behaviour.	Six week (18 sessions) high intensity interval training program.	MFI	Mean scores reduced pre- to post-intervention and pre-intervention to follow up for general, physical, and mental fatigue, with reported Cohen's *d* suggesting moderate–large effect sizes Qualitative reports suggest the experience of fatigue had not changed, but two reported that intensity was lower

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Driver and Ede (2009) USA	RCT	To examine the effect of a physical activity program on the mood states of individuals with a TBI.	Intervention: Individualised physical activity aquatic and aerobic sessions, 1 h/week for 8 weeks. Control: voc rehab class aimed at improving reading and writing skills post-injury, 1 h/week for 8 weeks	Fatigue subscale of Profile of Mood States (POMS)	Significant between -roup difference of total score of POMS. Significant within-group difference for the experimental group from pre- to post-program for fatigue. No significant differences seen in control group
Kolakowsky-Hayner *et al.* (2017) USA	RCT	To evaluate the impact of a graduated physical activity program on fatigue after a TBI.	Intervention: the walking module, a home-based program where each participant utilised a pedometer to track daily number of steps + frequent coaching. Control: nutrition module, to assist participants with learning healthy eating habits. Was created to provide coaching contact frequency and intensity equivalent to the coaching calls during the walking phase of the study. Both arms of the study were 12 weeks in duration, with participants switching groups after 12 weeks.	Global Fatigue Index Barrow Neurological Institute Fatigue Scale Overall Severity Index Score MFI	Significant improvement for fatigue across all scales at the end of the walking intervention. Improvements in fatigue persisted 12–24 weeks after
Lilliecreutz *et al.* (2017) Sweden	Cohort study	To examine whether a specific guided program of aerobic and mindfulness exercises could have an effect on estimated health status and occupational performance in individuals with an ABI. As secondary outcomes, the effects on health-related quality of life, cognition, and mental fatigue were analysed.	Combination of three sessions of aerobic exercise (outdoor walking) and six sessions of mindfulness exercises (3× group setting and 3× individually guided by audio file) every week for 12 weeks.	Mental Fatigue Scale	There was a statistically significant positive change in mental fatigue after the intervention
Complementary and alternative medicine					
Nelson and Esty (2010) USA	Conference abstract: case control	Reports on a series of patients seen in a clinical practice who underwent the Flexyx Neurotherapy System (FNS) intervention as an initial step in documenting the potential promise of this approach.	FNS involves minute pulses of electromagnetic energy to stimulate changes in brainwave patterns, delivered via specially designed headset equipment. Number of treatment sessions ranged from 3 to 38.	Self-report of symptoms on a 0–10 visual analogue scale (10 being worst)	Curve estimation regression analyses indicated linear trends in evidence for significant decrease in fatigue

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Nelson and Esty (2015) USA	Case report	To explore if FNS treatment may be of benefit to address longer duration of TBI and post-traumatic stress disorder symptoms.	FNS as described above. Participants attended 25 sessions (2–3 sessions per week).	Self-report of symptoms on a 0–10 visual analogue scale (10 being worst)	Reduced pre- to post- for both participants
Schoenberger *et al.* (2001) USA	RCT	To evaluate the efficacy of FNS for people who have experienced a TBI.	FNS therapy, 25 sessions of treatment administered over a 5–8 week period.	MFI	Between-group differences were not significant for the total score on the MFI; however, the treatment group was significantly improved compared with the control group on the General Fatigue and Mental Fatigue subscales. Within-group analysis for fatigue subscales showed greatest improvement in their mental fatigue. Significant improvement was observed after treatment and maintained at follow up
Shirvani *et al.* (2021) Iran	RCT	To compare transcranial direct current stimulation (tDCS) and MBSR in mental fatigue, quality of life, and aggression in mTBI patients.	Three tDCS electrical stimulations delivered eachweek for 8 weeks compared to MBSR 8 week group program delivered face-to-face.	Mental Fatigue Scale	Significant decrease from pre- to post-phase and from pre- to follow-up phase for tDCS and MBSR groups. Significant changes in the follow-up stage in the MBSR group. Mental fatigue was significantly reduced in MBSR group compared to tDCS and control groups and was significantly reduced in the tDCS group compared to control
Connolly *et al.* (2021*a*) Australia	Case report	To describe the development and implementation of the intervention, providing an in-depth description of the personalised intervention methodology, and examining its feasibility and acceptability and responses on various measures in two case studies.	Exposure to a home-based dynamic light therapy, in which treatment consisted of ambient exposure to blue-enriched white light during the daytime and blue-depleted white light for 3 h prior to sleep. Compared with control lighting usual lighting (3000–4000 K during the day and evening). Two month intervention condition (treatment and control conditions) with 1-month follow-up.	BFI FSS Intervention satisfaction questionnaires	Case study 1: clinically significant reductions from baseline to mid- and end-treatment assessment points in fatigue. Questionnaire rated a 'considerable improvement' in fatigue during the treatment condition. All of these domains were found to worsen during the control condition. Mild–moderate side effects reported. Reported 'very high' satisfaction. Case study 2: clinically significant reductions were observed from baseline to mid- and end-treatment assessment points in fatigue symptoms. Mild side effects reported. One questionnaire response reported a 'considerable improvement' in fatigue and reported 'mostly satisfied' with the treatment

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Table 4. (*Continued*)

Study, year, and location	Design	Objectives	Intervention description	Fatigue outcomes measures	Fatigue results
Connolly *et al.* (2021*b*) Australia	RCT	To compare the impact of exposure to a dynamic light schedule with participants' usual lighting on fatigue.	Home-based dynamic light therapy as described in Connolly *et al.* (2021*a*).	BFI FSS Intervention satisfaction questionnaires	Treatment was not associated with statistically significant change on either measure of fatigue, although there was a medium effect size of improvement found. Most participants reported positive experiences during the study in terms of their symptoms; 17 participants were 'mostly satisfied' or 'very satisfied' with the treatment
Connolly *et al.* (2021*c*) Australia	RCT secondary analysis of Connolly, Rajaratnam *et al.* 2021	To investigate which factors moderated response to in-home light therapy for individuals with fatigue following TBI and stroke.	Home-based dynamic light therapy as desribed in in Connolly *et al.* (2021*a*)	BFI	There were no variables that were significantly associated with changes in fatigue, although several factors did show associations with medium or large effect sizes. Evening chronotype; lighter eye colour; greater injury severity, as indicated by longer post-traumatic amnesia; and lower baseline depressive symptoms were associated with greater post-treatment reduction in fatigue
Sinclair *et al.* (2014) Australia	RCT	To investigate the efficacy of blue light therapy in reducing fatigue in patients with TBI.	Four week, 45 min/morning, home-based treatment with short wavelength (blue) light therapy compared with yellow light therapy (containing less photons in the short wavelength range) and a no treatment control group.	FSS	Those in the blue light therapy group experienced a greater overall decline in fatigue relative to controls. There was evidence of trend to imply that the effects of blue light exposure did not persist after treatment cessation
Meek *et al.* (2021) Canada	Cohort study	To investigate the feasibility, tolerability, and efficacy of twice-daily, low frequency repetitive transcranial magnetic stimulation (rTMS) over the right dorsolateral prefrontal cortex in the reduction of chronic post-concussion symptoms in patients who have suffered a mild TBI.	Two treatment sessions rTMS administered each day, excepting weekends and holidays, with a 15 min break between sessions. Participants received a total of 30 treatment sessions over the course of 3 weeks.	Post-Concussion Symptom Scale – Fatigue subscale FSS	Significant improvements were observed in the severity of post-concussion symptoms scale; however, detail on fatigue subscale not reported. There was no significant change in fatigue severity on the FSS
Quera Salva *et al.* (2020) France	RCT	To explore whether face-mounted, blue-enriched bright white light therapy could reduce fatigue in survivors of TBI.	Bright light therapy was delivered via a face-mounted device resembling glasses. Treatment was administered every day at awakening for 30 min for 4 weeks.	FSS	A significantly higher reduction in fatigue was found during treatment phase and at week 4 in patients who received light therapy compared with the control group. This effect stopped after cessation of treatment (week 8)

Pharmacological interventions

Most of the RCTs in this study were of pharmacological interventions, with mixed outcomes reported. Johansson *et al.* (2012*b*) and Carlsson (2012) reported statistically significant positive fatigue outcomes for the drug (−)-OSU6162. However, the RCT by Berginström *et al.* (2017) found no interventional effect on fatigue compared to placebo, and Nilsson *et al.* (2020) only found a positive treatment effect for fatigue in 10 of 28 participants after a secondary analysis. A series of longitudinal studies explored Methylphenidate with a large group of participants, and although attrition impacted sample sizes, mental fatigue was shown to significantly improve with medication over time (Johansson *et al.* 2014, 2015*c*, 2017, 2018, 2020). An RCT exploring Melatonin found the intervention group reported a significant reduction in the impact of fatigue during daily activities (Grima *et al.* 2018). rhGH was shown not to have an effect on skeletal muscle fatigue (Mossberg *et al.* 2017) but was associated with significant improvements in subjectively rated fatigue (Mossberg *et al.* 2017; Wright *et al.* 2020). Modafinil was explored in two RCTs, which found no statistically significant difference between intervention and placebo (Jha *et al.* 2008; Kaiser *et al.* 2010).

Psychological interventions

CBT demonstrated positive results for fatigue management with varying levels of statistical significance. The RCTs by Ymer *et al.* (2021*a*) and Potter *et al.* (2016) each demonstrated CBT intervention groups with significant improvement in fatigue scores, especially therapy sessions provided over shorter time intervals. Ymer *et al.* (2021*b*) also suggested that response to CBT interventions for fatigue was impacted by the severity of fatigue, pre-morbid intelligence and condition (a TBI diagnosis was more likely to see improvement in fatigue earlier, whereas stroke had longer lasting positive response). In Nguyen *et al.* (2017), the RCT intervention group demonstrated similar improvements in fatigue but did not reach statistical significance. A case control (Ouellet and Morin 2007) and case report (Lu *et al.* 2016) showed clinically significant positive responses to CBT intervention, but methodological limitations cautioned result interpretation.

Multifaceted psychosocial education groups were a common fatigue management intervention, but a variety in methodology designs revealed mixed results. The Audrit *et al.* (2021) RCT of a TBI education group demonstrated significant improvement in fatigue complaints for the intervention, even though fatigue was only addressed in one of the four sessions. The Howe *et al.* (2019) cohort study also looked at a general TBI education group; however, design limitations made it difficult to determine any significant differences at follow up. Studies exploring fatigue-specific education groups did not demonstrate any statistical significant results on formal fatigue measures; however, qualitative results revealed improvements in understanding fatigue patterns (Humphries 2017) and implementing fatigue management strategies (Cooper *et al.* 2009; Killington *et al.* 2021). Formalised interventions, such as the MAX intervention, demonstrated varied results, with one RCT demonstrating significant improvements for fatigue over time (Whyte *et al.* 2015) whereas another with similar study size and methodology only recorded small–medium effect sizes (Raina *et al.* 2016). A subsequent paper (Raina *et al.* 2022) applying more sophisticated analysis techniques demonstrated significant differences for the MAX group at post-intervention and 8 week follow up.

Positive results were seen in studies using MBSR for fatigue management. The Johansson *et al.* (2012*a*) RCT demonstrated a significant difference in improved fatigue symptoms, with these levels being maintained in a prospective study of the same participants 8 months later (Johansson *et al.* 2015*b*). When exploring MBSR mode of delivery, there were greater improvements in terms of mental fatigue when the intervention was accessed online compared to face-to-face (Johansson *et al.* 2015*a*).

Activity-based interventions

All activity-based interventions demonstrated statistically significant results. Independent aerobic interventions demonstrated significantly lower fatigue scores post-intervention (Chin *et al.* 2015) as well as follow-up periods of 12–24 weeks (Kolakowsky-Hayner *et al.* 2017). Combination intervention studies of aerobic and aquatic (Driver and Ede 2009) and outdoor walking and mindfulness (Lilliecreutz *et al.* 2017) demonstrated statistically significant positive change in mental fatigue. A high intensity interval training program demonstrated reductions in fatigue scores with moderate–large effect sizes (Dornonville de la Cour *et al.* 2022). Even a novel task stimulation headset game demonstrated that attaining a rewarding outcome resulted in on-task fatigue reduction in individuals with a TBI (Dobryakova *et al.* 2020).

CAM interventions

CAM intervention outcomes were mixed due to varieties in study designs and methodologies. Studies on light therapy showed medium–large effect sizes of improvement and positive patient experiences; however, all studies reported reduction in effect after treatment cessation (Quera Salva *et al.* 2020; Connolly *et al.* 2021*a*, 2021*b*). One study on symptom correlation discussed whether a greater injury severity and lower baseline depressive symptoms were associated with a greater reduction in post-traumatic fatigue (Connolly *et al.* 2021*c*). Shirvani *et al.* (2021) compared transcranial stimulation to MBSR and a control, demonstrating a statistically significant decrease in mental fatigue for transcranial stimulation compared to the control but not in comparison to MBSR. For FNS, an RCT found no statistically significant difference between intervention and health

controls (Schoenberger *et al.* 2001). In two case-controlled studies, a reduction in symptoms were reported; however, these must be interpreted with caution given their study design limitations (Nelson and Esty 2010, 2015).

ICF framework correlations to fatigue management

To explore the fifth and final research questions, a content analysis of meaningful concepts of fatigue measures, interventions, and outcomes in relation to ICF framework components was completed (see supplemental material in online dataset (Spalding 2022)). The following identifies aspects of the health conditions that have been captured by these methods and highlights any gaps that need to be considered when selecting such methods for future studies or clinical practice implementation.

Fatigue measures

Body function was the most common ICF component focus of the fatigue outcome measures in the reviewed studies. Body functions refer to physiological functions such as those required for cognition, cardiovascular function, motor functions, pain or emotion (Cieza *et al.* 2005). Sixteen measures, including the Mental Fatigue Scale, FSS, and Brief Fatigue Inventory (BFI), focused strongly on mental function categories such as energy and drive, used to meet specific needs and goals in a persistent manner and energy levels that produce vigour and stamina. They also focused on physical function categories such as exercise tolerance and fatiguability that relate to respiratory and cardiovascular capacity as required for enduring physical exertion.

Over half of the fatigue outcome measures in the reviewed studies explored additional ICF components alongside the body function component. Eight measures such as the Multidimensional Fatigue Inventory and Modified Fatigue Impact Scale explored activities and participation which refers to the individual's execution of tasks and involvement in everyday life situations (Cieza *et al.* 2005). Specifically, these measures focused on determining one's ability to carry out a daily routine under the impact of fatigue. Personal factors refers to characteristics that are unique to each individual such as age, gender, ethnicity, personality, resilience or experiences (Cieza *et al.* 2005). Three measures explored the fatigue experience: the Intervention Satisfaction Questionnaire and two qualitative interviews. No environmental factors for fatigue were assessed by the outcome measures in this review.

Fatigue interventions

Body functions was again the most popular ICF component for interventions of fatigue management in 45 of the 49 reviewed articles. Intervention focus varied and included specific mental function categories such as attention, memory, executive functions, sleep functions, orientation, consciousness and emotional functions of affect, sadness, and emotional lability. Body structures, that is the anatomical structure required for cognition, cardiovascular and motor functions, pain or emotion (Cieza *et al.* 2005) was the focus for all of the pharmacological and some of MBSR interventions. The intent for fatigue treatment was to improve cellular efficiency, monoaminergic systems, or nerve cell stimulation.

Activities and participation were a focus for interventions that had educational and practical components such as CBT, MBSR or the MAX intervention. They looked at categories of learning and applying knowledge of fatigue management such as understanding new concepts, making decisions and solving problems, as well as undertaking multiple tasks, carrying out a daily routine and handling stress. None appeared to focus on personal, domestic or employment activity categories for fatigue management. Environmental factors of assistive technology and natural and man-made changes to the environment was a focus for light therapy interventions, but no studies explored a focus on relationship or support aspects of fatigue treatment.

Fatigue outcomes

All fatigue intervention outcomes reported by the reviewed studies aligned with the body functions ICF component. There was a strong focus on reporting change in cognitive and emotional function categories including energy and drive, sleep, energy levels and motivation.

Less than half of the outcomes reported explored the activities and participation ICF component. For those that did, they reported changes in categories of knowledge, daily routine, general ability to undertake multiple tasks and handling stress. There were no fatigue outcomes reported against specific personal, domestic or employment activities or participation levels. Several articles did conclude that future studies should explore outcomes in relation to return to work and other complex occupational tasks (Cooper *et al.* 2009; Audrit *et al.* 2021; Killington *et al.* 2021).

Five studies explored the ICF component of personal factors by reporting patient experiences of the intervention. Killington *et al.* (2021) was the only study to report on qualitative themes in relation to personal experiences of fatigue and its management. Two studies reported that future work exploring personal factors of symptom and injury perceptions and broader personality traits would aid to refine interventions and identify mediators for change (Cooper *et al.* 2009; Potter *et al.* 2016).

There were no outcomes reported that could be linked to environmental factors of fatigue treatment such as impact of relationships and support, assistive technology, or environmental changes.

Discussion

Current literature has outlined the complexity of post-traumatic fatigue, indicating the need for a multimodal

clinical treatment approach, however little guidance is available on how a multidisciplinary team could and should approach this. This scoping review was conducted to explore fatigue management interventions for post-TBI in the context of the ICF framework, focusing on how health and functioning is addressed within the multidisciplinary team. The results of this scoping review indicate that the post-traumatic fatigue interventions in the literature are conducted by singular professions, that there is a strong focus on a body functions approach and that there is a discrepancy between intervention intent and measurement.

The importance of a multidisciplinary approach to brain injury rehabilitation is well documented. The complexities of problems post brain injury vary, and as such different combinations of interventions are required to meet the needs of patients (Turner-Stokes *et al.* 2015). What was interesting in the results of this review was that no fatigue interventions were found to use a multidisciplinary approach. This silo style reported patient outcomes at different levels of the ICF framework impacting the ability to conceptualise the impact and use of more than one approach at a time. Several did conclude that the impact of other discipline interventions for fatigue should be explored alongside their intervention (Lilliecreutz *et al.* 2017; Audrit *et al.* 2021; Killington *et al.* 2021).

The issue of clinicians working in silos has long been investigated. A silo mentality in the workplace can cause a reduction in efficiency, difficulties in sharing information, adapting to innovation and committing to flexibility, with often negative effects on healthcare consumers including protracted and reduced quality of care (Meneses and Caseiro 2018). Pain management is one example of how a change in this mentality can improve the care of complex conditions. There is currently consensus across pain clinical guidelines (Caneiro *et al.* 2020; Lin *et al.* 2020) encouraging clinicians to focus on the patient as a whole, and to refer for co-care in the presence of comorbid mental and physical health complaints. The introduction of multidisciplinary pain clinics has enabled integrated care, with consistent messages across the team to prevent care fragmentation and patient distress (Lewis and Bean 2021). Pain disorders are frequently comorbid and share common biopsychosocial disability profiles to fatigue (Lenaert *et al.* 2018). Perhaps a similar multidisciplinary approach to post-traumatic fatigue may work towards addressing the complex constructs of this symptom of brain injury.

Alongside the notion of approaching fatigue management from a multidisciplinary viewpoint is the idea of addressing management of the whole person. By using a biopsychosocial model like the ICF, different perspectives of a person's health and function can be addressed. This review found fatigue management interventions with a strong bias towards addressing fatigue at a body function level only. In fact, 43 of the 47 interventions addressed cognitive or emotional functions with less than half exploring activities and participation abilities, and none addressing social or environmental aspects of the individual. This contrasts with the growing evidence that fatigue management should be multifaceted, addressing different aspects of the individual in order to achieve best outcomes (Ponsford *et al.* 2015; Shuman-Paretsky *et al.* 2017). Whilst some interventions in this review could be classified under the activities and participation function, these were mainly linked with improving knowledge, such as learning about fatigue, energy conservation techniques or mindfulness activities. The act of implementing such techniques into everyday activities, where ultimately fatigue is experienced the most, was largely unexplored. Further investigation into these other components could add to the richness of multifaceted fatigue management.

Finally, it was evident in this review that there was disparity in the intent of fatigue interventions and outcomes measures used. Whilst there was a significant focus on body function interventions, over half of the measures explored the impact of fatigue on activities and participation. For example, two of the top three most prevalent measures, the FSS and the BFI explore one's ability to carry out daily routines, work, employment, and even interpersonal interactions. However, these elements were not included in any interventions. There has been a push in rehabilitation practice to accurately measure and report on the intent of the intervention. For those clinicians wishing to incorporate a client-centred practice approach, the use of meaningful assessments for the individual and intervention are crucial to demonstrate clinical effectiveness (Whalley Hammell 2013). This is important for clinicians looking to translate research evidence into practice. The use of the ICF framework in this review not only highlights these gaps but begins to provide clinicians better choice and tailoring of interventions and outcome measurement for their client's needs.

Implications for future research, practice, and policy

It is evident from this review that continuing research is required to build understanding of fatigue interventions and their impact on function in relation to ICF components of activities and participation, environmental and personal factors. A multidisciplinary approach to fatigue management could be developed from the current research evidence, clinical expertise, and experiences of people with TBI, with further research required to evaluate its effectiveness versus a single discipline approach.

Limitations

The authors acknowledge that additional stakeholders such as the consumer or other disciplines could have added a richer perspective to the understanding of this issue, but finite resources limited that level of engagement. As the

nature of the methodology and intent of this scoping reviews was not to directly analyse and synthesise primary research papers, results cannot be generalised and should be interpreted with caution.

Conclusion

There is a growing body of evidence for fatigue interventions post-TBI. This scoping review has used the ICF framework to conceptualise fatigue management and highlight focus areas for multidisciplinary teams when tailoring selection and implementation of interventions. Results show that majority of fatigue interventions and measures focus on a the ICF component of body functions. Whilst positive results have been reported from a variety of interventions including pharmacological, behavioural, or psychological, their singular focus on addressing fatigue at a body functions level may limit a multidisciplinary team's ability to comprehensively address the impact of fatigue on people following TBI. Further opportunities to develop interventions that target other health and function components including activities and participation, environment and personal factors may enable a greater impact of fatigue management approaches.

Supplementary material

Supplementary material is available online.

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