REVIEW



Frequency and extent of cognitive complaint following adult civilian mild traumatic brain injury: a systematic review and meta-analysis

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(Received 7 February 2022; revised 28 June 2022; accepted 6 July 2022; first published online 30 August 2022)

Abstract

Objective: Cognitive symptoms are associated with return to work, healthcare use and quality of life after mild traumatic brain injury (mTBI). Additionally, while overall 'post-concussion' symptoms are often present at similar levels in mTBI and control groups, cognitive complaints may be specifically elevated in mTBI. A systematic review and meta-analysis was conducted to investigate the frequency and extent of cognitive complaints following adult civilian mTBI, and compare it to the frequency and extent of complaints in control populations (PROSPERO: CRD42020151284).

Method: This review included studies published up to March 2022. Thirteen studies were included in the systematic review, and six were included in the meta-analysis. Data extraction and quality assessment were conducted by two independent reviewers.

Results: Cognitive complaints are common after mTBI, although reported rates differed greatly across studies. Results suggested that mTBI groups report cognitive complaints to a significantly greater extent than control groups (Hedges' g = 0.85, 95% CI 0.31–1.40, p = .0102). Heterogeneity between studies was high ($\tau^2 = 0.20$, 95% CI 0.04–1.58; $I^2 = 75.0\%$, 95% CI 43.4%–89.0%). Between-group differences in symptom reporting were most often found when healthy rather than injured controls were employed.

Conclusions: Cognitive complaints are consistently reported after mTBI, and are present at greater levels in mTBI patients than in controls. Despite the importance of these complaints, including in regards to return to work, healthcare use and quality of life, there has been limited research in this area, and heterogeneity in research methodology is common.

Keywords: mild traumatic brain injury; concussion; cognitive symptoms; cognitive complaints

Mild traumatic brain injury (mTBI) is the most common type of traumatic brain injury, making up approximately 70%–90% of all traumatic brain injuries, and resulting in about 100-300/ 100,000 hospital-evaluated cases per year worldwide (Cassidy et al., 2004). Since many people with mTBI do not seek medical attention, researchers have estimated that the true prevalence of mTBI may be upwards of 600 people per 100,000 (Cassidy et al., 2004).

Note: The protocol for this systematic review and meta-analysis was preregistered through PROSPERO (registration number: CRD42020151284). Data and analysis code has been made available on the Open Science Framework and can be accessed at: https://osf.io/ckjg6/?view_only=b582da431f6b4bd98ed9998eddd0cb5d.

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The prognosis following mTBI is considered to be largely positive, with reports suggesting that the majority of individuals recover fully within approximately 3 months (Carroll, Cassidy, Peloso, et al., 2004). Nevertheless, there is a subgroup of patients who experience poor recovery, evident by the reporting of ongoing 'post-concussion' symptoms. Recent research has suggested that this subgroup may be much larger than previously recognised, with potentially a majority of patients experiencing long-term post-concussion symptoms (Machamer et al., 2022).

Some of the most common self-reported post-concussion symptoms are cognitive symptoms, or *cognitive complaints* (Clarke et al., 2012). These refer to subjective reports of reduced cognitive ability, typically within the domains known to be affected in mTBI, including memory, attention, processing speed and executive function (Clarke et al., 2012; Ngwenya et al., 2018; Rabinowitz & Levin, 2014). Research suggests these symptoms can persist even several years following injury (Theadom et al., 2018), emphasising the need for further research in this area.

Cognitive complaints have received limited attention in mTBI research, possibly due to the fact that these symptoms do not reliably correspond to objective cognitive performance (Anderson, 2021; Stillman et al., 2019). In fact, research on cognitive performance suggests that the majority of individuals return to premorbid levels of cognitive functioning after mTBI (Iverson et al., 2019; Schneider et al., 2022). Nevertheless, cognitive symptoms continue to be reported, and these symptoms are associated with other important outcome factors after mTBI, including quality of life and return to work (Schraa, 1995; Theadom et al., 2017; Voormolen et al., 2019; Wrightson & Gronwall, 1981; Yousefzadeh-Chabok et al., 2021). In addition, cognitive symptoms are often the precipitant for referral to specialist neuropsychological services. Thus, it is important to understand these symptoms in order to improve patient outcomes, and to minimise the substantial financial burden of mTBI, of which healthcare use and delayed return to work are both large contributors (Te Ao et al., 2014). There is a paucity of research in this area, however, as most mTBI symptomatology research focuses only on overall post-concussion symptoms.

Cognitive symptoms are also particularly important because, in contrast to general postconcussion symptoms, cognitive complaints may differentiate between mTBI patients and control groups. There is a large body of research on the non-specificity of overall post-concussion symptoms, which are often found to be present at similar levels in mTBI patients and controls (Dean et al., 2012; Meares et al., 2011). There are intuitive reasons to expect that cognitive complaints, specifically, might be elevated in mTBI, and there is an assumption in clinical practice that this is the case. However, this assumption has not been formally assessed through prior review studies, and in actuality, cognitive symptoms are observed in a range of populations, including in nonbrain-injured trauma patients and healthy individuals (Cargin et al., 2008; Iverson & Lange, 2003; Meares et al., 2011; Pullens et al., 2010). Thus, it is not currently clear whether these symptoms are greater (in frequency and/or severity) in patients with mTBI than in control populations, and further research is necessary to examine this hypothesis.

There are a number of factors to consider when exploring cognitive complaints after mTBI. Psychological factors (e.g. depression and anxiety) and female sex have consistently been linked to increased post-concussion symptoms after mTBI (Anderson & Jordan, 2021; Cnossen et al., 2018; Meares et al., 2006), and are therefore relevant, potentially confounding factors to consider in this area of research. Age is also known to affect symptoms after mTBI and is therefore another potential confound to consider (Cassidy, Boyle, et al., 2014; Hu et al., 2017; Li et al., 2017). Symptom reporting is also likely to be impacted by the duration after injury at which follow-up occurs (McCrea et al., 2009). Other considerations involve how mTBI is defined and how diagnosis is ascertained. Both of these factors determine the nature and representativeness of mTBI samples, and both commonly vary between studies and contribute to variability in study findings (Carroll, Cassidy, Holm, Kraus & Coronado, 2004).

This review is specifically interested in the patterns of cognitive complaints observed following civilian mTBI, as this represents the majority of mTBI. Civilians with mTBI represent a distinct subgroup in the mTBI literature as they experience different symptom burdens than individuals with military- or sports-related injuries (Beauchamp et al., 2021; Chapman & Diaz-Arrastia, 2014).

Inclusion Criteria	Exclusion Criteria
 Publication in English Inclusion of an mTBI sample Reporting of cognitive complaint data Participant sample within the ages of 18-60 (or data reported separately by age with at least one age category falling within this range)^a 	 Conference abstract Non-civilian population (military or athlete sample) Inclusion of mixed-severity TBI sample with no reporting of mTBI data separately No reporting of cognitive complaint subscale or item data^b Sample selected due to being symptomatic (e.g. participants recruited from brain injury rehab; participants seen in brain injury clinic with no indication of it constituting routine follow-up), or asymptomatic Sample selected from a population not representative of general adult civilian mTBI due to specific characteristics expected to potentially affect outcome variable (e.g., litigants, assault victims, single sex [e.g. only females], college students, substance users, participants with mental health conditions) Duplicate paper, or overlapping participant sample/data Age range information not reported

Table 1. Inclusion and exclusion criteria for each study

^aIf studies included an mTBI group within the required age range and a control group outside of the age range, the study was included and treated as a case series.

^bThis includes studies that reported overall post-concussion symptom data without reporting cognitive complaint data separately, and studies that only reported inferential statistics involving cognitive complaint data (e.g. correlation coefficients or beta values) as there was no way to extract participant ratings of cognitive complaint from these studies.

The aim of this systematic review and meta-analysis is to determine (1) the frequency and extent of cognitive complaints following adult civilian mTBI, and (2) whether these complaints are greater in mTBI relative to control groups. An additional aim is to review the quality of the existing literature on this topic.

Methods

Study protocol and search strategy

The protocol for this systematic review and meta-analysis was preregistered through PROSPERO (registration number: CRD42020151284). Reporting of this review followed Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines (Moher et al., 2009; Stroup et al., 2000).

The following databases were searched for studies published prior to 25 March 2022: Medline, PsycINFO, Emcare, Embase, Web of Science and Scopus. The full electronic search strategy is given in the Appendix (see Supplementary Material).

Inclusion and exclusion criteria

Studies of interest for inclusion in the systematic review were peer-reviewed journal articles reporting cognitive complaint data following adult civilian mTBI. Studies were eligible for inclusion whether they reported this data as frequency data (e.g. the proportion of a sample reporting cognitive complaints) or as continuous data (e.g. scores on a cognitive complaint scale). Note that continuous data was interpreted as representing the overall extent of cognitive complaint, as higher scores on each scale could indicate either a greater number of symptoms endorsed, symptoms endorsed to a greater severity or both. Studies were also eligible whether or not they included a control group. The complete list of inclusion and exclusion criteria is listed in Table 1.

Study screening, data extraction and quality analysis

Covidence online systematic review software (Veritas Health Innovation, 2019) was used for study screening, data extraction and quality analysis. The first author conducted title and abstract screening and full-text screening. Studies that passed full-text screening were reviewed with the final author for consensus for inclusion in the review.

Two independent reviewers completed data extraction and quality analysis for each included study. Any disagreements were settled through discussion until consensus was reached. Where the two primary reviewers could not reach consensus, a third reviewer was engaged and majority opinion was taken. Data extracted from each study included study design data, participant characteristics and demographics, and cognitive symptom data. Study authors were contacted for numerical data values in cases where symptom data was reported in figures.

The quality of each study was evaluated using the Newcastle–Ottawa Scale (NOS), designed to assess the quality of non-randomised studies included in systematic reviews (Wells et al., 2000). The NOS is recommended by the Cochrane Collaboration as well as various methodological review papers (Deeks et al., 2003; Higgins & Green, 2011; Zeng et al., 2015). The cohort study version of this scale evaluates studies on the domains of group selection, comparability of study groups and ascertainment of outcome. Studies are eligible for a maximum of one 'star' for each item within the selection and outcome categories, and a maximum of two stars for the comparability item. The form was modified to fit the current research question. As several included studies were case series and did not include a control group, the scale was additionally modified for use with these studies, similar to previous approaches (Lawley et al., 2015; Murad, Sultan, Haffar & Bazerbachi, 2018).

Data analysis

Intended analyses included determining the overall frequency of cognitive complaints, subgroup analyses examining cognitive domain and time since injury, and comparison of the extent of cognitive complaints in mTBI and control groups. Due to their non-comparability, frequency data and continuous data were analysed separately.

The summary measure used for meta-analysis was the standardised mean difference (SMD). The SMD is a measure of effect size that allows for pooling of outcome data across the use of different outcome scales through standardising the difference between groups in each study. The current meta-analysis used Hedges' *g*, a specific form of SMD, which corrects for bias in effect size estimations when small samples are used (Borenstein et al., 2009).

A random-effects model was used to pool outcomes, based on the expectation that included studies would differ in their underlying true effects, a scenario that is highly likely due to methodological differences in studies being combined (Borenstein et al., 2009). The Hartung–Knapp adjustment was applied to the model to reduce the risk of a false positive result, which metaanalyses can be particularly susceptible to when they contain a small number of studies with substantial heterogeneity (Inthout, Ioannidis & Borm, 2014).

Heterogeneity between studies was quantified using τ^2 and I^2 . τ^2 is defined as the variance of the true effect sizes of the population of studies, on the same scale as the SMD. Thus, on a distribution of the true underlying effect sizes, the SMD is the estimate of the mean of the distribution, and τ^2 is the variance of the distribution (Borenstein et al., 2009). To estimate τ^2 , the restricted maximum-likelihood method was used, as recommended by Veroniki et al. (2016). I^2 gives the percentage of the total observed variation that is attributed to differences in true effect sizes underlying the included studies, as opposed to random error (where total variation can be thought of as the sum of the true between-studies variation and the within-study error) (Borenstein et al., 2009). I^2 can range from 0% to 100% and I^2 values of 25%, 50% and 75% can be interpreted as indicating low, moderate and high heterogeneity, respectively (Higgins, Thompson, Deeks & Altman, 2003).

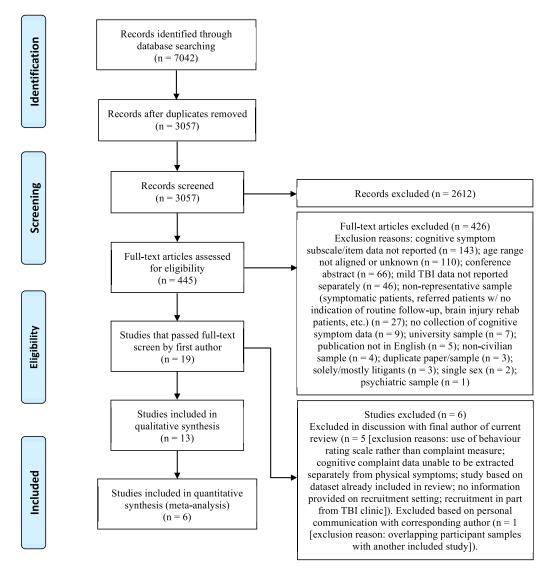


Figure 1. PRISMA flow diagram. Modified from Moher et al. (2009).

All quantitative analysis was conducted in R (version 3.6.1; R Development Core Team, 2011) using the following packages: tidyverse (Wickham et al., 2019), meta (Balduzzi, Rücker & Schwarzer, 2019) and dmetar (Harrer, Cuijpers, Furukawa & Ebert, 2019).

Results

As shown in Fig. 1, 3057 studies were screened by the first author for inclusion in the systematic review, of which 445 were assessed through full-text review. The resulting 19 papers underwent review by the first and last author, with a further 6 papers excluded by consensus (see Fig. 1 for exclusion reasons). The 13 remaining papers were included in the systematic review (Anderson, 2021; Clarke, Genat & Anderson, 2012; Hou et al., 2012; Landre et al., 2006; Marsh & Smith, 1995; Mayer et al., 2015; Norman, Shah & Turkstra, 2019; Pacella, Prabhu, Morley, Huang & Suffoletto,

2018; Raz et al., 2011; Shumskaya, Andriessen, Norris & Vos, 2012; Studerus-Germann et al., 2017; Stulemeijer, Vos, Bleijenberg & van der Werf, 2007; Sullivan et al., 2017).

One of the most common reasons for exclusion during full-text review was on the basis of age range of participants. Importantly, this was often due to insufficient reporting of information, as approximately one quarter of the studies excluded on this basis did not report participant age range.

Of the 13 included papers, study authors were contacted for numerical data values in the case of four studies where outcome data was reported in figures (Hou et al., 2012; Pacella et al., 2018; Studerus-Germann et al., 2017; Stulemeijer et al., 2007). This additional data was provided for one study (Studerus-Germann et al., 2017). For the remaining studies, figures reporting cognitive complaint data were used to derive ranges of symptom endorsement. These data ranges were included in the qualitative synthesis but were not included in the meta-analysis.

Systematic review

Quality assessment of included studies

There was 83.33% agreement between raters across the three NOS domains. Inter-rater reliability yielded a Cohen's kappa of 0.73. This reflects moderate agreement by conservative approaches, and is high relative to previous research using the same scale (Hartling et al., 2012; McHugh, 2012).

Table 2 presents ratings on the modified NOS scale for each included study. The total number of stars that each study was eligible for varied due to variability in study design. Only four of the 13 included studies were awarded a star on 80% or more of the eligible items (Clarke et al., 2012; Hou et al., 2012; Landre et al., 2006; Raz et al., 2011).

Each study was deemed to have a sample that was sufficiently representative of adult civilian mTBI, which was expected given that this was an inclusion criterion for the review. Additionally, almost all studies were considered to have employed a follow-up length sufficient for outcomes to occur, defined as follow-up \geq 24 h after injury. However, there were some methodological short-comings in other areas assessed by the NOS scale. Where follow-up was present, nearly all studies either had insufficient follow-up rates – defined as rates <80% (Marsh & Smith, 1995; Pacella et al., 2018; Studerus-Germann et al., 2017) – or failed to provide this information (Stulemeijer et al., 2007). Studies were also likely to introduce potential bias through failing to ensure comparability of mTBI and control cohorts by not controlling for sex (Landre et al., 2006; Norman et al., 2019) or psychological factors (Clarke et al., 2012; Norman et al., 2019; Pacella et al., 2018; Shumskaya et al., 2012).

Characteristics of included studies

The characteristics of included studies are listed in Table 3. The sample size of each study ranged from 15 mTBI participants to 107 mTBI participants. Across the included studies, there were a total of 546 mTBI participants with cognitive complaint data available.

The features required for diagnosis of mTBI differed greatly between included studies, despite many studies basing their criteria on the same published definitions of mTBI. A comparison of mTBI definition between studies is shown in Table 4. This table highlights the variation in definitions of mTBI across studies. Note that if study definitions were equivalent, each column of the table would be identical.

Ten of the 13 studies included a control group, but only seven had control groups within the required age range of this review (i.e. age 18–60) and with cognitive complaint data available. Of these studies, three employed healthy controls (Anderson, 2021; Mayer et al., 2015; Shumskaya et al., 2012), three employed injured controls (Landre et al., 2006; Norman et al., 2019; Pacella et al., 2018) and one employed both (Clarke et al., 2012). One study also employed a 'head injury'

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Table 2. Star ratings on the modified NOS scale for each included study

	Anderson (2021)	Clarke et al. (2012)	Hou et al. (2012)	Landre et al. (2006)	Marsh & Smith (1995)	Mayer et al. (2015)	Norman et al. (2019)	Pacella et al. (2018)	Raz et al. (2011)	Shumskaya et al. (<mark>2012</mark>)	Studerus- Germann et al. (2017)	Stulemeijer et al. (2007)	Sullivan et al. (2017)
Representativeness of exposed (mTBI) cohort	*	*	*	*	*	*	*	*	*	*	*	*	*
Selection of non- exposed cohort ^a	-	*		*		-	*	*		-			
Ascertainment of mTBI exposure	*	*	*	*	-	-	*	*	*	-	*	-	-
Comparability of cohorts ^a	*	*		*		**	-	*		*			
Follow-up length suffi- cient for outcomes to occur?	*	*	*	*	*	*	*	-	*	*	*	*	*
Adequacy of cohort fol- low-up ^a			*		-			-			-	-	
# of stars out of total eligible	4/6	5/6	4/4	5/6	2/4	4/6	4/6	4/7	3/3	3/6	3/4	2/4	2/3
% of stars out of total eligible	67%	83%	100%	83%	50%	67%	67%	57%	100%	50%	75%	50%	33%

altems not relevant for specific studies are left blank. This includes studies that did not include a control group, and/or those that did not involve a longitudinal component.

Table 3. Characteristics of studies included in systematic review

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Study ^a	Study type	mTBI recruitment details	Control group type ^b	n ^c	Sample age ^d [Mean (SD), Range]	Sex (% female)	Follow-up time post- injury ^e	Scale	Type of data reported	Format of reported data	Findings ^f
Anderson (2021)	Prospective	Patients admitted to hospital	НС	mTBI: 52	mTBI: 35.75 (14.70), 18–60;	mTBI: 21%	6-12 weeks	ССАМСНІ	Scale total	Means, SDs	Average total scores were 94.09 (SD = 7.33) for the mTBI group
				HC: 57	HC: 31.04 (11.11), 18-56	HC: 65%					and 85.34 (SD = 7.70) for the HC group. The difference between groups was significant ($p = .002$)
Clarke	Prospective	Patients admitted to	SI; HC	mTBI: 21	mTBI: 35.6, 19–60	mTBI: 33%	3-12 months	PACCQ	Scale total	Means, SDs	Average total scores were 96.90
et al. (<mark>2012</mark>)		neurosurgery unit of hospital		SI: 19	SI: 34.1, 18–58	SI: 26%					(SD = 8.20) for the mTBI group, 92.53 $(SD = 3.64)$ for the SI group
				HC: 20	HC: 19.0, 18-28	HC: 40%					and 88.20 (SD = 10.84) for the HC group. The difference between the mTBI and HC groups was significant (mean difference = 8.70, SE = 2.56, $p = 0.004$)
Hou et al. (2012)	Prospective, longitudi- nal	Patients presenting to hospital ED	N/A	107	38.32 (14.14) ⁸ , <i>18–60</i>	37%	3 months; 6 months	RPQ	Item data (Forgetfulne- ss, poor memory; poor concen- tration; tak- ing longer to think)	Frequencies	'Forgetfulness, poor memory' was endorsed by 25–30% of the sam- ple at 3 months and 15–20% of the sample at 6 months. Poor concentration was endorsed by 15–25% of the sample at 3 months and 15–20% at 6 months. Taking longer to think was endorsed by 20–25% of the sam- ple at 3 months and 15–20% at 6 months
Landre	Prospective	Patients admitted to	тс	mTBI: 37	18-60	mTBI: 38%	mTBI:	Modified	Scale subscore	Means, SDs	
et al. (2006)		hospital trauma department			mTBI: 33.11 (9.97);		3.87 ± 4.40 days; TC:	version of PCSC			subscale was 12.51 (SD $=$ 5.00) for the mTBI group and 11.38
				TC: 39	TC: 36.46 (11.20)	TC: 26%	5.08 ± 5.47 days				(SD = 4.29) for the TC group. The difference between groups was not significant
Marsh & Smith (1995)	Prospective, longitudi- nal	Patients "treated for concussion" at hospital	N/A	15 (<i>n</i> = 11 for first fol- low-up)	27.07 (12.60), 18–56	20%	2 weeks; 1 month; 3 months	CFQ	Scale total	Means, SDs	Mean total scores were 46.27 (SD = 22.81), 39.67 (SD = 19.66) and 28.93 (SD = 14.93) at 2 weeks, 1 month and 3 months, respectively

Study ^a	Study type	mTBI recruitment details	Control group type ^b	n ^c	Sample age ^d [Mean (SD), Range]	Sex (% female)	Follow-up time post- injury ^e	Scale	Type of data reported	Format of reported data	Findings ^f
-	Prospective	Recruitment setting	HC	mTBI: 46	18-55	mTBI: 48%	13.7 ± 5.0	NSI	Scale subscore	Means, SDs	Ŭ
(2015)		not specified			mTBI: 28.9 (9.8)		days				was 4.7 (SD = 3.4) for the mTBI group and 1.4 (SD = 2.3) for the
				HC: 46	HC: 28.4 (9.9)	HC: 48%					HC group. This difference was significant ($F_{1,89} = 28.53$, p < 0.001, d = 1.12)
Norman et al.	Prospective	Patients presenting to hospital ED	OI	mTBI: 20	mTBI: 29.20 (10.77), 19.6–52;	mTBI: 57%	3-12 weeks	NSI	Scale subscore	Means, SDs	was 3.75 (SD = 2.83) for the mTBI
(2019)				OI: 21	OI: 28.23 (7.58), 18.5–48	OI: 73%					group and 2.76 (SD $=$ 3.25) for the OI group. This difference was not significant
Pacella	Prospective,	Patients presenting	HI (i.e. injury	mTBI: 39	18-55	mTBI: 49%	1–14 days	RPQ; RPQ-	Item data	Frequencies	In the mTBI group, 40-60% experi-
et al. (2018)	longitudi- nal	to hospital ED	to the head with-		mTBI: 32 (12.1)			based experi-	(Concentrati- on difficulty)		enced concentration difficulties every day, and 0–20% did not
			out mTBI);	HI: 16	HI: 36 (9.9)	HI: 50%		ence			experience concentration difficul-
			TC	TC: 53	TC: 34 (11.1)	TC: 45%		sam- pling			ties on any day. In the TC group, 20–40% experienced concentration
								ques-			difficulties every day, and 20-40%
								tions			of the group did not experience
											any concentration difficulties. No
											differences were detected between the mTBI group and HI group. The
											odds difference in symptom
											reporting between the mTBI and
											TC groups became non-significant
											by day 8 post-injury. Pre-injury
											concentration difficulties were
											reported by 36%, 25% and 28% of
											the mTBI, HI and TC groups,
											respectively.

https://doi.org/10.1017/BrImp.2022.19 Published online by Cambridge University Press

Study ^a	Study type	mTBI recruitment details	Control group type ^b	n ^c	Sample age ^d [Mean (SD), Range]	Sex (% female)	Follow-up time post- injury ^e	Scale	Type of data reported	Format of reported data	Findings ^f
Raz et al. (2011)	Prospective	Recruited from hos- pital records and ED	N/A	28	35.6 (10.4), <i>18–60</i>	32%	MRI 559 ± 803 days; symptom data within 24 h of MRI	PCSS	Item data (Memory loss)	Frequencies	8 patients (29% of sample) reported experiencing memory loss
Shumskaya et al. (2012)	Prospective	Patients admitted to hospital ED	нс	mTBI: 32 HC: 32	mTBI: 39, 18–60 ^h HC: 38, 19–59 ^h	mTBI: 37% ^h TC: 37% ^h	2-28 days (mean = 9 days)	RPQ	Scale subscore	Means, IQR, score range	The average cognitive score for the mTBI group was 25.0 ($IQR = 24.3$; range 0–75) and the average cognitive score for the HC group was 0.0 ($IQR = 16.3$; range 0–50). The difference between groups was significant ($p = 0.010$).
Studerus- Germann et al. (2017)	Prospective	Patients presenting to hospital ED	N/A	23	35.0, 18–55 ⁱ	47% ⁱ	3 months	ImPACT PCSS	Item data (Difficulty concentrat- ing, difficulty remembering, feeling slowed down, feeling men- tally "foggy")	Means	Mean scores on the rating scale were as follows, for the 3-day and 7-day return to work groups, respectively: 1.45 and 0.75 ('diffi- culty concentrating'); 1.09 and 1.25 ('difficulty remembering'), 0.55 and 0.25 ('feeling slowed down'); and, 0 and 0 ('feeling mentally "foggy"). ^J Note: partici- pants did not follow the return to work recommendations; the 3- day group returned to work later than the 7-day group on average

Table 3.	(Continued)
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Study ^a	Study type	mTBI recruitment details	Control group type ^b	n ^c	Sample age ^d [Mean (SD), Range]	Sex (% female)	Follow-up time post- injury ^e	Scale	Type of data reported	Format of reported data	Findings ^f
Stulemeijer et al. (2007)	Prospective, longitudi- nal	Patients presenting to hospital ED	N/A	79	18-60 CCs: 37.7 (13.5) No CCs: 36.8 (12.3)	38%	6 months (longitudi- nal follow-up over 12 days)	RPQ; SOL	Scale subscore [RPQ]; Item data [SOL] (memory problems, concentration problems)	Frequencies	39% of sample reported 'serious' CCs. No difference was found in diary ratings of cognitive prob- lems between groups; memory problems were experienced 10% and 9% of the time in these groups, respectively, and concen- tration problems were experi- enced 11% and 6% of the time, respectively. Memory and concen- tration problems were highest around the middle of the day and lowest at the start and end of the day
Sullivan et al. (2017)	Prospective	Patients admitted to ED of tertiary- referral hospital	N/A	38	34.71 (11.81), 18–60	42%	11.5 ± 6.49 days (median: 10.5, range: 2- 33)	NSI	Scale subscore	Means, SDs	The mean response on the cognitive items was 0.52 (SD = 0.90), and the average total score for these items was 2.07 (SD = 3.61)

CC, cognitive complaint; CCAMCHI, Cognitive Complaint After Mild Closed Head Injury; CFQ, Cognitive Failures Questionnaire; ED, emergency department; HC, healthy control; HI, head injury; ImPACT PCSS, Immediate Post-Concussion Assessment and Cognitive Test post-concussion symptom scale; IQR, interquartile range; MRI, magnetic resonance imaging; NSI, Neurobehavioral Symptom Inventory; OI, orthopedic injury; PCSC, Post-concussive Symptom Checklist, PACCQ, Post-Hospital Admission Cognitive Complaint Questionnaire; RPQ, Rivermead Post-Concussion Symptoms Questionnaire; SD, standard deviation; SI, spinal injury; SOL, Self-Observation List; TC, trauma control

^aStudies included in the quantitative synthesis are listed in bold.

^bControl groups are only listed if they are within the required age range for this review (18–60), with cognitive complaint data reported.

^cBased on participants with cognitive complaint data available.

^dWhere information on age of study participants was not reported, this information was based on study inclusion criteria (indicated by italics).

eFollow-up times are only listed for those follow-ups where cognitive complaint data was reported.

Where frequency data was reported in figures and raw data was unable to be obtained from study authors, frequency ranges (extracted from figures) are given.

^gBased on characteristics of sample at baseline before dropout (n = 126).

^hBased on characteristics of full sample including those with cognitive complaint data unavailable (*n* = 35). Age data represents median values, not means.

ⁱBefore dropout, for n = 30.

^jAs cognitive outcome data for this study was reported in a figure, numerical values were obtained from study authors.

Table 4. Definition of mTBI in studies included in systematic review

https://doi.org/10.1017/BrImp.2022.19 Published online by Cambridge University Press

Key features of definition	Anderson (2021)	Clarke et al. (2012)	Hou et al. (<mark>2012</mark>)	Landre et al. (2006)	Marsh & Smith (1995)	Mayer et al. (2015)	Norman et al. (2019)	Pacella et al. (2018)	Raz et al. (<mark>2011</mark>)	Shumskaya et al. (<mark>2012</mark>)	Studerus- Germann et al. (2017)	Stulemeijer et al. (2007)	Sullivan et al. (2017)
Alteration in mental state	(✔)		(✔)	(✔)		1	(✔)	(✓)	1				
Loss of con- sciousness:													
\leq 15 mins			(🗸)										
\leq 20 mins					(🗸)								
<30 mins											(✔)	(🗸)	
\leq 30 mins	(🗸)	1		(🗸)		(🖌)		(✔)	1	(✔)			
1–30 mins													(🖌)
Any duration							(🗸)						
Post-traumatic amnesia:													
\leq 60 mins			(🗸)										
<60 mins												(🗸)	
<24 h	(🗸)										(✔)		
≤24 h		1		(🗸)		(🗸)		(✔)	1				(🖌)
Any duration										(✔)			
GCS Score:													
13–15	1	1	1	1		1	1		1	1	1	1	(🖌)
15								1					
CT findings:													
Present													
Absent		1			1		1				1		

Table 4. (Continued)

Key features of definition	Anderson (2021)	Clarke et al. (2012)	Hou et al. (<mark>2012</mark>)	Landre et al. (2006)	Marsh & Smith (1995)	Mayer et al. (<mark>2015</mark>)	Norman et al. (2019)	Pacella et al. (2018)	Raz et al. (<mark>2011</mark>)	Shumskaya et al. (2012)	Studerus- Germann et al. (2017)	Stulemeijer et al. (2007)	Sullivan et al. (2017)
Focal neurologi- cal deficit(s):													
Present	(🖌)			(🖌)									
Absent			1		1								
Skull fracture/ penetrating injury:													
Present										(✔)			
Absent					1		✓						1
Published mTBI definition ref- erenced?	WHO	-	ACRM	ACRM	-	-	ICD9 Codes 850, ICD10 Codes S06.0	ACRM	ACRM	-	-	EFNS	WHO

Note. A standard checkmark indicates required features, and a checkmark in brackets indicates features that were considered in the definition but not specifically required (i.e. optional features, or situations in which only one of a set of features was required). Some definitions were unclear; this represents best interpretation. For studies where comprehensive diagnostic information was not provided (Norman et al., 2019; Stulemeijer et al., 2007), additional information was obtained from published definitions cited within these studies (Eisenberg et al., 2014; Vos et al., 2002). The variation both in features of the definition (represented by each row) and whether the feature was required (represented by each symbol) highlights the degree of heterogeneity in definitions of mTBI across studies.

ACRM, American Congress of Rehabilitation Medicine; EFNS, European Federation of Neurological Societies; GCS, Glasgow Coma Scale; ICD, International Classification of Diseases; WHO, World Health Organization

group of trauma patients who sustained an injury to the head but did not meet criteria for mTBI (Pacella et al., 2018). Across these studies, there were a total of 148 injured controls and 155 healthy controls with cognitive complaint data available.

Follow-up times within included studies ranged from approximately 1 day post-injury (Pacella et al., 2018) to approximately 1.5 years post-injury (Raz et al., 2011). Six studies collected cognitive complaint data at or within an average of 2 weeks post-injury (Landre et al., 2006; Marsh & Smith, 1995; Mayer et al., 2015; Pacella et al., 2018; Shumskaya et al., 2012; Sullivan et al., 2017), three studies collected this data between 2 weeks and 3 months post-injury (Anderson, 2021; Marsh & Smith, 1995; Norman et al., 2019), five studies collected this data at or between 3 and 12 months post-injury (Clarke et al., 2012; Hou et al., 2012; Marsh & Smith, 1995; Studerus-Germann et al., 2017; Stulemeijer et al., 2007) and one study collected this data at more than 1 year post-injury (Raz et al., 2011). Four studies reported cognitive complaint data at multiple time-points (Hou et al., 2012; Marsh & Smith, 1995; Pacella et al., 2018; Stulemeijer et al., 2007).

Most studies reported continuous outcome data rather than frequency data. This was either in the form of mean total scores on a scale of cognitive complaints (n = 3; Anderson, 2021; Clarke et al., 2012; Marsh & Smith, 1995) or mean cognitive subscores on a scale of post-concussive symptoms (n = 6; Landre et al., 2006; Mayer et al., 2015; Norman et al., 2019; Shumskaya et al., 2012; Studerus-Germann et al., 2017; Sullivan et al., 2017). The specific cognitive functions assessed by each scale are listed in Table 5.

In contrast to the studies reporting continuous outcome data, four studies reported dichotomous outcome data (Hou et al., 2012; Pacella et al., 2018; Raz et al., 2011; Stulemeijer et al., 2007), that is, frequencies or percentages of the sample endorsing cognitive complaints.

Cognitive symptoms overall

One study looked at the overall prevalence of cognitive complaints (Stulemeijer et al., 2007). This study found that 39% of their sample reported 'serious' cognitive complaints, defined as scores on a cognitive subscale that fell two or more standard deviations above the mean of an injured control group.

With respect to overall cognitive symptoms over time, one study found that subjective cognitive symptoms decreased significantly from 2 weeks to 1 month to 3 months (Marsh & Smith, 1995). Results from a second study appeared to suggest a slight decrease in frequency of cognitive symptom endorsement from 3 months to 6 months, but this was not statistically investigated (Hou et al., 2012).

Cognitive symptoms in patients versus controls

All studies employing healthy control groups found a greater extent of cognitive complaints in mTBI patients relative to controls (Anderson, 2021; Clarke et al., 2012; Mayer et al., 2015; Shumskaya et al., 2012). This was the case early after injury and in the chronic phase post-injury.

In the studies employing injured control groups, three found no differences in cognitive complaint between mTBI and control groups (Clarke et al., 2012; Landre et al., 2006; Norman et al., 2019). These studies were conducted at a range of time points post-injury, at less than 1 week, 3– 12 weeks and 3–12 months post-injury. A fourth study found that on day 1 following injury, mTBI patients were 39 times more likely to report concentration complaints than trauma controls, but the odds difference between groups was non-significant by day 8 post-injury (Pacella et al., 2018). The study also found no difference in concentration difficulties between mTBI patients and 'head injured' controls who did not meet criteria for mTBI. Table 5. Cognitive functions assessed by each scale

argeted cognitive co Cognitive Failures Q	
Perception	
Memory	
Motor function	
Post-Hospital Admis Closed Head Injury	sion Cognitive Complaint Questionnaire (PACCQ) and Cognitive Complaint After Mild (CCAMCHI) ^b
Memory	
Attention	
Processing speed	
Executive function	
Post-concussion symp	tom scales ^c
Rivermead Post-con	cussive Symptoms Questionnaire (RPQ)
Forgetfulness, poor	memory
Poor concentration	
Taking longer to th	ink
ImPACT Post-Concus	sion Symptoms Scale (PCSS)
Difficulty remembe	ring
Difficulty concentra	ting
Feeling slowed dov	'n
Feeling like you are	' 'in a fog'
Neurobehavioral Syr	nptom Inventory (NSI)
Forgetfulness	
Poor concentration	
Difficulty making d	ecisions
Slowed thinking	
Modified Post-Concu	ssion Syndrome Checklist (PCSC)
Memory problems	
Trouble concentrat	ing
Difficulty finding w	ords when speaking

^aList represents cognitive domains assessed by each scale, with multiple items evaluating each domain.

^bThe CCAMCHI is a modified version of the PACCQ scale, and assesses the same domains.

^cList represents individual cognitive items from each scale.

Cognitive symptoms by cognitive domain

With regard to the assessment of individual cognitive domains, most studies reported this data in the form of frequencies of symptom endorsement. The two domains most commonly assessed individually were memory (n = 3; Hou et al., 2012; Raz et al., 2011; Stulemeijer et al., 2007) and concentration (n = 3; Hou et al., 2012; Pacella et al., 2018; Stulemeijer et al., 2007). Only one study reported frequency of endorsement of processing speed symptoms (Hou et al., 2012). None of the studies individually reported executive function symptom data.

With respect to memory symptoms, the frequency of symptom endorsement ranged from 9% to approximately 30% across studies (Hou et al., 2012; Raz et al., 2011; Stulemeijer et al., 2007). It is noteworthy that these studies used different methods of symptom evaluation, making the data non-equivalent. The higher end of the range (15%–30%) represents studies reporting the percentage of their sample endorsing memory complaints, based on ratings on symptom scales (Hou et al., 2012; Raz et al., 2011). The lower end of this range (9% and 10%) was drawn from a study involving daily self-monitoring of memory symptoms and represents the percentage of the time during the 12-day study period that memory symptoms were experienced (Stulemeijer et al., 2007).

With respect to concentration symptoms, frequency of endorsement ranged from 6% to approximately 60% across studies (Hou et al., 2012; Pacella et al., 2018; Stulemeijer et al., 2007). As with memory symptom data, concentration symptom data was derived using varied approaches, limiting between-study comparison. Point estimates for daily self-monitoring of symptoms fell at the lower end of the range (6% and 11%; Stulemeijer et al., 2007), estimates of frequency of the sample experiencing symptoms fell in the middle of the range (15%–25%; Hou et al., 2012) and estimates of the percentage of a sample experiencing concentration difficulties every day over 14 days fell at the higher end of the range (40%–60%; Pacella et al., 2018). In regards to symptoms over time, the latter study showed that concentration complaints decreased over the first 14 days after injury, with about a 28% reduction each day in the odds of reporting these complaints (Pacella et al., 2018).

Processing speed symptoms were reported by between 15% and 25% of individuals in one mTBI sample, with this range again based on extrapolation from a figure (Hou et al., 2012).

In addition to the studies that reported individual cognitive domain data as frequency data, one study reported this as continuous data, that is, mean scores on a symptom scale (Studerus-Germann et al., 2017). Symptom scores were highest for the items 'difficulty concentrating' and 'difficulty remembering', lower for 'feeling slowed down' and zero for the symptom 'feeling mentally "foggy".

Meta-analysis

A meaningful meta-analysis on frequency data was not feasible as a result of the limited number of studies reporting frequency data, methodological differences between studies (e.g. variation in cognitive domains assessed), lack of control groups employed and lack of availability of numerical outcome data (i.e. where data was reported in figures). Therefore, a single meta-analysis was conducted, synthesising studies reporting continuous data. These studies were also highly varied in their methodology. However, they were consistent in reporting overall cognitive symptom scores rather than differing cognitive domains, and most studies had control data available. We therefore included studies that 1) reported continuous outcome data, and 2) employed a control group, to address the research question, *Do patients with mTBI report cognitive symptoms to a greater extent than control groups?* Based on the small number of included studies, intended subgroup analyses were unable to be conducted.

A total of six studies were included in the final meta-analysis (Anderson, 2021; Clarke et al., 2012; Landre et al., 2006; Mayer et al., 2015; Norman et al., 2019; Shumskaya et al., 2012). Three of the studies employed healthy controls (Anderson, 2021; Mayer et al., 2015; Shumskaya et al., 2012) and two employed injured controls (Landre et al., 2006; Norman et al., 2019). The remaining study employed both healthy and trauma controls, and in this case the trauma group was used as the control group in the analysis, as this was expected to be a closer comparison (Clarke et al., 2012). The resulting meta-analysis included a total of 208 mTBI participants and 214 control participants (135 healthy controls and 79 injured controls).

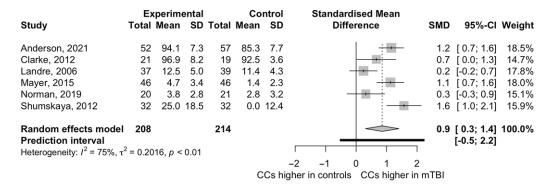


Figure 2. Results of the meta-analysis.

Each of the six included studies reported cognitive symptom data for a single time point only; these studies ranged from assessing participants approximately 4–5 days after injury (Landre et al., 2006), to assessing participants 3–12 months after injury (Clarke et al., 2012).

Five different symptom scales were employed across the six studies. Available data from the five studies consisted of cognitive subscores on measures of post-concussive symptoms (Landre et al., 2006; Mayer et al., 2015; Norman et al., 2019; Shumskaya et al., 2012) or total scores on a specific cognitive symptom scale (Anderson, 2021; Clarke et al., 2012). In one case where standard deviations were not reported, they were estimated from interquartile ranges using published methods (Wan et al., 2014).

The results of the meta-analysis are presented in Fig. 2. Given the structure of the symptom scales, scores represent the number of symptoms endorsed in combination with the severity of endorsed symptoms.

The meta-analysis revealed significant effects for cognitive symptom reporting in mTBI patients versus controls, suggesting that mTBI patients report cognitive symptoms to a greater extent than controls (SMD = 0.85, 95% CI 0.31–1.40, p = .0102). There was a large degree of heterogeneity between studies ($\tau^2 = 0.20$, 95% CI 0.04–1.58; $I^2 = 75.0\%$, 95% CI 43.4%–89.0%). This was expected due to the methodological differences between studies, including differences in control groups employed and in time post-injury at which assessments took place.

No statistical outliers were detected in the analysis. Statistical tests of publication bias were not conducted given the low power of these tests when the number of included studies is low (Murad, Chu, et al., 2018).

Discussion

This review has demonstrated that cognitive complaints are consistently reported after mTBI, although reported rates differed greatly across studies. Importantly, this study has provided the first meta-analytic evidence to suggest that cognitive complaints are reported to a greater extent (using a combined measure of frequency and severity) in mTBI patients than in control groups. This indicates that cognitive complaints may be specifically elevated in mTBI, in contrast to overall post-concussion symptoms which are typically found to be present at similar levels in mTBI and control groups (Dean et al., 2012; Meares et al., 2011). The current review also highlighted several limitations in the literature, including inconsistencies in methodology between studies and insufficient reporting of study information.

The finding that cognitive complaints occur to a greater extent in mTBI patients than in control groups (in frequency and/or severity) indicates that, after mTBI, cognitive complaints are present

beyond 'normal' levels. Given cognitive complaints are highly important for successful return to work and extent of healthcare use (Schraa, 1995; Theadom et al., 2017, 2018; Wrightson & Gronwall, 1981), they clearly warrant further attention. Further, whereas measures of overall post-concussion symptoms often do not differ between mTBI and control groups (Dean et al., 2012; Meares et al., 2011), this review suggested that cognitive symptoms, when isolated from other post-concussion symptoms, are specifically elevated in mTBI. Thus, cognitive symptoms may be of specific clinical importance in individuals who are recovering after a mTBI, and deserve further investigation.

The meta-analysis revealed large amounts of heterogeneity between studies, of which underlying causes could not be statistically explored due to insufficient sample size. However, one potentially important source of heterogeneity may have been due to differences in the type of control groups employed. The systematic review revealed that differences in cognitive symptoms between mTBI patients and controls were most often found when healthy controls, rather than injured controls, were employed. This appeared to hold true whether studies were conducted in the acute or chronic phase following injury. Further, in the meta-analysis, the three studies that had the greatest between-group differences were those that employed healthy controls. It is therefore possible that the significant results from the meta-analysis were in part driven by the subgroup of studies that employed healthy controls rather than injured controls.

Due to the limited numbers of studies available for inclusion, the current meta-analysis was unable to determine whether mTBI patients report more cognitive complaints than injured controls specifically. This is an important question to pursue. If there is no difference in cognitive complaints between these groups, it suggests that some of the factors contributing to cognitive complaints in mTBI patients may also be present in injured control patients. In particular, cognitive symptoms may be related to stressors associated with general injury rather than mTBI-related impairment (Cassidy, Cancelliere, et al., 2014). It is also possible, however, that there are factors specific to mTBI which elevate cognitive complaints, either due to true cognitive changes resulting from brain injury or due to psychosocial factors inherent to mTBI (e.g. illness perceptions (Anderson & Fitzgerald, 2018; Whittaker et al., 2007) or 'diagnosis threat' (Ozen & Fernandes, 2011)).

With regards to time since injury, findings from the systematic review suggested that cognitive symptoms appear to decrease over time. This aligns with previous research, which has shown that overall post-concussive complaints decrease over time, and that cognitive performance normalises over time (Carroll, Cassidy, Peloso, et al., 2004; Frencham et al., 2005). It is important to consider that the studies included in this review spanned a very wide range with regard to when participants were assessed post-injury, ranging from days to years. Unfortunately, intended subgroup analyses on time since injury could not be conducted due to small sample size. However, given the likely role of time since injury in the reporting of cognitive complaints, it will be important for future studies to investigate this topic in samples that are within discrete post-injury time periods.

With regards to cognitive domains, mTBI patients endorsed symptoms across each of the domains that were individually assessed, that is, memory, attention and processing speed. However, studies varied greatly in regards to how domain-level data was derived, making the data non-equivalent and limiting between-study comparison. Across all included studies, including those that examined domains collectively, memory, attention and processing speed symptoms were commonly assessed. This is consistent with the literature that shows that these are common domains of objective impairment after mTBI (Rabinowitz & Levin, 2014). In contrast, only three of the 13 included studies assessed executive function symptoms, despite this domain also being commonly impaired after mTBI (Frencham et al., 2005; Rabinowitz & Levin, 2014). Given that intended subgroup analyses on type of cognitive complaint were unable to be conducted due to limited sample size, further research is warranted to determine the domain(s) most commonly subjectively impaired after mTBI.

In considering these findings, it is noteworthy that the quality of included studies varied, with four studies meeting less than or equal to 50% of evaluated criteria, and four studies meeting over 80% of evaluated criteria. Similarly, this review found a large degree of inconsistency in methodology between studies, and this was identified as one of the primary methodological issues in the current literature. In particular, inconsistencies and vagueness in defining mTBI have been apparent in the literature for several decades now (Carroll, Cassidy, Holm, et al., 2004; Pertab et al., 2009; Ruff et al., 2009) and this review has shown that these issues remain prevalent.

It is important to note that there were a large number of studies excluded from this review on the basis of the age of included participants. There is a well-established relationship between age and outcome after mTBI, both at the higher and lower ends of the spectrum (Cassidy, Boyle, et al., 2014; Jacobs et al., 2010; Li et al., 2017). Given this relationship, including studies involving older or younger participants – or studies where the age of participants could not be determined – would have created a potential bias for this review. Therefore, to minimise bias, only studies that directly specified that their sample fell between the ages of 18 and 60 were included. Given the impact of age on recovery from mTBI, it is recommended that future studies consider younger and older adults with mTBI as separate, unique populations.

Study limitations

The primary limitation of this systematic review and meta-analysis was small sample size. This resulted in an inability to conduct subgroup analyses, as well as an inability to formally evaluate publication bias. When only a small number of studies are available for quantitative synthesis, limitations primarily include difficulties in accurately estimating meta-analysis parameters (Borenstein et al., 2009). Despite these difficulties, it is still preferable to synthesise studies statistically through meta-analysis in these situations, as this provides for a more accurate representation of data than intuitive ad hoc data summaries, which can be misleading (Borenstein et al., 2009). This limitation was mitigated in the current study through the use of the Hartung-Knapp model adjustment in our meta-analytic approach, which reduces the risk of obtaining a false positive result in the presence of a small number of studies (Inthout et al., 2014). The possibility of small sample sizes within studies was addressed through the use of Hedges' g, which allows for unbiased estimates of effect size even in the presence of small samples (Borenstein et al., 2009). A final limitation of this study was the absence of a second reviewer for initial screening of relevant literature, due to the large number of studies identified for screening. In order to minimise the potential impact of this limitation, any screening decisions that were unclear were discussed with the second and final authors until consensus was reached; a low threshold was used for initiating this discussion.

Directions for future research

Further research is required to determine whether mTBI patients report greater cognitive complaints than injured control groups, and if so, for what time period post-injury. This will have important implications from a rehabilitation perspective, as it would contribute to understanding the relative specificity of cognitive complaint in mTBI, which could assist with patient management.

Current measures of symptom reporting typically combine symptom frequency and symptom severity into a single score. It will be important for future research to examine cognitive complaints in a manner that allows for the evaluation of complaint frequency and severity as separate entities. The disentanglement of these components will allow for understanding of whether increased levels of cognitive complaint in mTBI are a result of increased complaint frequency, increased complaint severity or both. Future research would also benefit from executive function difficulties being routinely included in symptom assessment, to enable comprehensive investigation of cognitive symptoms. Similarly, future research would profit from thorough reporting of study information including: age ranges of included participants, how exposure to mTBI was determined, rates of participant follow-up and recruitment setting and selection procedure for control groups. Future studies are encouraged to control for factors known to impact symptom reporting, including sex and psychological factors. Direct adherence to standardised definitions of mTBI, for example, the World Health Organization definition (Carroll, Cassidy, Holm, et al., 2004), would further improve comparability between studies.

Conclusions

This study has confirmed that cognitive complaints are consistently reported after mTBI. Findings have provided clear evidence to suggest that these complaints are reported to a greater extent, using a combined measure of frequency and severity, in mTBI patients than in control groups. Results suggest that this difference in symptom reporting may be greater when healthy controls, rather than injured controls, are employed. Given the importance of elevations in cognitive symptom reporting for outcome after mTBI, including in the context of return to work and healthcare use (Donovan et al., 2014; Theadom et al., 2017), it is evident that cognitive complaints warrant investigation. It is clear from this review, however, that there has been limited research regarding the nature and time course of cognitive complaint after mTBI. Future research into cognitive complaint, including examination of the factors contributing to these complaints, will provide an evidence-based context for clinicians to consider these complaints with respect to management and intervention.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/BrImp.2022.19

Data availability. Data and analysis code is available at the Open Science Framework and can be accessed at: https://osf.io/ ckjg6/?view_only=b582da431f6b4bd98ed9998eddd0cb5d.

Acknowledgements. We would like to acknowledge: Jacquie Eyres, who acted as the second reviewer on this project; and Cameron Patrick (Melbourne Statistical Consulting Platform), who provided statistical consulting on this project.

Financial support. This work was supported by a Melbourne Research Scholarship from the University of Melbourne, awarded to the first author.

Conflicts of interest. Arielle M. Levy has no conflicts of interest to disclose. Michael M. Saling has no conflicts of interest to disclose. Jacqueline F. I. Anderson has no conflicts of interest to disclose.

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Cite this article: Levy AM, Saling MM, and Anderson JFI (2023). Frequency and extent of cognitive complaint following adult civilian mild traumatic brain injury: a systematic review and meta-analysis. *Brain Impairment* 24, 309–332. https://doi.org/10.1017/BrImp.2022.19