Apathy After Traumatic Brain Injury: Prevalence, 12-Month Trajectory, and Clinical Implications

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signature:

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Date: 04/06/2025

Overview

This thesis contributes to the growing recognition of apathy as a clinically meaningful outcome following traumatic brain injury (TBI). The thesis consists of three parts:

Part one presents a systematic review and meta-analysis estimating the prevalence of apathy after TBI. Eighteen studies were included, and the pooled prevalence was over one-third. Subgroup and meta-regression analyses identified moderators of prevalence, including cause of injury, injury severity, population type, and sex. These findings reinforce the importance of routine apathy screening.

Part two reports an empirical study using data from the TRACK-TBI cohort. The study compared apathy trajectories in individuals with TBI versus orthopaedic injuries over 12-months and explored whether early apathy was associated with long-term functional outcomes. Apathy scores were higher in the TBI group and remained higher throughout the 12-months. However, this association was reduced when the model was adjusted for co-occurring mental health difficulties. Early apathy was associated with poorer functioning at 12 months, particularly in social and interpersonal domains. These findings support the clinical relevance of apathy as an early marker of long-term outcomes.

Part three is a critical appraisal that reflects on the evolving understanding of apathy, highlighting the challenges of capturing its complexity within existing frameworks. It explores key methodological decisions, including the use of secondary data and the development of an ad-hoc apathy scale, and considers how open-science principles and clinical experience shaped the research process. The appraisal also discusses the clinical relevance of apathy following TBI and outlines future directions for improving its measurement and recognition in practice.

Impact statement

This thesis explores apathy as a multidimensional outcome of traumatic brain injury (TBI), highlighting its prevalence, clinical relevance, and long-term impact on recovery. The findings have potential to inform academic research, clinical practice, and policy.

Academic Impact

This work includes the first meta-analytic synthesis of apathy prevalence following TBI, addressing a critical gap in the literature. While apathy prevalence has been estimated in other neurological populations, no previous review had quantified this in TBI. By establishing that over one-third of individuals experience apathy post-TBI, the review provides a robust foundation for future research. The review also identifies key methodological inconsistencies and moderators, highlighting the need for more standardised and comparable approaches in future studies. Both the review and the empirical paper highlight the lack of a consensus definition and the absence of gold-standard measures for apathy in TBI, reinforcing the need for conceptual clarity and measurement development in future research.

Clinical and Professional Impact

Identifying apathy as a prevalent and functionally significant outcome helps raise awareness among clinicians that it is an important focus for recovery. The findings support routine screening and early identification of apathy in both acute and community rehabilitation settings. By demonstrating that apathy emerges early and is associated with poorer long-term functional outcomes, this research supports its integration into multidisciplinary team (MDT) formulations, care planning, and psychological assessments. Framing apathy as a neuropsychiatric consequence of brain injury can enhance psychoeducation for caregivers. Highlighting its links with everyday functioning may also improve caregiver understanding and engagement in care planning.

Policy and Service-Level Impact

The findings reinforce the need for longer-term psychological support in TBI pathways, extending beyond physical rehabilitation. Understanding the prevalence of apathy after TBI can facilitate the planning of services accordingly. Given apathy's impact on social reintegration, return to work, and independence, its high prevalence has broader economic and societal implications, strengthening the case for service provision that includes neuropsychiatric outcomes.

Pathways to Impact

The systematic review has been submitted for peer-reviewed publication, with a preprint, dataset, and analysis code made publicly available to support open-science and knowledge accessibility. The empirical paper will also be prepared for submission to ensure broad dissemination of findings to clinical and academic audiences.

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Part 1: Literature Review

Prevalence and moderators of apathy after traumatic brain injury: a systematic review and meta-analysis

Abstract

Aims: This study aimed to quantify the pooled prevalence of apathy in individuals with traumatic brain injury (TBI) and identify factors that may moderate its occurrence. By synthesising findings from previous studies, we sought to address inconsistencies in reported prevalence rates and enhance understanding of apathy as a neuropsychiatric outcome of TBI.

Methods: We conducted a pre-registered meta-analysis (PROSPERO CRD42024552306), searching three databases (APA PsycINFO, MEDLINE, and EMBASE) for primary studies assessing apathy in individuals with TBI. Eighteen studies met inclusion criteria, and data were extracted for meta-analysis to estimate the pooled prevalence of apathy. Subgroup analyses and meta-regressions explored the influence of potential moderating factors including demographic characteristics, injury-related factors, and methods of apathy assessment.

Results: The meta-analysis found the prevalence of apathy following TBI to be 37.6% [95% CI 28.5 – 47.2%]. Key moderators included cause of injury, TBI severity, sex and population type. Specifically, transport accidents were associated with higher apathy prevalence, while mild TBI, male sex, and veteran status were associated with lower apathy prevalence.

Conclusions: Apathy is a prevalent and significant symptom following TBI, affecting over one-third of individuals in the reviewed studies. These findings highlight the need for increased clinical focus on apathy as an important aspect of TBI recovery.

Introduction

Traumatic brain injury (TBI) is a significant public health concern. It occurs when an external force damages the brain, which can result in a range of physical, cognitive, emotional, and behavioural impairments (Menon et al., 2010). It is the leading cause of disability and mortality among individuals aged 1 to 45, with only 25% of those who have had a serious TBI gaining long-term functional independence (Ahmed et al., 2017). The consequences of TBI extend beyond the individual, often causing significant distress for families and contributing to broader societal and economic challenges (Faul et al., 2010; Rubiano et al., 2015). In 2019, there were 27.16 million new cases of TBI worldwide, with 48.99 million people living with TBI (Guan et al., 2023). In the UK, a report by the Centre for Mental Health estimated the annual cost of TBI to be £15 billion (Parsonage, 2016). Importantly, while some of the symptoms of TBI may be immediately apparent, other, predominantly neuropsychiatric, symptoms, may be less so. It is because of this that TBI is often referred to as the 'silent epidemic'.

Apathy is a well-recognised neuropsychiatric outcome in individuals with TBI, with significant impact on functioning and recovery (Azouvi et al., 2017; Ciurli et al., 2011; Worthington & Wood, 2018). Marin (1991) first defined apathy as a neuropsychiatric syndrome characterised by a persistent lack of motivation that cannot be explained by diminished consciousness, cognitive deficits, or emotional distress. It is considered to be a multidimensional construct involving reduced motivation, goal-directed behaviour, and emotional indifference (Marin, 1996). These characteristics make apathy a critical focus in clinical assessment and intervention, given its substantial impact on daily functioning and overall quality of life.

Apathy has been consistently linked to significant impairments in psychosocial functioning. Individuals with apathy face difficulties in activities of daily living (Green et al.,

2022; Tierney et al., 2018), reduced independence after hospital discharge (Arnould et al., 2015), and limited community integration (Cattelani et al., 2008). Apathy has also been associated with less progress in rehabilitation (Resnick et al., 1998), increased reliance on caregivers (Landes et al., 2001) and significant caregiver distress which can strain family dynamics (Marsh et al., 1998). Moreover, apathy has been associated with passive coping strategies (Finset & Andersson, 2000), poorer employment outcomes such as reduced working hours and financial independence (Bull et al., 2016; Funayama et al., 2022). These findings highlight the pervasive and multifaceted impact of apathy, reinforcing its importance as a focus for clinical assessment and intervention.

Apathy is prevalent across various other neurological conditions. A meta-analysis found that apathy affects 33% of individuals post-stroke (Zhang et al., 2023) and is reported to be up to three times more prevalent than depression in dementia (Caeiro et al., 2013).. Similarly, 39.8% of individuals with Parkinson's disease experience apathy (den Brok et al., 2015), and it was reported as the most common neuropsychiatric symptom in Alzheimer's disease (Mega et al., 1996; Nobis & Husain, 2018; Zhao et al., 2016). However, our understanding of the prevalence of apathy following TBI is limited.

A recent review by Quang et al. (2024) explored factors associated with apathy in moderate-to-severe TBI and reported the limited role of injury severity and demographics. Instead, they highlighted the influence of factors like caregiver burden and self-efficacy. While this review emphasised the need for a multifaceted biopsychosocial approach to understanding apathy, it did not meta-analyse apathy prevalence, leaving the overall rate across studies unclear. Additionally, their focus on moderate-to-severe TBI limited insight into how apathy and its moderators vary across the full spectrum of injury severity.

Thus, despite recognition of its seriousness, the prevalence of apathy after TBI remains unclear and a robust meta-analysis addressing this is needed. Estimates of the

prevalence of apathy in TBI vary widely, ranging from 16% (Zomeren & Burg, 1985) to 71% (Kant et al., 1998), making it difficult to estimate the scale of the problem and plan services accordingly. The extent of this variability also hints at the existence of factors moderating the relationship between TBI and apathy, whether this is the case and which factors may be relevant remains unclear. Potentially contributing to this inconsistency are definitional challenges. Apathy has been conceptualised as both a symptom and a syndrome (Levy & Dubois, 2006; Robert et al., 2018) and often co-occurs with related conditions such as depression and fatigue, which complicates differential diagnosis (Worthington & Wood, 2018). In addition, the lack of a gold-standard apathy measure validated for TBI populations (Clarke et al., 2011) further limits comparability across studies.

This systematic review and meta-analysis aimed to address these important issues by providing a comprehensive estimate of apathy prevalence across mild, moderate, and severe TBI populations while identifying potential moderators influencing variability in reported rates.

Methods

Search Strategy

The protocol was pre-registered on PROSPERO (CRD42024552306). We performed comprehensive searches on the Ovid platform across three databases: APA PsycINFO, MEDLINE, and EMBASE. The search was conducted in August 2024 with no date restrictions. Exact search terms are provided in appendix A. The search strategy included terms such as ‘traumatic brain injury’, ‘head injury’, ‘apathy’, ‘amotivation’ and ‘disinterest’. A wide-ranging selection of apathy-related terms was used (e.g. ‘loss of motivation, ‘indifference’). References of included papers were searched to identify additional studies.

Eligibility Criteria and Screening

Eligibility criteria were defined using the Population, Intervention, Comparison, Outcomes, and Study (PICOS) framework:

- Population: Adults (≥18 years) with a history of TBI, assessed at least once for apathy.
- Intervention: Apathy assessed through clinical evaluation, structured interviews, or questionnaires.
- Comparison: Studies with or without comparison groups were eligible.
- Outcome: Prevalence of apathy reported as cases per sample.
- Study Design: Peer-reviewed primary research articles.

We included studies published in English only due to resource limitations but imposed no restrictions on publication date, geographic location, or care setting. We did not include studies which did not differentiate between TBI and other neurological conditions or acquired brain injury. Studies were excluded if participants were selected based on apathy symptoms, to avoid bias in prevalence estimates due to selective recruitment.

As a wide range of apathy-related terms were captured in the search, we applied explicit decision rules to determine whether a construct or measure was considered to reflect apathy. Studies were included when the target construct was explicitly labelled ‘apathy’ by the original authors and the assessment (questionnaire, structured interview, or an apathy subscale within a broader measure) contained items that directly indexed diminished motivation, initiation, persistence, or interest, and was interpreted as apathy by the authors. For instruments spanning multiple domains, we extracted only the apathy-specific subscale or item set. Ambiguities were resolved by reviewer discussion until consensus.

Search results were imported into Rayyan, an online screening platform. Two authors (JL and LHS) independently screened titles and abstracts for eligibility. Studies passing this

initial screening underwent full-text review for final inclusion by the two authors (JL and LHS). Any disagreements were resolved through discussion or consultation with a third author (VB) when necessary.

Data Extraction

Data were extracted independently by two authors (JL and LHS), with discrepancies resolved through discussion and consensus. A third author (VB) was consulted if necessary. Data were extracted into a pre-designed spreadsheet, capturing the following:

1. Study characteristics: Authors, publication year, study design, population and setting.
2. Sample demographics: Age, sex distribution, percentage of non-white participants and sample size.
3. Clinical characteristics: TBI severity, time since injury, and cause of TBI.
4. Apathy assessment: Measurement tool and rater (e.g., clinician, self-report, caregiver/informant).
5. Outcome: Prevalence of apathy (number of cases and sample size).

In three studies, multiple apathy prevalence rates were reported. In each case, two reviewers (JL and VB) selected the most appropriate estimate for inclusion in the overall prevalence analysis. In one study, both self- and caregiver-reported measures were available; the caregiver rating was chosen to align with the most common method across studies. In another, two validated measures were used within the same sample; the scale with stronger psychometric support was selected. In the third, prevalence was reported at multiple timepoints, so the mid-point estimate was used to ensure consistency.

Quality Assessment

Risk of bias was evaluated using the JBI Critical Appraisal Checklist for Prevalence Studies which assesses aspects of study validity such as measurement reliability, sample size and sampling methods (see appendix B for criteria and how each item was interpreted for this review). Two authors (JL, LHS) rated independently, resolving disagreements by consensus. For comparability, we scored Yes=1 and No/Unclear=0, excluding Not Applicable items from the denominator; totals (0–10) summarised study quality. Across 18 studies, the mean score was 8.3/10. Item-level ratings are in Appendix C.

Statistical analysis

The meta-analysis was carried out using R (version 4.4.2) with the meta and metafor packages. Random-effects models were used to calculate the pooled prevalence of apathy after TBI. Heterogeneity was assessed using I^2 statistics to quantify the proportion of variability due to heterogeneity rather than sampling error. Heterogeneity is typical among prevalence studies and therefore a random effects model accounts for $I^2 \geq 50\%$. Prevalence rates were transformed using a Freeman-Tukey double arcsine transformation to stabilize variance.

To assess potential publication bias, we constructed funnel plots and performed Egger's regression test. Sensitivity analyses were completed to include a leave-one-out procedure, wherein each study was sequentially removed to examine its impact on the overall effect size.

Subgroup analyses were conducted to explore variations in prevalence based on study design, study location, setting, apathy measure and apathy rater. Meta-regressions were used to assess whether age, gender, study quality, TBI severity, length of time since TBI and cause of injury moderated the prevalence of apathy.

Results

Search results

Out of 710 studies screened, 18 met the final inclusion criteria. The full screening and study selection process is detailed in the PRISMA flowchart (Figure 1). There was substantial agreement between both reviewers for the title and abstract screening (Cohen's kappa = 0.72).

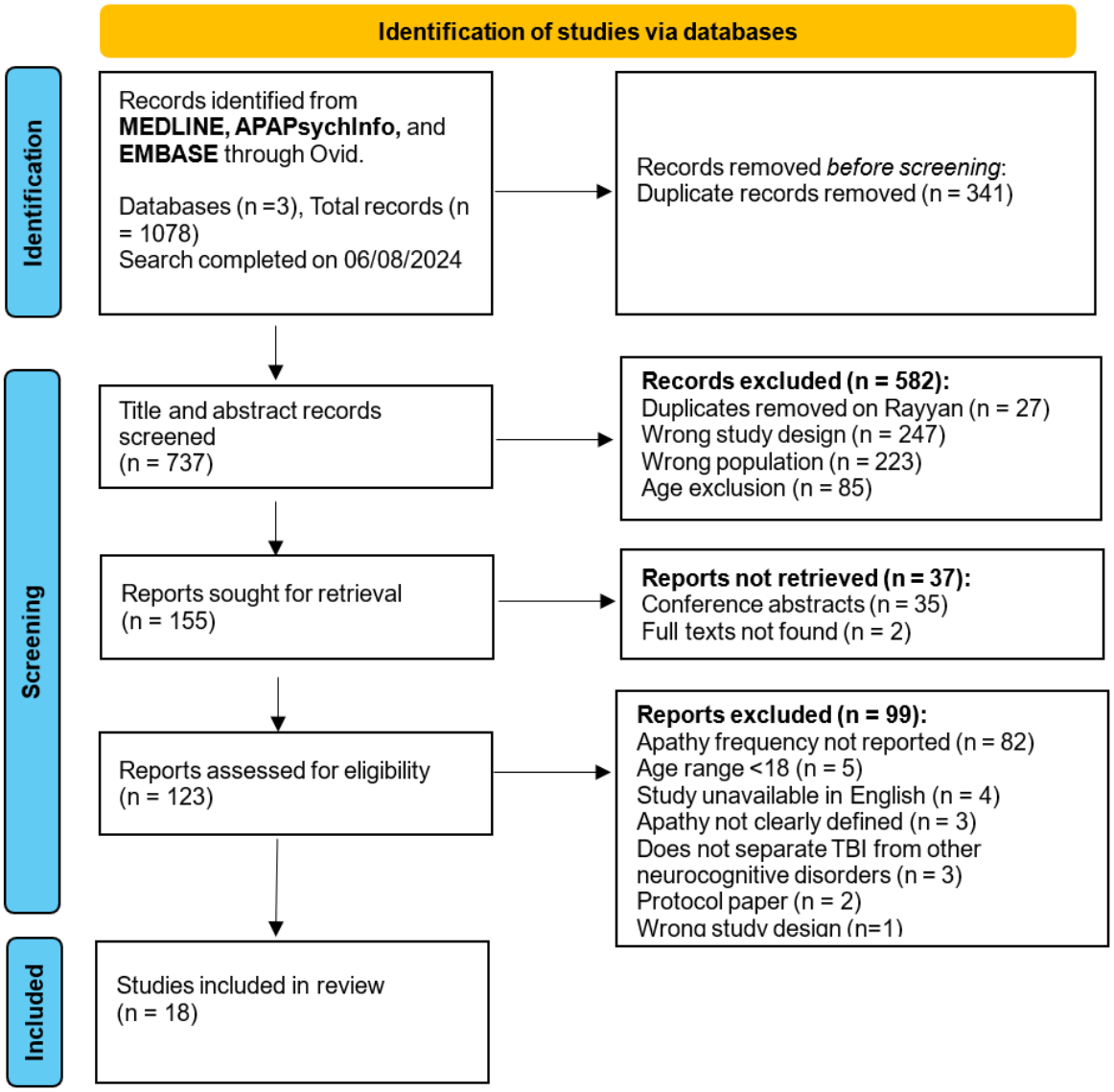

Figure 1. *PRISMA flowchart for identification of included studies*

Study characteristics

Eighteen studies were included in the analysis, spanning publication years from 1991 to 2024, Table 1 outlines basic characteristics of each included study (see appendix D for full study extraction details). The studies were conducted across five continents, with the majority based in North America (k = 6), Asia (k = 5) and Europe (k=5). Only two of the studies (both in North America) reported details on the proportion of non-white participants, limiting our ability to assess how representative the included samples were or explore potential differences in apathy prevalence by ethnicity. A total of 1,136 participants with a TBI were included, with a mean of 63 participants per study. The mean age of participants was 37.8 years, and males comprised 79% of the sample, reflecting the well-documented gender imbalance in reported TBI rates (Bruns Jr. & Hauser, 2003).

One study (Nygren DeBoussard et al., 2017) provided demographic data for a larger sample (n=114) than the 81 that were assessed for apathy, limiting the demographic details we could report for this study. Sixteen studies reported the TBI severity of their sample, which overall was found to be 13.2% mild, 34.0% moderate-to-severe and 52.8% severe. Seven of the studies used the Glasgow Coma Scale (GCS) to categorise severity: mild (score 13-15), moderate (9-12), and severe (3-8). Two studies used the GCS alongside other factors, such as the duration of loss of consciousness, post-traumatic amnesia, and intracranial neuroimaging abnormalities. One study combined these factors without relying on the GCS, while another used the Glasgow Outcome Scale. Seven studies did not specify their method of categorisation.

Eleven studies reported TBI causes: transport accidents (74.5%), falls (11.36%), combat (4.3%), assaults (4.5%), and other causes (3.8%). Seventeen studies reported a mean or median time since TBI, with a pooled average of 43.4 months. The average time since injury across studies ranged from 3 to 133.2 months (SD = 44.3), based on study-level summary values. One study (Nygren DeBoussard et al., 2017) reported apathy prevalence at

3 weeks (35%), 3 months (32%), and 1 year (37%) post-injury; the 3-month estimate was selected for inclusion in the meta-analysis. Fourteen studies did not specify whether participants had a single or multiple TBIs. Of the four that did, two included only single TBI cases, while the other two included participants with varying numbers of TBIs.

Apathy was assessed using a variety of measures, including the Neuropsychiatric Inventory (NPI; k = 5), Apathy Evaluation Scale (AES; k = 3), Frontal Systems Behavior Scale (FrSBe; k = 2), Dimensional Apathy Scale (DAS; k = 1), Apathy Scale (k = 1), Head Injury Symptom Checklist (k = 1), Frontal Behavioural Inventory (k = 1), and Apathy Inventory (k = 1).

For the purposes of this review, the AES and FrSBe were considered validated measures of apathy in TBI, based on psychometric evidence in this population (Lane-Brown & Tate, 2009a). The AES and NPI have also been identified as the most psychometrically robust apathy measures across neurological populations (Clarke et al., 2011). Preliminary evidence supports the NPI's validity in TBI populations specifically (Kilmer et al., 2006), and it was therefore also included as a TBI-validated measure. Several other tools such as the DAS, Apathy Inventory and Frontal Behavioural Inventory lack validation in TBI populations, though have been validated in other neurological populations (Radakovic et al., 2019; 2020; Kertesz et al., 2000). In total, ten studies used TBI-validated measures and eight used non-validated ones.

Most measures were caregiver-rated (k = 10), with four self-reported and three clinician-rated. One study (Lengenfelder et al., 2015) reported both self-reported (43%) and caregiver-reported (35%) apathy prevalence; the caregiver-reported estimate was included in the meta-analysis to align with the dominant reporting method across studies. Reported apathy prevalence ranged widely, from 4% to 87%.

Study authors	*Year*	*Country*	*TBI N*	*Severity categorisation method*	*Apathy measure*	*Rater*	*Apathy N*
Venkatesan & Rabinowitz	2024	USA	106	GCS + other factors	Frontal Systems Behaviour Scale	Self-report	53
Nguyen et al.	2023	Vietnam	75	GCS	Neuropsychiatric Inventory	Caregiver	46
Quang et al.,	2023	Vietnam	45	GCS	Dimensional Apathy Scale	Caregiver	20
Ubukata et al.	2022	Japan	88	GCS	Apathy Scale	Self-report	51
Balan et al.	2021	Brazil	41	NA	Apathy Evaluation Scale	Caregiver	12
Devi et al.	2020	India	50	GCS	Neuropsychiatric Inventory	Caregiver	5
Huang et al.	2020	USA	25	GCS + other factors	Head Injury Symptom Checklist – adapted	Self-report	1
Nygren DeBoussard et al.	2017	Sweden	81	GCS	Clinical interview	Clinician	26
Arnould et al.	2015	France	68	NA	Apathy Inventory	Caregiver	14
Lengenfelder et al.	2015	USA	33	NA	Frontal Systems Behaviour Scale	Caregiver	11.55
Knutson et al.	2014	USA	176	NA	Neuropsychiatric Inventory	Caregiver	28
Wiart et al.	2012	France	47	Glasgow Outcome Scale	Clinical interview	Clinician	20
Lane-Brown & Tate	2009	Australia	34	NA	Apathy Evaluation Scale	Caregiver	23.46
Kilmer et al.	2006	USA	51	Other factors	Neuropsychiatric Inventory	Caregiver	19
Al-Adawi et al.	2004	Oman	80	GCS	Apathy Evaluation Scale	Self-report	16
Cantagallo & Dimarco	2002	Italy	53	GCS	Neuropsychiatric Inventory	Caregiver	25
Pąchalska et al.	2001	Poland	15	NA	Frontal Behavioural Inventory	Caregiver	13
Dunlop et al.	1991	USA	68	NA	Neuropsychiatric scale devised for the study	Clinician	28.56

Table 1. *Characteristics of 18 included studies. GCS = Glasgow Coma Scale; NA = Not reported; Other factors = Length of post traumatic amnesia, length of loss of consciousness, trauma-related intracranial neuroimaging abnormalities*

Main Findings

The pooled prevalence of apathy after TBI was 37.58% (95% CI: 28.45–47.15%) under a random-effects model (Figure 2). Heterogeneity was high (I^2 = 90.3%, 95% CI: 86.2–93.2%), with a significant test of heterogeneity (Q = 174.88, p < 0.001) and between-study variance (τ^2 = 0.037, 95% CI: 0.021–0.098). Study weights ranged from 4.4% to 6.1%, indicating no single study disproportionately influenced the estimate. A Freeman-Tukey double arcsine transformation and Clopper-Pearson method were applied to address extreme values and calculate confidence intervals.

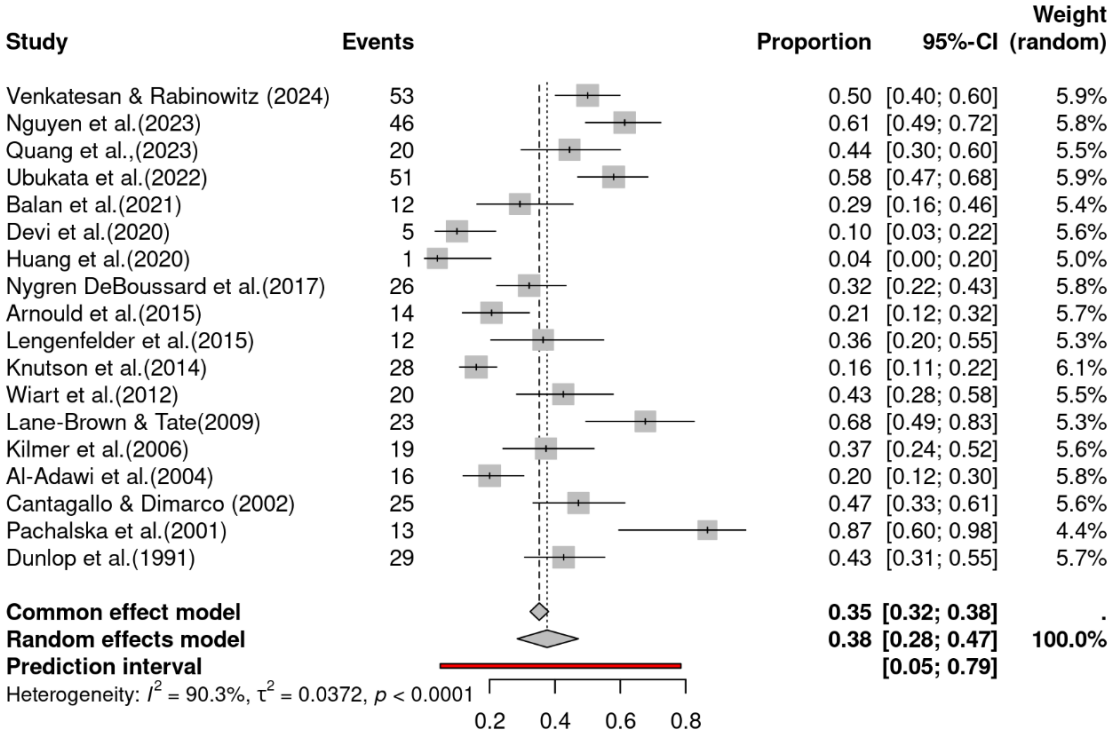

Figure 2. *Forest plot of overall apathy prevalence across 18 included studies*

Subgroup analyses

We conducted subgroup analyses for study design, setting, population, continent, apathy measure, validated measures and apathy rater; see Table 2 for results. Groups with single studies only were excluded. The only significant difference was found was in population subgroups, where veterans had a lower apathy prevalence than the general public ($p < 0.001$). No other subgroups were found to significantly moderate the apathy prevalence. One study (Lengenfelder et al., 2015) included both self and caregiver-reported apathy. We ran a sensitivity analysis using the self-report measure in place of the caregiver rated measure, although the subgroup comparison for rater remain non-significant ($p = 0.876$).

Subgroup	*Category (k)*	*Prevalence (%)*	*95% CI*	*p*
Study Design	Cross-sectional (14)	40.09	28.97–51.72	0.306
	Other designs (4)	29.66	15.20–46.46	
Setting	Outpatient (8)	43.23	29.24–57.78	0.600
	Inpatient (5)	40.45	24.30–57.69	
	Study registry database (3)	30.69	13.46–51.21	
Population	General public (16)	41.52	32.77–50.54	< 0.001
	Veterans (2)	10.92	2.47–23.56	
Continent	Europe (5)	43.18	26.89–60.22	0.513
	Asia (5)	37.46	17.94–59.30	
	North America (6)	29.87	15.95–45.90	
Apathy Measure	Frontal Systems Behaviour Scale (2)	45.12	32.63–57.92	0.672
	Apathy Evaluation Scale (3)	37.66	13.20–65.91	
	Clinical Interview (2)	36.23	26.47–46.58	
	Neuropsychiatric Inventory (5)	32.71	14.47–54.09	
Validated Measures	Validated (10)	36.21	23.83–49.55	0.740
	Non-validated (8)	39.39	25.82 – 53.80	
Apathy Rater	Caregiver (11)	39.60	26.45–53.52	0.836
	Self-report (4)	31.49	11.61–55.60	
	Clinician (3)	38.27	31.12–45.67	

Table 2. *Subgroup Analyses of Apathy Prevalence in TBI Populations*

Meta regression analyses

We also ran several meta-regressions to explore the impact of further demographic factors (age and sex), TBI factors (severity, time since TBI and cause of TBI) and study factors (year published and study quality) on apathy prevalence.

Demographic factors

A mixed-effects meta-regression model found no significant relationship between mean age and apathy prevalence ($\beta = 0.001$, $p = 0.930$). An analysis of 17 studies revealed a significant effect of sex, with males showing a lower prevalence of apathy ($\beta = -0.90$, $p = 0.03$). The model explained 10.56% of the heterogeneity, but residual heterogeneity remained high ($I^2 = 90.03\%$).

TBI factors - severity

Three meta-regression analyses were conducted to examine whether TBI severity moderated the relationship between TBI and apathy prevalence. Fifteen studies were included, with three excluded due to missing data.

A significant negative association was found between mild TBI and apathy prevalence ($\beta = -0.40$, $p = 0.044$), suggesting that individuals with mild TBI experience lower apathy prevalence compared to other severity levels. The model explained a modest proportion of variability ($R^2 = 5.16\%$), though residual heterogeneity remained high ($I^2 = 87.79\%$). No significant associations were found for moderate-to-severe TBI ($\beta = 0.10$, $p = 0.469$) or severe TBI ($\beta = 0.09$, $p = 0.473$) with apathy prevalence.

TBI factors - time since TBI and cause of TBI

A meta-regression analysis investigating the relationship between the mean months since TBI and apathy prevalence revealed no significant association (β = 0.002, p = 0.130). Regarding the cause of TBI, additional meta-regression analyses were conducted to assess how specific causes influenced apathy prevalence. For transport accidents, an analysis of 11 studies demonstrated a significant positive association, indicating that individuals with TBI resulting from transport accidents exhibited higher apathy prevalence (β = 0.417, p = 0.028). This model explained 26.02% of the variability and residual heterogeneity remained high (I^2 = 89.56).

When exploring the same 11 studies, no significant relationship was identified between falls as a cause of TBI and apathy prevalence (β = 0.125, p = 0.908). Similarly, an analysis focusing on assault as a cause of TBI, which included nine studies where this was reported, found no significant association with apathy prevalence (β = 1.150, p = 0.397).

Study factors

A meta-regression analysis found no significant relationship between the year of study publication and apathy prevalence (β = -0.004, p = 0.428). Similarly, no significant effect was found for study quality (β = -0.014, p = 0.601).

Publication bias and sensitivity analysis

The LFK index was 0.4 and so below the threshold for asymmetry suggesting no significant evidence of publication bias in the Doi plot (Figure 3).

Figure 3. *Doi plot*

Outlier and influence analysis

Outlier analysis identified seven studies (Devi et al., 2020; Huang et al., 2020; Knutson et al., 2014; Lane-Brown & Tate, 2010; Nguyen et al., 2023; Pąchalska et al., 2001; Ubukata et al., 2022) as outliers. After excluding these outliers, the random-effects model was based on 11 studies with 673 observations and 246 events although the pooled apathy prevalence estimate was similar at 36.11% (95% CI: 29.37–43.13) although with reduced heterogeneity ($I^2 = 70.4\%$, $\tau^2 = 0.009$). Sensitivity analysis using leave-one-out diagnostics showed minor fluctuations in the pooled prevalence (ranging from 33.34% to 39.23%), with similarly minor fluctuations in overall heterogeneity ($I^2 = 87.9\%$ to 90.8%), indicating the robustness of the meta-analytic results.

Similarly, the influence diagnostics (appendix E) did not identify any studies as having an effect on the pooled effect size and heterogeneity. Baujat diagnostics identified Pąchalska et al. (2001) and Huang et al., (2020) as potentially influential studies (appendix F). However, a sensitivity analysis omitting these studies indicated a similar prevalence

estimate although with slightly improved heterogeneity (38% CIs 29% – 47%; I^2 = 89.4%), similarity indicating robustness.

Discussion

To our knowledge, this is the first review to meta-analyse the pooled prevalence of apathy in individuals with a history of TBI. We also examined potential moderators, including demographic characteristics, TBI-related factors, and methods of apathy assessment. Drawing on data from 18 studies published between 1991 and 2024, we found an overall prevalence of 37.6%, emphasising the high occurrence of apathy in this population. The prevalence estimate remained robust with little change in the overall estimate in subsequent sensitivity analyses.

This prevalence rate is comparable to other neurological conditions, such as 33% in stroke (Zhang et al., 2023) and 39.8% in Parkinson's disease (den Brok et al., 2015), although it is lower than the 49% prevalence found in Alzheimer's disease (Zhao et al., 2016). These findings indicate that over a third of individuals with TBI are likely to experience apathy. Given its significant negative impact on psychosocial functioning, rehabilitation outcomes, and family well-being, this underlines the need for greater clinical attention to apathy as a critical issue in TBI recovery.

Significant heterogeneity was observed across studies, with apathy frequency ranging from 4% to 87%. This wide variability suggests the influence of various moderating factors. Our subgroup analyses and meta-regressions identified four factors that significantly influenced apathy prevalence: cause of injury, TBI severity, sex and population type. Specifically, transport accidents were associated with higher apathy prevalence, while mild TBI, male sex, and veteran status were associated with lower apathy prevalence. We will consider each of these in turn.

We found that males had a significantly lower prevalence of apathy compared to females. Previous studies, including a large cohort study and meta-analysis, have found that females reported a higher symptom burden and more mental health difficulties following TBI (Farace & Alves, 2000; Mikolić et al., 2021). This difference was more pronounced after mild TBI than after severe TBI (Mikolić et al., 2021; Starkey et al., 2022). The mechanisms underlying these disparities in sex remain unclear, with some clinical opinions contrasting this and suggesting that females tend to experience better outcomes after TBI. While biological factors may contribute to these differences, an additional explanation could be that females are more likely to self-report symptoms or have greater self-awareness of TBI-related deficits (Barsky et al., 2001; Niemeier et al., 2014). Interestingly, a review on apathy after TBI (Quang et al., 2024) found no significant sex differences. However, this review focused only on moderate-to-severe TBI and may not reflect differences that emerge more clearly in mild TBI, which our study includes. Given the male predominance in TBI cases (79% in our sample), further research is needed to explore sex-specific differences in apathy and their clinical implications. No significant impact of other demographic factors, such as age, was found on apathy prevalence in this review.

Regarding TBI severity, we conducted three meta-regressions to examine whether the severity of TBI (mild, moderate-to-severe, and severe) moderated the relationship between TBI and apathy prevalence. Our results indicated that only mild TBI had a significant moderating effect, suggesting that individuals with mild TBI may be less likely to experience apathy. However, this effect was small, and substantial heterogeneity remained, indicating that additional factors may contribute to apathy in this group. The lack of significant findings for moderate-to-severe and severe TBI suggests that apathy prevalence may not increase in direct proportion to injury severity alone. Neuropsychiatric outcomes after mild TBI are influenced by a complex, multifactorial aetiology, with psychological mechanisms such as

coping styles or pre-injury mental health difficulties potentially playing a significant role in this group (Mooney et al., 2005; Ponsford et al., 2000; van der Horn et al., 2020). Given that mild TBI accounted for only 10% of the participants in this review, these findings should be interpreted with caution and further research on apathy in mild TBI is needed.

Road traffic accidents were found to moderate the relationship between TBI and apathy, suggesting that individuals with traffic accident-related TBIs may be more likely to experience apathy. One potential explanation for this finding is that road traffic accidents may lead to more complex neurological damage or additional injury-related factors that influence apathy. In high-income countries, road traffic accidents account for the highest proportion of TBI-related hospitalisations (Hyder et al., 2007), indicating that these injuries often necessitate more intensive medical intervention. Furthermore, TBIs resulting from road traffic accidents tend to be more severe than those caused by other incidents (Rahman et al., 2025). The increased severity of injury and the heightened burden of hospitalisation following road traffic accidents may contribute to the higher prevalence of apathy observed in this group.

Veterans had a significantly lower prevalence of apathy (10.9%) compared to the general population (41.5%). However, this result should be interpreted cautiously, given the small number of studies on veterans ($k = 2$; Knutson et al., 2014; Huang et al., 2020). Notably, both veteran cohorts were composed entirely of males. Given that we found males had a significantly lower prevalence of apathy than females, one possibility is that this difference is explained entirely by sex. Alternatively, the lower prevalence in veterans could be attributed to other factors, such as distinct TBI aetiologies, the effects of military training or rehabilitation, or differences in symptom reporting. One of these studies used self-report measures, while the other relied on caregiver ratings. Some research suggests that veterans may underreport psychological symptoms due to cultural influences such as military norms

around emotional resilience and concerns about stigma (Hoge et al., 2004; Vogt et al., 2014). If underreporting is a factor, the true prevalence of apathy in veterans may be underestimated.

Further research using clinician-rated measures is needed to determine whether the lower prevalence reflects a genuine difference or is influenced by reporting biases. Additional studies with larger and more diverse veteran cohorts, including female participants, are needed to clarify and expand upon these findings. This result also underscores the broader importance of contextual influences such as cultural norms, identity-related factors, and psychosocial context, in shaping how apathy is experienced and reported across populations. For instance, Quang et al. (2024) found that apathy was associated with increased loneliness and lower self-efficacy, highlighting complex interactions between environmental and individual-level factors. These influences may contribute to variability in prevalence estimates and warrant greater attention in future research.

We found no evidence that the length of time since injury influenced apathy prevalence, suggesting that apathy may persist over time. This might indicate that apathy is a chronic symptom, possibly driven by neurobiological changes affecting brain regions involved in motivation and emotion. The lack of significant change over time may also reflect insufficient clinical focus on apathy post-TBI. Notably, a systematic review on interventions for post-TBI apathy identified only one randomised controlled trial addressing this symptom (Lane-Brown & Tate, 2009b). This study examined cranial electrotherapy stimulation but lacked between-group analyses, preventing conclusions on effectiveness. Our finding highlights both the potential persistence of apathy and the scarcity of evidence on effective treatments. However, there was substantial variability in the time since injury across included studies, with a range of 3 to 133.2 months, which may have limited our ability to detect consistent associations. Future research should use longitudinal designs with repeated

assessments to clarify the trajectory of apathy over time and identify key windows for intervention.

Our analysis found that apathy prevalence remained consistent across study designs, settings, and continents, and was not influenced by the type of apathy measure used or whether it was validated. This suggests our pooled estimate may be robust across assessment approaches. However, this finding should be interpreted with caution. Validated apathy measures for use in TBI populations are limited, and even these appear to capture different characteristics of the construct (Lane-Brown & Tate, 2009a). Additionally, the lack of a clear consensus on how apathy is defined complicates efforts to compare prevalence estimates across studies. Together, these limitations highlight important gaps in the literature and point to the need for greater conceptual and measurement clarity in future research.

The study has several methodological strengths. By pooling data from multiple studies and using meta-analytic techniques, we achieved high statistical power, which allowed for more precise and reliable estimates of apathy prevalence. The use of subgroup analyses and meta-regressions further enabled us to explore potential moderating factors, helping to address the considerable variability in reported apathy rates. Moreover, the inclusion of studies spanning different TBI severities strengthens the generalisability of our findings across a wide range of patient populations.

Despite these strengths, several limitations warrant consideration. While the review included studies from five continents, no studies from Africa and only one from Oceania were identified, narrowing the global applicability of the findings. We also only included studies published in English. Moreover, most studies failed to report the ethnicity of their samples, which limits the ability to explore whether apathy prevalence may differ across ethnic groups or cultural contexts. The findings are further constrained by the underrepresentation of certain groups, such as females and individuals with mild TBI,

hindering the understanding of sex-specific differences and limiting the applicability to milder forms of TBI. Furthermore, the categorisation of TBI severity was not consistently reported across studies, and variability in classification systems could have impacted the results.

In addition, our search strategy focused on peer-reviewed empirical studies and included three key databases. The extent to which including additional databases improves article identification for any particular topic is debated in the literature. Our review complies with recommendations to select databases based on their coverage of the topic (Dhippayom et al., 2023) and to include at least three databases in systematic reviews related to clinical neurology (Vassar et al., 2017). However, although we included backward citation searching we did not include forward citation searching which can improve article identification and grey literature was excluded, which may have missed prevalence estimates published in theses, pre-prints and other sources outside the peer-reviewed literature.

Additionally, pooled prevalence estimates were not adjusted for co-occurring mental health conditions such as depression, meaning we were unable to understand to what extent apathy prevalence was associated with co-morbid mental health difficulties, or alternatively, overlap between measures. The extent to which apathy and other mental health problems co-occur, overlap, or are on causal pathways for each other is a matter of debate, although this is not easily tested meta-analytically, and may be better addressed by primary data studies.

Lastly, while our meta-analysis identified several factors that are likely to explain some of the variability in prevalence estimates, it is notable that these estimates were still extremely wide (ranging from 4% to 87%). Comparing prevalence across studies is challenging, as apathy can be conceptualised as both a symptom and a syndrome, and different measures may capture distinct dimensions (e.g., emotional, behavioural, cognitive). Contextual influences such as cultural norms, rehabilitation engagement, and individual

differences, may also shape how apathy is experienced and reported. Future research should investigate these factors to support a more biopsychosocial understanding of apathy.

Our findings highlight the high prevalence of apathy following TBI, yet treatment options remain limited. There is little research investigating how pharmacological or rehabilitative interventions might influence apathy in this population, which limits understanding of how best to support recovery. In dementia, acetylcholinesterase inhibitors have shown the strongest evidence for reducing apathy (Berman et al., 2012), while motivation-based behaviour therapy has demonstrated benefits in a single-case experimental study (Lane-Brown & Tate, 2010). Multi-sensory stimulation and music therapy have also shown promise in dementia populations (Holmes et al., 2006; Verkaik et al., 2005). Given the multifaceted nature of apathy, clinical research should prioritise developing and evaluating pharmacological, psychological, and rehabilitative interventions tailored to TBI-related apathy.

In conclusion, this meta-analysis is the first to systematically quantify the prevalence of apathy in individuals with TBI and identify the influence of moderating factors. Our findings demonstrate that apathy is prevalent following TBI, affecting over one-third of individuals in the reviewed studies. However, this pooled estimate should be interpreted with caution given the substantial heterogeneity between studies, the limited representation of individuals with mild TBI and females, and the absence of studies from non-Western contexts. The review identified several factors that may contribute to variability in prevalence: specifically, transport accidents were associated with higher apathy rates, while mild TBI, male sex, and veteran status were linked to lower prevalence. Further research is needed to clarify how apathy manifests across diverse populations and settings. These findings highlight the importance of recognising apathy as a key aspect of TBI recovery and underscore the need for greater clinical attention to its assessment and management.

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Part 2: Empirical paper

Apathy After Traumatic Brain Injury: Longitudinal Trajectories, Mental Health Overlap, and Functional Recovery in TRACK-TBI

Abstract

Aims: This study examined (1) whether apathy is elevated in individuals with TBI versus orthopaedic injuries over 12 months and its association with injury severity; (2) how co-occurring mental health symptoms influence this relationship; and (3) whether early apathy is associated with long-term functional outcomes.

Methods: Data came from TRACK-TBI, a multi-centre longitudinal study. A composite apathy score was derived from validated mental health items at 2 weeks, 3-, 6-, and 12-months post-injury. Multilevel models compared apathy trajectories between TBI and orthopaedic groups, adjusting for demographic and mental health covariates. Regression analyses tested associations between injury severity and apathy, and between 2-week apathy and 12-month functional outcomes.

Results: Apathy scores were higher in the TBI group than orthopaedic controls ($\beta = 0.88$, 95% CI [0.45–1.30]), peaking at 3 months. This peak and group difference weakened after adjusting for depression and anxiety, though apathy remained elevated in TBI overall. Injury severity (GCS, LOC, PTA) was not consistently associated with apathy at 12 months. Early apathy (2 weeks) was associated with poorer global functioning at 12 months ($\beta = –0.12$, 95% CI [–0.14, –0.09]), particularly in social domains.

Conclusions: Apathy emerges early after TBI, is only partly explained by mood symptoms, and is associated with poorer long-term outcomes. It is a clinically important outcome that warrants routine monitoring after TBI.

Introduction

Traumatic brain injury (TBI) is a leading global cause of death and disability (Ahmed et al., 2017), with an estimated 69 million new cases occurring each year (Dewan et al., 2018). In the European Union alone, TBI accounts for approximately 1.5 million hospital admissions annually (Maas et al., 2017). TBI causes lasting impairments across physical, cognitive, behavioural, and psychosocial domains, though outcomes vary widely due to differences in injury severity, pathology, and individual factors (Maas et al., 2017; Ritter et al., 2021). TBI is associated with increased risk for neurodegenerative disease, psychiatric disorders, cognitive decline, and long-term health complications (Deb et al., 1999; Kumar et al., 2020; Masel & DeWitt, 2010). For many, the impact of TBI extends well beyond the acute phase, with some researchers arguing it should be viewed as a chronic health condition due to its lasting effects on health, comorbidities and mortality (Masel & DeWitt, 2010).

While early clinical care often prioritises physical recovery, growing evidence highlights the long-term significance of cognitive, emotional, and behavioural impairments. These are often considered the most disabling, as they are associated with persistent functional difficulties, including challenges returning to work, maintaining social relationships, and engaging in everyday activities (Dams-O'Connor et al., 2013; Thurman et al., 1999; Zahniser et al., 2019). In mild TBI, early emotional distress at two weeks post-injury was associated with poorer six-month recovery (Naalt et al., 2017), whereas structural indicators like computed tomography (CT) abnormalities have shown limited prognostic value for long-term recovery (McMahon et al., 2014), suggesting that psychological factors may be more informative than structural findings in mild TBI.

Greater attention is needed to identify early neuropsychiatric features that may shape recovery trajectories. Apathy is a common and clinically significant neuropsychiatric consequence of TBI, with prevalence estimates ranging from 20% to 70% (Worthington &

Wood, 2018). Originally defined by Marin (1991) as diminished motivation for goal-directed behaviour not attributable to reduced consciousness, global cognitive impairment, or primary emotional distress, contemporary accounts conceptualise apathy as a multidimensional construct spanning executive, emotional, and initiation deficits (Levy & Dubois, 2006; Radakovic & Abrahams, 2018). It is widely recognised as a distinct clinical syndrome and is frequently linked to disruption of frontal–subcortical circuits (Arnould et al., 2013; Lanctôt et al., 2017; Levy & Dubois, 2006).

Theoretical models have framed apathy both as a symptom and as a syndrome, reflecting disciplinary perspectives. In neurology, it is typically treated as a neuropsychiatric syndrome of diminished motivation marked by impaired initiation, emotional responsiveness, and goal-directed behaviour (Starkstein & Leentjens, 2008; Lanctôt et al., 2017). In psychiatry, it is often framed as amotivation secondary to broader difficulties, such as anhedonia in depression or negative symptoms in schizophrenia (Foussias & Remington, 2010; Thomsen et al., 2015; Treadway & Zald, 2011). To provide greater conceptual clarity, Robert et al. (2009) proposed diagnostic criteria for apathy syndrome as a reduction in motivation relative to previous functioning, with impairment in at least two of three domains (behaviour, cognition, emotion), causing significant disruption to daily life and not explained by reduced consciousness, motor disability, or substance effects. These criteria have since been validated across neurological and psychiatric conditions (Husain & Roiser, 2018), with later work highlighting subtypes such as social apathy (Sockeel et al., 2006; Ang et al., 2017).

Apathy must be distinguished from related constructs such as depression, with which it frequently co-occurs after TBI (Andersson et al., 1999; Starkstein et al., 2006). Although both are linked to poorer functional outcomes (Naalt et al., 2017), their profiles are distinct. Apathy is associated with disruption of frontal–subcortical motivation networks and shows limited response to antidepressants, whereas depression involves different neural correlates

(Lanctôt et al., 2017; Ruthirakuhan et al., 2018). Anhedonia, a key feature of depression, is defined as a diminished capacity to experience pleasure and is also understood to involve reduced motivation to pursue rewarding activities (Treadway & Zald, 2011; Radakovic & Abrahams, 2018). This brings it conceptually closer to apathy, but the two remain distinct. Apathy reflects impairments in anticipatory or effort-related processes (e.g., generating, evaluating, sustaining actions toward rewards), whereas anhedonia reflects deficits in consummatory processes, namely the hedonic experience of reward itself (Le Heron et al., 2019; Husain & Roiser, 2018). Effort-based decision-making models integrate these distinctions by mapping where motivation can fail, including option generation, cost–benefit evaluation, effort maintenance, and outcome learning (Husain & Roiser, 2018; Le Heron et al., 2019; Pessiglione et al., 2018). Within this framework, apathy arises when engagement is not initiated or sustained despite intact hedonic capacity, whereas anhedonia reflects blunted pleasure. These insights reinforce apathy as a distinct syndrome within a broader class of motivational disorders.

Beyond definitions, apathy after TBI is best understood within a biopsychosocial framework. Rather than reflecting neuropathology alone, it emerges from the interaction of neurobiological, psychological, and social factors. Neuropathological disruption after TBI to prefrontal–subcortical circuits and dopaminergic pathways provides a biological substrate (Levy & Dubois, 2006; Knutson et al., 2014; Navarro-Main et al., 2021). However, apathy expression is shaped by psychological and environmental influences such as executive dysfunction, caregiver burden, family dynamics, and the loss of rewarding roles (Marin & Wilkosz, 2005; Arnould et al., 2015; Quang et al., 2022; Ponsford, 2013). Individual characteristics such as pre-injury personality and self-efficacy further moderate vulnerability and outcomes (Fleming & Ownsworth, 2006; Bivona et al., 2019). The evidence highlights

apathy as a multidetermined phenomenon arising from interactions across neurobiological, psychosocial, and individual domains.

Building on these conceptual foundations, it is important to consider how apathy manifests in TBI populations and the extent to which it contributes to functional outcomes. In the context of moderate-to-severe TBI, apathy is associated with poorer engagement in activities of daily living (ADLs) (Green et al., 2022), reduced independence after hospital discharge (Arnould et al., 2015) and greater caregiver burden (Marsh et al., 1998). However, findings are not consistent across the spectrum of injury severity. A study in individuals with mild TBI found that apathy did not predict return-to-work, which was used as a proxy functional outcome (Zakzanis & Grimes, 2017). This suggests that the relationship between apathy and functional outcomes may depend on injury severity or on the specific domain of functioning assessed. Given its multifaceted nature, apathy likely affects multiple aspects of daily life, though which domains are most vulnerable remains unclear.

Although many studies have examined long-term outcomes following TBI (Corrigan & Hammond, 2013; Kumar et al., 2020), few have investigated whether early neuropsychiatric features, such as apathy, predict later functional outcomes. This represents a critical gap, as clinical assessments and interventions are typically concentrated in the early post-injury period, when healthcare engagement is at its highest, despite the enduring nature of TBI-related difficulties (Andelic et al., 2020; Mahoney et al., 2021). Apathy, though known to hinder rehabilitation engagement, is rarely prioritised in clinical care. Most existing research focuses on global disability outcomes, offering limited insight into the domain-specific effects of apathy or which individuals may be most vulnerable. Longitudinal studies tracking the emergence of apathy from the acute phase onward remain scarce, making it difficult to identify early predictors.

Studies exploring potential predictors of apathy—such as the Glasgow Coma Scale (GCS), duration of post-traumatic amnesia (PTA), and loss of consciousness (LOC)—have also been inconsistent. Some studies report no significant associations (Glenn et al., 2002; Knutson et al., 2014; Lane-Brown & Tate, 2009; Navarro-Main et al., 2021), while others, such as Arnould et al. (2018), have found relationships in severe TBI. Although GCS remains the most widely used acute severity measure, its ability to predict long-term functional outcomes, such as independence, appears to be limited in some contexts (Perrin et al., 2015). These inconsistencies raise important questions about the utility of traditional injury severity markers in predicting neuropsychiatric sequelae such as apathy. Moreover, few studies include trauma-exposed control groups, limiting our ability to isolate TBI-specific mechanisms underlying apathy.

The current study used data from the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) study—a large, multicentre longitudinal cohort including individuals with TBI and orthopaedic injuries followed across four timepoints in the first year post-injury. As the dataset lacks a validated apathy scale, reflecting a broader gap in TBI research and practice (van Reekum et al., 2005), a proxy measure was constructed using items reflecting behavioural, emotional, and motivational dimensions. This study addressed three research questions:

1. How does apathy differ between individuals with TBI and orthopaedic injuries over the first year post-injury, and is it associated with injury severity within the TBI group?
2. To what extent is the association between TBI and apathy explained by co-occurring mental health symptoms?
3. Is early apathy associated with poorer functional outcomes at 12 months post-injury, and does this association persist after adjusting for mental health symptoms?

Methods

Overview of the TRACK-TBI Dataset

This study utilised secondary data from the TRACK-TBI cohort, a multi-centre, prospective observational study conducted across 18 Level 1 trauma centres in the United States. The study recruited approximately 3,000 individuals with a TBI and a comparison group of around 350 individuals with orthopaedic injuries (OI). After applying inclusion/exclusion criteria and accounting for available data across all relevant timepoints, the final sample for this study comprised 2376 TBI participants and 281 orthopaedic controls. Participants were assessed within 24 hours of injury, with follow-up evaluations conducted at two weeks, three months, six months, and 12 months post-injury. All outcome measures were administered and scored by trained examiners certified on the TRACK-TBI outcome assessment battery.

Inclusion and Exclusion Criteria

Participants were included in the TBI group if they had sustained a head trauma resulting in altered mental status, such as unconsciousness, peritraumatic amnesia, or other signs of altered consciousness. Additionally, a head CT scan confirming the injury was required, and participants had to be enrolled within 24 hours of the injury.

For the OI group, participants were required to have sustained orthopaedic injuries without any evidence of head trauma, amnesia, or altered consciousness.

Exclusion criteria for both groups included:

- Pregnancy
- Being in police custody
- Non-survivable trauma
- Inability to speak English or Spanish

- A history of debilitating neurological or psychiatric disorders

Ethical Considerations

All participants or their legally authorised representatives provided written informed consent. Demographic, injury, and outcome variables were collected in accordance with the TBI Common Data Elements (Hicks et al., 2013; Maas et al., 2010; Wilde et al., 2010). The use of TRACK-TBI data for this study was approved by the UCL Research Ethics Committee (Ref: CEHP/2023/593). Data were securely stored in UCL's Data Safe Haven, and researchers handling the data completed NHS Digital's Data Security Awareness course to ensure compliance with data protection protocols.

Measures

Apathy Score Development

Because TRACK-TBI did not include a validated apathy instrument, we constructed a proxy scale by aggregating conceptually relevant items from available measures. Item selection was guided by definitions emphasising reduced motivation, diminished interest, and impaired initiation/energisation of goal-directed behaviour (Levy & Dubois, 2006). The composite showed good internal consistency at each time point (Cronbach's $\alpha = .82–.84$).

We reduced contamination by excluding items indexing low mood, fatigue, and social rejection. Conceptually, the selected items align with domains covered by validated apathy instruments (Apathy Evaluation Scale [AES]: Marin, 1991; Neuropsychiatric Inventory apathy domain [NPI]: Cummings et al., 1994). Appendix G provides item-by-item mapping to apathy definitions and to AES/NPI content, and flags where anhedonia overlap is most likely.

The final apathy score included five items, each rated on a Likert scale ranging from 0–3 or 0–4, yielding a total possible score of 19. Higher scores indicated greater apathy. The items included were:

1. "Little interest or pleasure in doing things" (0–3 scale) from the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001)**.**
2. "Feeling no interest in things" (0–4 scale) from the Brief Symptom Inventory-18 (BSI-18**;** Derogatis, 1982)**.**
3. "Problems initiating activities without being prompted" (0–4 scale) from the Mayo-Portland Adaptability Inventory-4 (MPAI-4; Malec et al., 2003).
4. "Loss of interest in activities that were previously enjoyable" (0–4 scale) from the Post-Traumatic Stress Disorder Checklist (PCL-5; Blevins et al., 2015).
5. "Feeling emotionally numb or being unable to have loving feelings for those close to you" (0–4 scale) from the PCL-5 (Blevins et al., 2015).

Injury Characteristics

- The Glasgow Coma Scale (GCS; Teasdale & Jennett, 1974), a validated measure of consciousness post-injury, was used to classify TBI severity: mild (13–15), moderate (9–12), and severe (3–8).
- Loss of Consciousness (LOC) and Post-Traumatic Amnesia (PTA) duration were also used as clinical markers of injury severity. These indicators are widely employed in TBI research and practice to differentiate between mild, moderate, and severe TBI, with longer durations associated with greater injury severity (Russell & Smith, 1961; Teasdale & Jennett, 1976). These were collected via self-report, witness reports, or clinical interviews.

Mental Health Outcomes

Mental health measures were primarily completed via self-report, with informant reports used only when participants were unable to complete assessments themselves, in line with TRACK-TBI protocols.

- Brief Symptom Inventory-18 (BSI-18**;** Derogatis, 1982)The BSI-18 is a short, validated self-report screening tool designed to assess psychological distress across three domains: depression, anxiety, and somatisation. Participants rate symptom severity over the past seven days on a 5-point Likert scale.
- Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001)**:** The PHQ-9 is a validated 9-item measure of depressive symptoms, assessing frequency over the past two weeks. It is widely used in medical care settings. Scores range from 0 to 27, with higher scores indicating more severe symptoms.

Functioning Outcome

- The Glasgow Outcome Scale-Extended (GOS-E; Wilson et al., 1998) was used to assess functional recovery and level of disability. This is a widely used and validated tool for TBI populations. It captures return to work, independence across settings, relationship quality, and participation in social and leisure activities relative to pre-injury levels. This measure was completed by either the participant or an informant. For the purposes of this study, we used binary outcomes which were derived by dichotomising subdomain items (e.g., return to work at pre-injury capacity vs. not).

Covariates

Covariates were selected a priori with the aim of either a) accounting for potential confounders (research questions 1-3), or b) understanding to what extent apathy is explained by cooccurring psychopathology (research questions 2-3).

Potential confounders

All models were adjusted for age, sex, ethnicity, household income, reported history of TBI prior to the index injury, and pre-injury depression. Demographic data were sourced from medical records and self-report; clinical variables were self-reported and coded as binary (yes/no).

These covariates were selected due to their known associations with both TBI risk and neuropsychiatric outcomes. For instance, young males are more likely to sustain a TBI, while women and older adults tend to show poorer recovery (Frost et al., 2012; Maas et al., 2022; Polinder et al., 2018). Ethnicity and socioeconomic status are linked to disparities in injury risk, healthcare access, and long-term functioning (Bruns Jr. & Hauser, 2003; Gary et al., 2009; Kraus et al., 1986; Maas et al., 2022; Venturini et al., 2024).

Prior TBI was included due to its association with heightened risk of subsequent injuries and cumulative cognitive and psychiatric burden (Fehily & Fitzgerald, 2017; Gronwall et al., 1997). A reported pre-injury diagnosis of depression was included given its association with both the risk of sustaining a TBI and poorer post-injury neuropsychiatric outcomes (Ahmed et al., 2017; Gould et al., 2011; Vassallo et al., 2007).

Additional Covariates

For Research Questions 2 and 3, we adjusted for co-occurring psychopathology using PHQ-9 and BSI-18 scores that were re-scored to exclude items conceptually overlapping with

apathy (the items used in our apathy proxy scale). This was intended to reduce construct contamination and better isolate the association between TBI and the apathy proxy (van Reekum et al., 2005; Worthington & Wood, 2018).

Data Analysis

Power Sensitivity Analysis

A sensitivity analysis using G*Power indicated that, for our main research questions, the study is powered to detect a minimum odds ratio of 1.17 in logistic regression analyses, a small effect size. For linear regression models, the minimum detectable effect size was $f^2 = 0.03$. These results suggest the study is adequately powered to detect even small effects.

Missing data

All analyses were conducted using R version 4.4.1. Patterns of missingness were explored prior to analysis, and a visual summary of missing data for key variables is provided in appendix H. Missing data were handled using regression-based imputation with the missForest package, under the assumption that data were missing at random. This method allows for simultaneous imputation of categorical and numerical variables without relying on distributional assumptions (Kokla et al., 2019; Shah et al., 2014). To enhance accuracy, the imputation model included related variables such as demographics, apathy scores across timepoints, and other mental health measures.

Variables with a high proportion of missingness (>40%) , including some injury severity indicators such as post-traumatic amnesia (PTA) and loss of consciousness (LOC) duration, were excluded from imputation and handled using complete-case analysis. Key identifiers, including participant ID and injury type, were also not imputed.

At 2 weeks post-injury, there were several psychological outcomes which had moderate levels of missing data (e.g., PHQ-9, BSI-18 and apathy scores at 2 weeks, each with

~37% missing). These data were imputed due to their central relevance to the research questions, with the aim to maximise statistical power while reducing bias. To assess the robustness of findings, primary analyses were then repeated using non-imputed data as a sensitivity check. Results were compared to evaluate whether the imputation procedure meaningfully influenced observed associations.

Research Question 1: How does apathy differ between individuals with TBI and orthopaedic injuries over the first year post-injury, and is it associated with injury severity within the TBI group?

To assess whether apathy was specific to TBI and how it evolved over time, we used a multi-level linear regression model using the lme4 package in R, with a random intercept for participant to account for repeated measures across time. Injury type (TBI vs. orthopaedic injury) was entered as a between-subjects factor, and timepoint (2 weeks, 3 months, 6 months, 12 months) as a within-subjects factor. The outcome was the continuous total apathy score. Main effects of injury type and time, as well as their interaction, were tested to assess group differences and trajectories over time.

Follow-up linear regressions were conducted within the TBI group to assess whether injury severity was associated with apathy at 12 months. Predictor variables included GCS score, LOC duration, and PTA duration. Severity variables were first entered as continuous predictors: GCS was reverse-coded (so that higher scores indicated greater severity), and LOC/PTA were converted from ordinal to numeric scales. Additional models treated these predictor variables categorically: GCS (mild, moderate, severe) and LOC/PTA (seven levels: none, <1 minute, 2–29 minutes, 30–59 minutes, 1–24 hours, 1–7 days, >7 days); with ‘mild’ and ‘none’ as reference categories used in the analysis.

Research Question 2: To what extent is the association between TBI and apathy explained by co-occurring mental health symptoms?

To examine whether TBI was associated with apathy independently of broader mood symptoms, the RQ1 multi-level model was extended to include time-varying PHQ-9 and BSI-18 scores (with apathy-related items removed) at each timepoint. The model retained a random intercept for participant and treated timepoint as a categorical variable.

Research Question 3: Is early apathy associated with poorer functional outcomes at 12 months post-injury, and does this association persist after adjusting for mental health symptoms?

To assess whether early apathy was associated with overall functional recovery, linear regression models were used with total GOS-E score at 12 months as the outcome and 2-week apathy scores (continuous) as the predictor. Models were run unadjusted, then adjusted for confounders, and finally for co-occurring depressive and anxiety symptoms (PHQ-9 and BSI-18 scores, excluding apathy items).

To examine domain-specific outcomes, separate binary logistic regressions were conducted for each GOS-E subdomain (e.g., return to work, social engagement), using 2-week apathy as the predictor. Outcomes were coded as binary indicators of recovery (e.g., returned to work: yes/no), with the same adjustment as above.

Results

Participant Characteristics

A total of 2,838 participants were included in this study, with 2,539 in the TBI group and 299 in the orthopaedic injury group. 181 participants then died or dropped out before the

2-week follow-up. Therefore, the final sample comprised of 2657 participants (2376 TBI; 281 OI). The demographic characteristics of these participants are summarised in Table 1 and injury details are summarised in Table 2.

Category	*Traumatic Brain Injury N (%) N = 2376*	*Orthopaedic Injury N(%) N = 281*
Age (m, sd)	40.6 (17.1)	39.7 (15)
Sex		
Female	738 (31%)	93 (33%)
Male	1638 (69%)	188 (67%)
Ethnicity		
White	1820 (79%)	216 (79%)
Black	397 (17%)	44 (16%)
Asian	82 (3%)	8 (3%)
Other	15(1%)	4 (1%)
Unknown	62	9
Family Income		
Less than 25k	752 (45%)	74 (34%)
25k-50k	407 (25%)	63 (29%)
50k – 100k	325 (20%)	44 (20%)
More than 100k	169 (10%)	39 (18%)
Unknown	723	61
Employment status		
Paid work	1633 (73%)	218 (83%)
Student	116 (5.2%)	8 (3.0%)
Retired	206 (9.2%)	15 (5.7%)
Unemployed	219 (9.8%)	20 (7.6%)
Other	64 (2.9%)	3 (1.1%)
Unknown	138	17
History of mental health diagnoses		
No diagnosis	1831 (77%)	215 (77%)
One or more	545 (23%)	66 (23%)
Depression diagnosis	339(14%)	44 (16%)
Previous TBI		
Previous TBI reported	663 (28%)	62 (22%)

Table 1. *Demographic Characteristics of Participants*

Category	*N (%)*
Cause of injury	
Road Traffic Accident	396 (51%)
Accidental Fall	302 (39%)
Violence/Assault	68 (8.7%)
Other	14 (1.8%)
Admission type	
ED Discharge	502 (21%)
Hospital Admit (No ICU)	836 (35%)
Hospital Admit (With ICU)	1038 (44%)
TBI severity (based on GCS score)	
Mild (score 13-15)	1513 (64%)
Moderate (score 9-12)	505 (21%)
Severe (score 3-8)	358 (15%)

Table 2. *Injury Details*

Research Question 1: How does apathy differ between individuals with TBI and orthopaedic injuries over the first year post-injury, and is it associated with injury severity within the TBI group?

The unadjusted multi-level model demonstrated that participants with TBI showed significantly higher apathy scores than those with orthopaedic injury. This difference remained after adjusting for confounders, although the effect size was slightly reduced (Adjusted $\beta = 0.88$, 95% CI [0.45, 1.30]). Apathy scores peaked at 3 months post-injury ($\beta = 0.58$, 95% CI [0.23, 0.92] vs. 2-week baseline) and remained elevated, though the injury type × time interactions were non-significant. See Table 3 and Figure 1 for model estimates and predicted trajectories.

Predictor	*Unadjusted β [95% CI]*	*Adjusted β [95% CI]*
Injury Type (TBI)	1.00 [0.55 – 1.44]	0.88 [0.45 – 1.30]
Timepoint	Unadjusted EMM [95% CI]	Adjusted EMM [95% CI]
2 weeks	2.33 [2.10 – 2.55]	2.96 [2.53 – 3.40]
3 months	3.02 [2.80 – 3.24]	3.66 [3.23 – 4.10]
6 months	2.31 [2.08 – 2.53]	2.95 [2.51 – 3.38]
12 months	2.30 [2.08 – 2.52]	2.94 [2.51 – 3.38]

Table 3. *Multi-level linear regression model of injury type (TBI vs. Orthopaedic Injury) and time on apathy scores. EMM = Estimated Marginal Means. Adjusted models include covariates: age, sex, ethnicity, household income, prior TBI, and pre-injury depression diagnosis.*

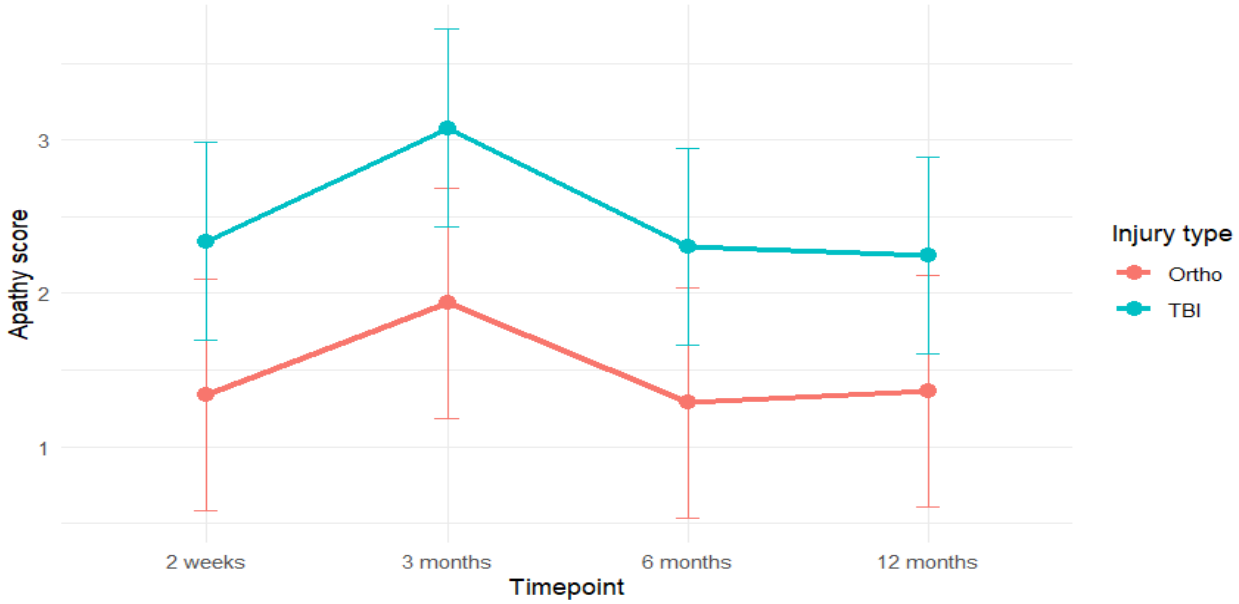

Figure 1. *Estimated Apathy Trajectories Over Time by Injury Type (TBI vs. Orthopaedic Injury), With 95% Confidence Intervals.* Estimates are based on adjusted linear multi-level models adjusted for age, sex, ethnicity, household income, prior TBI, and pre-injury depression diagnosis.

Sensitivity analysis

To test the robustness of findings given ~37% missing data at 2 weeks, analyses were repeated using only participants who had complete data at 2 weeks post-injury (n = 1255).

The injury type–apathy association remained significant, though attenuated (β = 0.24, 95% CI [0.03, 0.45]). Results were consistent: apathy was higher in the TBI group across timepoints, with no significant injury type × time interactions.

TBI severity and apathy score at 12 months post-TBI

Injury severity as indicated by continuous GCS, LOC or PTA duration was not significantly associated with apathy at 12 months post-TBI. (see Table 4).

Injury characteristic	*Unadjusted β [95% CI]*	*Adjusted β [95% CI]*
GCS (reversed)	0.02 [-0.03 – 0.06]	0.03 [-0.01 – 0.07]
LOC duration score	0.07 [-0.06 – 0.20]	0.09 [-0.04 – 0.22]
PTA duration score	0.04 [-0.07 – 0.16]	0.09 [-0.01 – 0.19]

Table 4. *Linear Regression Models of Injury Characteristics and Apathy Score at 12 Months Post-TBI. Adjusted models include covariates: age, sex, ethnicity, household income, prior TBI, and pre-injury depression diagnosis*

When TBI severity was modelled categorically, apathy scores at 12 months did not significantly differ between participants with severe and mild TBI (adjusted β = 0.36, 95% CI [–0.06, 0.78]), nor between those with moderate and mild TBI (adjusted β = 0.06, 95% CI [–0.56, 0.68]). Model-estimated apathy scores by TBI severity level are presented in Figure 2.

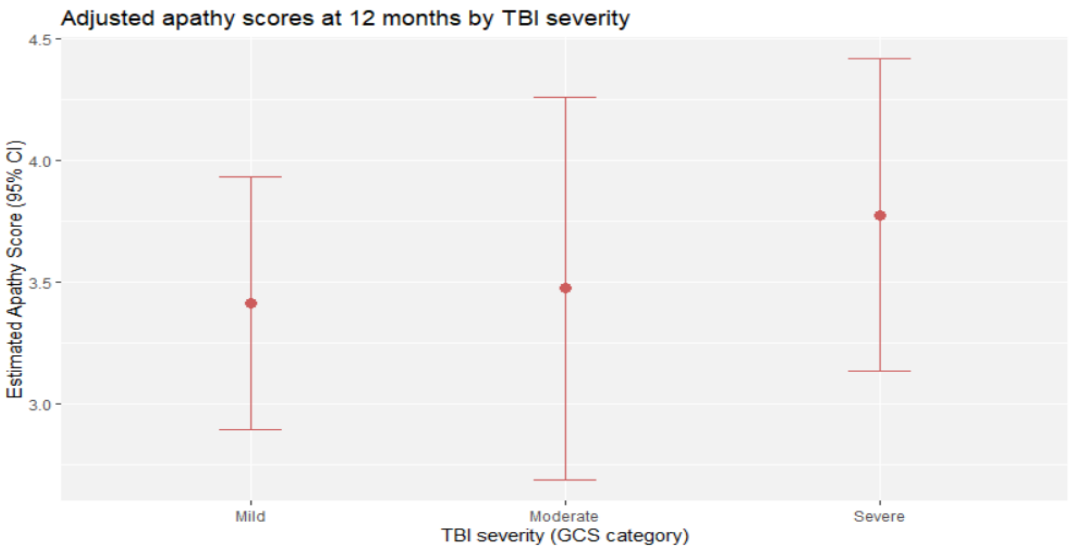

Figure 2. *Estimated Apathy Scores at 12 Months by TBI Severity (Glasgow Coma Scale Categories) Linear regression models were adjusted for age, sex, ethnicity, household income, prior TBI, and pre-injury depression diagnosis. Error bars represent 95% confidence intervals.*

As shown in Figure 3, none of the LOC duration categories were significantly associated with apathy scores at 12 months when compared to the reference group (no LOC). In contrast, participants with PTA lasting more than 7 days had significantly higher apathy scores than those with no PTA (β = 0.89, 95% CI [0.06, 1.70], p = .003).

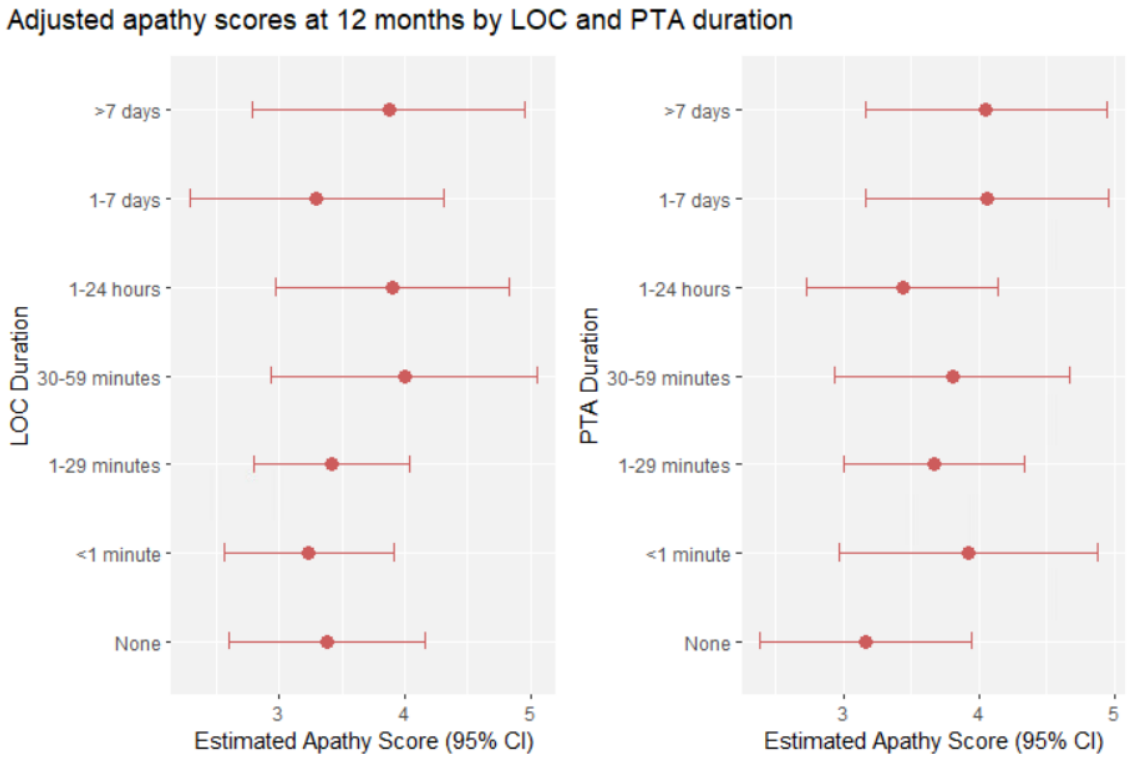

Figure 3. *Estimated Apathy Scores at 12 Months by Duration of Loss of Consciousness (LOC) and Post-Traumatic Amnesia (PTA). Estimates are derived from adjusted linear regression models. Models were adjusted for age, sex, ethnicity, household income, prior TBI, and pre-injury depression diagnosis. Error bars represent 95% confidence intervals.*

Research Question 2: To what extent is the association between TBI and apathy explained by co-occurring mental health symptoms?

The multilevel model was re-estimated with additional adjustment for PHQ-9 and BSI-18 scores at each timepoint (excluding apathy-related items). The main effect of injury type remained statistically significant but was reduced (adjusted β = 0.31, 95% CI [0.08, 0.54]).

Adjustment for mental health symptoms also altered the temporal pattern of apathy. At 3 months, apathy scores were significantly lower than at 2 weeks (β = –0.36, 95% CI [–0.62, –0.10]), reversing the early peak observed in the unadjusted model. Although apathy

remained higher overall in the TBI group, group differences were only observed at two timepoints: 2 weeks and 6 months post-injury (see Figure 4).

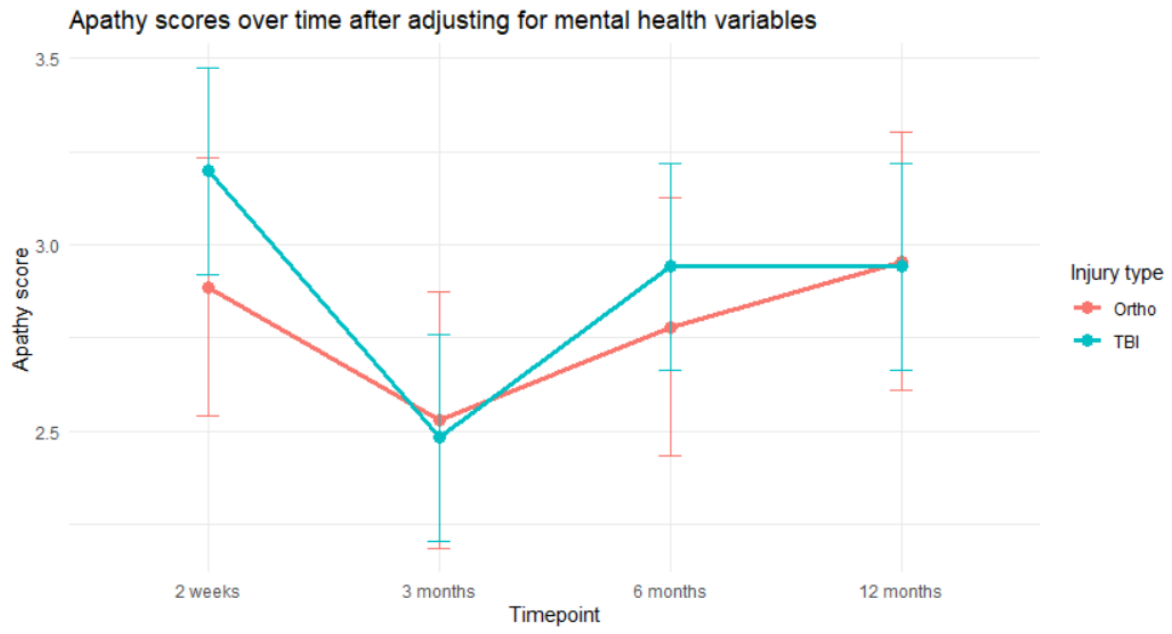

Figure 4. *Predicted Apathy Scores Over Time by Injury Type (TBI vs. Orthopaedic), Adjusted for Demographics, Mental Health History, and Concurrent Symptoms of Depression and Anxiety. Estimates are adjusted for age, sex, ethnicity, household income, prior TBI, pre-injury depression diagnosis, and time-varying PHQ-9 and BSI-18 scores (with apathy items removed). Error bars represent 95% confidence intervals.*

Research Question 3: Is early apathy associated with poorer functional outcomes at 12 months post-injury, and does this association persist after adjusting for mental health symptoms?

In the unadjusted linear regression model, higher apathy at 2 weeks post-TBI was significantly associated with poorer functional outcomes, as indicated by lower GOS-E scores at 12 months ($\beta = -0.15$, 95% CI [–0.17, –0.14]), though with a relatively small effect size.

This association remained unchanged after adjustment for confounding variables (β = –0.15, 95% CI [–0.17, –0.14]).

Following further adjustment for co-occurring symptoms of depression and anxiety (PHQ-9 and BSI-18 scores with apathy items removed), the effect size was slightly reduced but remained statistically significant (β = –0.12, 95% CI [–0.14, –0.09]).

Association between early apathy and sub-domains of functional recovery

Logistic regression analyses indicated that higher apathy at 2 weeks post-TBI was most strongly associated with increased odds of family and friendship strain at 12 months (adjusted OR = 1.41, 95% CI [1.36, 1.46]). The next strongest association was with reduced odds of returning to normal social and leisure activities (adjusted OR = 0.79, 95% CI [0.77, 0.81]). After further adjustment for co-occurring mental health symptoms (PHQ-9 and BSI-18 scores with apathy items removed), these domains remained the most strongly associated, though effect sizes were slightly reduced.

GOS-E Domain	*Unadjusted OR [95% CI]*	*Adjusted OR [95% CI]*	*Fully adjusted OR [95% CI]*
Family and friendship strain	1.42 [1.37, 1.47]	1.41 [1.36, 1.46]	1.27 [1.19, 1.33]
Assistance needed	1.11 [1.07, 1.16]	1.13 [1.08, 1.18]	1.21 [1.11, 1.33]
Social and leisure activities normal	0.80 [0.78, 0.82]	0.79 [0.77, 0.81]	0.79 [0.76, 0.84]
Work capacity normal	0.81 [0.79, 0.83]	0.80 [0.78, 0.82]	0.85 [0.80, 0.89]
Shop without assistance	0.89 [0.86, 0.93]	0.88 [0.84, 0.92]	0.81 [0.75, 0.89]
Travel without assistance	0.90 [0.86, 0.93]	0.88 [0.85, 0.92]	0.81 [0.74, 0.89]

Table 5. *Logistic Regression Analyses Examining the Association Between Apathy 2 Weeks Post-TBI and GOS-E domains 12 Months Post-TBI. Adjusted models include demographic and pre-injury confounders. Fully adjusted models additionally include PHQ-9 and BSI-18 scores with apathy items removed.*

Discussion

Using a proxy apathy index, we found that apathy scores were higher in the TBI group than orthopaedic controls at all timepoints across 12 months. Injury severity markers were not associated with apathy at 12 months. After adjusting for co-occurring mental health symptoms, the TBI–apathy association was attenuated. Apathy remained higher overall in the TBI group, but group differences were no longer significant at 3 and 12 months. The apathy proxy score at 2 weeks post-injury was associated with poorer functioning at 12 months, even after adjusting for mental health symptoms, with the strongest association seen in family and friendship strain.

The results from research question 1 demonstrated that across the first post-injury year, apathy-like scores from the proxy index were consistently higher in the TBI group than in orthopaedic controls, with a transient peak around 3 months in both groups. This pattern aligns with prior reports of elevated and persistent apathy after brain injury relative to non–brain-injured samples (Arnould et al., 2018; Ciurli et al., 2011; Lengenfelder et al., 2015; Quang et al., 2022).

Apathy symptoms were evident as early as two weeks post-TBI, with scores already significantly higher than in orthopaedic controls. This aligns with prior reports of apathy emerging within weeks post-TBI (Nygren DeBoussard et al., 2017), and echoes findings in stroke populations, where apathy has emerged within four days (Caeiro et al., 2013). Because several proxy items capture loss of interest/pleasure, early post-injury distress may inflate scores via anhedonia, complicating interpretation of timing. Although a peak was observed at 3 months, it disappeared after adjusting for mood symptoms, emphasising the need to distinguish transient motivational disruption from persistent apathy. This aligns with proposed diagnostic criteria, which require symptoms to persist for at least four weeks (Mulin et al., 2011; Starkstein et al., 2001), highlighting the value of repeated assessment over time.

When depression and anxiety were included as covariates, the group difference in apathy was reduced. Although apathy remained higher overall in the TBI group, differences at 3 and 12 months were no longer significant. The previously observed 3-month peak also disappeared, suggesting that early increases in apathy may partly reflect shared variance with emotional distress. Noting the construct overlap, part of this signal may reflect anhedonia rather than apathy, and residual confounding from mood symptoms likely persists despite covariate adjustment. This comorbidity and conceptual overlap make disentangling apathy from depression an ongoing clinical and research challenge (Arnould et al., 2013; Marin, 1991; Starkstein et al., 2006). While previous cross-sectional studies have shown that apathy remains elevated in TBI after adjusting for depressive symptoms (Bivona et al., 2019; Ubukata et al., 2022), our longitudinal data suggest this relationship may fluctuate over time, with the strongest overlap evident at 3 months post-injury. This pattern is consistent with biopsychosocial accounts of apathy and suggests that subacute contextual pressures and transient neurophysiological changes may amplify symptom overlap.

The pronounced overlap between apathy and mood symptoms at three months may reflect psychosocial stressors common in early recovery, such as reduced independence, social isolation, and disrupted routines (Cristofori et al., 2019; Ponsford, 2013; van Reekum et al., 2016; Vincent et al., 2015). This period may also coincide with neuroplastic changes in brain networks involved in motivation and affect regulation (Cicerone et al., 2006; Sharp et al., 2014) which may temporarily disrupt goal-directed behaviour. Together, these factors could create a self-reinforcing loop in which reduced initiation limits exposure to rewarding activities, mood worsens, and motivation is further dampened. In some contexts, treating co-occurring depression alongside dopaminergic therapy has been reported to improve apathy, underscoring the interplay between affective and motivational systems (Skorvanek et al., 2015). This aligns with a biopsychosocial account of apathy development (Quang et al.,

2024). These patterns support repeated assessment to distinguish transient, context-driven motivational difficulties from more persistent apathy. Future work using time-varying approaches could clarify whether changes in apathy precede, follow, or co-evolve with mood symptoms across recovery phases.

After adjusting for mood symptoms, apathy appears partly independent, but interpretation remains constrained by the proxy index, complicating differential diagnosis and limiting temporal inference. The attenuation at three and twelve months may be driven either by real coupling of apathy and mood or by measurement factors inherent to the proxy and modelling. Evidence from other conditions points to partially distinct trajectories (e.g., apathy increasing while depression remains stable in dementia: Connors et al., 2023; greater overlap post-stroke: Withall et al., 2011). Within that context, our data suggest that apathy emerges early after TBI and fluctuates alongside emotional distress. Future work using validated apathy instruments, and time-varying models will be needed to clarify temporal patterns and more accurately separate diagnoses. Interventionist studies that selectively target anticipatory/energisation processes versus hedonic experience could further disentangle these pathways by testing whether effort-based initiation and consummatory pleasure show dissociable treatment responses.

The relationship between TBI severity and neuropsychiatric outcomes such as apathy is complex (van Reekum et al., 2000). In line with previous studies reporting inconsistent associations between apathy and injury severity markers such as GCS, LOC, or PTA (Andersson & Bergedalen, 2002; Glenn et al., 2002; Worthington & Wood, 2018; Zomeren & Burg, 1985), our findings showed no significant relationship between continuous or categorical measures of GCS, LOC, or PTA and apathy at 12 months post-injury. The only exception was that individuals with PTA longer than 7 days showed higher apathy scores

than those with no PTA. These findings suggest that traditional injury severity indicators may have limited value in predicting long-term apathy.

The absence of a consistent association between injury severity and apathy features suggests that apathy may not follow a clear dose–response relationship, whereby greater injury leads to greater neuropsychiatric disruption. This is particularly notable given that injury severity is often associated with the extent of cognitive impairment post-TBI (Draper & Ponsford, 2008), and cognitive dysfunction has been linked to apathy across neurological populations (Andersson & Bergedalen, 2002; Drijgers et al., 2011; Lohner et al., 2017). These findings support the theory that apathy may arise not solely from the overall severity of injury, but from more specific disruptions to frontostriatal circuits and psychosocial mechanisms not captured by traditional TBI severity indices (Kumfor et al., 2018; van Reekum et al., 2005).

In addressing our third research question, we found that the apathy score at two weeks post-TBI was significantly associated with poorer global functioning at 12 months, even after adjustment for mood symptoms. This pattern indicates a unique association with long-term outcomes. Residual confounding is plausible, so part of the observed effect may reflect hedonic loss rather than apathy. Nonetheless, the association between early apathy and later functioning aligns with prior work highlighting the functional impact of apathy. Green et al. (2022) proposed that while both apathy and depression impair daily functioning, the impact of depression may be mediated largely through apathy. Similarly, Ubukata et al. (2022) found that only apathy-related symptoms on the Beck Depression Inventory-II predicted reduced activity, underscoring apathy's distinct role in functional impairment.

The strongest associations between early apathy and long-term impairment were observed in interpersonal relationships and social leisure participation. This is consistent with prior research linking apathy to caregiver distress and strained interpersonal dynamics (Marsh

et al., 1998). The relationship between apathy and social outcomes post-TBI is likely multi-faceted and complex. Bivona et al. (2019) found that individuals with severe TBI and reduced insight showed higher apathy and greater difficulty describing emotions. Caregivers often report behaviours like emotional flatness and lack of initiative as especially distressing (Kelly et al., 2008), and personality changes post-TBI have been associated with increased apathy (Diaz et al., 2012). More recently, deficits in social cognition – including empathy, theory of mind, and alexithymia – have been shown to correlate with apathy in moderate-to-severe TBI (Filipčíková et al., 2024). Together, these findings suggest that apathy may undermine social engagement both directly—through reduced emotional responsiveness and impaired processing of social cues—and indirectly, by straining interpersonal relationships and increasing caregiver distress. These dynamics highlight the importance of addressing apathy within rehabilitation to support social reintegration and enhance long-term quality of life.

Strengths, Limitations and Future Directions

A key strength of this study was its prospective, multi-centre design, which enabled examination of apathy trajectories and their association with long-term functional outcomes in a large, diverse TBI sample spanning all severities. This design reduced selection bias and enhanced generalisability. Including a non-TBI control group further strengthened the interpretability of group differences by allowing comparison against typical recovery trajectories. Additionally, the study focused on clinically meaningful outcomes and showed that apathy contributes uniquely beyond co-occurring mental health symptoms, offering important implications for rehabilitation planning.

However, several limitations must also be acknowledged. Our apathy score was a proxy measure consisting of items from measures not designed to assess apathy. It was not

validated against established apathy scales, limiting conclusions about its psychometric robustness. Convergent validity could not be assessed, and we did not perform formal discriminant-validity testing against depression/anxiety measures. Adjusting models with modified PHQ-9/BSI-18 scores may reduce confounding but does not establish discriminant validity; some overlap with mood likely remains, with potential attenuation and residual confounding. Findings should therefore be viewed as preliminary and hypothesis-generating. Because some items capture loss of interest/pleasure, content overlap with anhedonia and mood symptoms more broadly is possible. Accordingly, estimates should be interpreted as an 'apathy-like' signal (see Appendix G for item-to-AES/NPI content mapping and points of anhedonia overlap). Item selection was based on content validity which, while pragmatic for secondary analysis in a large cohort, introduces subjectivity. Future research should formally assess convergent and discriminant validity against standardised apathy measures, or ideally use a validated instrument such as the AES to address similar questions more robustly.

Executive dysfunction, a correlate of apathy (Andersson & Bergedalen, 2002), was not accounted for, which may have confounded some findings. The reliance on self-report measures may underestimate apathy in individuals with reduced insight (Marin, 1991); incorporating caregiver or clinician ratings in future studies would strengthen assessment. Additionally, we were not able to examine lesion location or brain regions affected, which may be relevant given evidence linking apathy to damage in areas such as the prefrontal cortex.

While this study benefitted from data collected across 18 U.S.-based centres, all sites were located within a single country. Differences in healthcare systems, rehabilitation models, and sociocultural factors may limit the generalisability of findings internationally. Future cross-national studies are needed to determine whether similar patterns emerge across different care contexts.

Additionally, apathy and functional outcomes may continue to evolve beyond this 12-month window. Longer-term studies are needed to assess the persistence of apathy and whether distinct apathy subtypes or trajectories (e.g., transient vs. persistent) emerge over time and how these relate to recovery outcomes.

Despite these limitations, the use of a large, longitudinal, multi-site dataset with a non-brain-injured comparison group allowed for a robust examination of apathy features across timepoints and injury severities, contributing important insights into this often-overlooked neuropsychiatric outcome.

Finally, there is a clear need to develop and evaluate interventions for apathy after TBI. Despite its prevalence across neurological disorders, no evidence-based treatments are established. To date, only one randomised controlled trial has targeted apathy directly (Lane-Brown & Tate, 2009b), and its design limited conclusions about effectiveness. Small-scale studies suggest potential benefits of approaches such as motivation-based behaviour therapy (Lane-Brown & Tate, 2010), while evidence from dementia populations indicates that multisensory stimulation, music therapy, and acetylcholinesterase inhibitors may help to reduce apathy (Berman et al., 2012; Holmes et al., 2006; Verkaik et al., 2005). The scarcity of trials likely reflects diagnostic overlap with related constructs, under-recognition of apathy in TBI services, and the heterogeneity of TBI presentations. Future research should prioritise theoretically grounded, clinically feasible interventions developed through interdisciplinary collaboration. Interventionist designs can also serve as mechanistic tests to differentiate apathy from depression and anhedonia by selectively targeting anticipatory/energisation processes and measuring effects on effort-based initiation and maintenance separately from hedonic experience during reward. Divergent treatment effects would support construct separability and help improve personalised rehabilitation targets.

Conclusions

Apathy is a clinically important but frequently overlooked consequence of traumatic brain injury. This study shows that it can emerge as early as two weeks post-injury, remain elevated across the first year, and is only partly explained by co-occurring mental health symptoms. While mood symptoms influenced the pattern of apathy over time, particularly at three months, apathy remained more pronounced in individuals with TBI overall.

Early apathy was also independently associated with poorer 12-month functioning, particularly in interpersonal domains, highlighting its prognostic value for recovery and quality of life. While we operationalised apathy using a proxy index assembled from non-apathy scales, so some overlap with anhedonia/depression may persist despite covariate adjustment, the overall pattern aligns with prior work and supports treating apathy as a distinct neuropsychiatric outcome that warrants routine identification and targeted management in rehabilitation.

Increased awareness and routine screening for apathy in the early stages of recovery could help identify individuals at greater risk of poorer outcomes. In the absence of well-established treatments, screening remains valuable for ensuring it is not overlooked in early rehabilitation. Incorporating apathy into case formulations may be particularly important, as it is likely to influence how individuals and their caregivers engage with rehabilitation. Ultimately, however, screening alone may have limited clinical benefit; further research is essential to develop evidence-based interventions that can meaningfully address apathy after TBI.

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Part 3: Critical Appraisal

Introduction

This critical appraisal presents a reflective and evaluative account of a research project examining apathy following traumatic brain injury (TBI). The project comprised two components: a systematic review and meta-analysis estimating the prevalence of apathy post-TBI, and an empirical study using longitudinal data from the TRACK-TBI cohort. The empirical study compared apathy trajectories between TBI and orthopaedic injury groups, examined the influence of co-occurring mental health symptoms, and explored associations between early apathy and long-term functional outcomes.

This appraisal begins by outlining how my training as a clinical psychologist and adoption of a biopsychosocial framework shaped the development of the research questions and theoretical orientation. I then examine key conceptual challenges in defining and measuring apathy, and how these informed decisions throughout the research process. This is followed by a critical evaluation of methodological choices, strengths, and limitations. I also reflect on issues of generalisability and the implementation of open science practices. The chapter concludes by considering the clinical relevance and broader contribution of the findings, and by identifying priorities for future research and intervention. Throughout, I reflect on the role of the clinician–researcher in bridging the gap between scientific evidence and real-world clinical practice.

Clinical Orientation and Framework

My training in clinical psychology, underpinned by a biopsychosocial framework, shaped both the conceptual and methodological design of this research. I was particularly motivated to pursue questions that hold relevance for clinical practice and capture the lived experiences of individuals recovering from TBI.

Apathy was selected as the central outcome of interest due to its significant impact on long-term recovery and the limited attention it has received in both clinical and research settings for intervention. In my clinical work, I observed how 'hidden' symptoms, such as apathy, fatigue, and memory difficulties, could be profoundly disruptive to daily life. These difficulties affected relationships, employment, and independence, yet were often overlooked once more visible or acute symptoms had resolved. This observation is echoed in the literature, which notes that enduring cognitive and emotional symptoms are among the most disabling yet under-recognised effects of TBI (Dams-O'Connor et al., 2013; Thurman et al., 1999; Zahniser et al., 2019). The term 'silent epidemic' has been used to characterise TBI's long-term consequences (Vaishnavi et al., 2009), reinforcing the need for greater focus on subtle, functional difficulties in recovery research.

Although many studies on apathy have focussed on neural correlates and anatomical disruption (Knutson et al., 2014; Kos et al., 2016; Moretti & Signori, 2016), psychological and social perspectives are increasingly recognised as essential to a more complete understanding. Recent literature calls for an integrated biopsychosocial approach to apathy that reflects its multidimensional nature (Quang et al., 2024; Worthington & Wood, 2018). This theoretical stance influenced my decision to focus not only on injury severity and apathy, but also on functional outcomes that reflect how people engage with their lives post-injury.

As a clinician-researcher, I was aware that my professional orientation shaped the research throughout. My clinical experience highlighted the divergence that can occur between commonly measured research outcomes and the everyday challenges faced by individuals recovering from TBI. My goal was to design a project that bridged this gap by focussing on an outcome that is both clinically meaningful but not yet fully understood. My

clinical orientation ultimately helped to ensure the study remained relevant to practice and centred on outcomes that matter in everyday recovery.

Challenges in Defining and Measuring Apathy

At the outset of this project, my understanding of apathy was relatively narrow, primarily shaped by its overlap with depression and characterised as a passive lack of motivation. However, through the process of completing this research, I came to appreciate apathy as a complex, multidimensional construct that is challenging to define and measure. A major barrier in both clinical and research contexts is the lack of a universally accepted definition. Apathy has been variably described as a symptom, a syndrome, or a disorder in its own right (Levy & Dubois, 2006; Robert et al., 2018), with each framing carrying different implications for diagnosis and intervention. This definitional inconsistency complicates diagnosis, the development of targeted interventions, and the comparability of findings across studies (Lanctôt et al., 2017).

Apathy is often described in negative terms, such as the absence of motivation, emotion, or initiative, rather than by its own distinct features. It is conceptualised both as a syndrome with specific neurobiological underpinnings and as a symptom secondary to other conditions (Marin, 1991; Worthington & Wood, 2018). This ambiguity makes it difficult to distinguish apathy from overlapping constructs such as depression or fatigue (Green et al., 2022; Levy et al., 1998; Marin et al., 1993), contributing to the wide variability in reported prevalence after TBI. Measurement tools also vary across populations. For example, the Lille Apathy Rating Scale in Parkinson's disease (Sockeel et al., 2006) and the Neuropsychiatric Inventory in dementia (Kaufer et al., 2000), limiting cross-study and cross-condition comparisons.

Over time, more nuanced models of apathy have emerged. Marin (1991) proposed that apathy involves reductions in goal-directed behaviour, cognition, and emotion—later expanded by Levy and Dubois (2006) into subtypes with distinct neural pathways. Mulin et al. (2011) added reduced emotional responsiveness as a core feature. More recent work has incorporated psychological and contextual factors, including self-efficacy (Arnould et al., 2018; Bivona et al., 2019) and impulsivity (Rochat et al., 2008), further reinforcing the value of a biopsychosocial approach (Arnould et al., 2013; Quang et al., 2024).

This evolving understanding directly informed my approach, particularly in developing a proxy apathy scale using secondary data. In the absence of a gold-standard measure, I adopted a pragmatic strategy guided by face validity and theoretical coherence. As Worthington and Wood (2018) argue, apathy remains poorly understood across neurochemical, psychological, and environmental domains. Moving forward, there is a clear need for a unified, multidimensional framework that can meaningfully distinguish apathy from related constructs and support valid assessment across different clinical populations. This conceptual ambiguity also had practical implications throughout both phases of this research. In the meta-analysis, inconsistent definitions and varying measurement tools complicated study selection. This required careful judgement to assess conceptual alignment and to evaluate whether included measures had been validated in TBI populations. Similarly, the construction of the proxy apathy scale involved navigating substantial overlap between motivational, affective, and emotional items. Although the selected items were theoretically grounded, there remained a risk of the items overlapping with other traits, particularly in a dataset that also included measures of depression and anxiety.

These challenges are not limited to research. In clinical settings, brief screeners and checklists are often used to guide assessment. Without a clear and consistent definition, apathy may be missed or misinterpreted particularly when symptoms are seen through the

lens of low mood or disinterest, rather than broader motivational dysfunction (Robert et al., 2018). These definitional and measurement issues shaped key design decisions in both studies and highlighted the need for greater conceptual clarity in future apathy research.

Methodological Reflections

Advantages of Secondary Data

This project benefitted from the use of secondary data from the TRACK-TBI study, a large, multi-site longitudinal cohort that employed Common Data Elements (CDEs) to ensure standardised data collection across sites. Access to this dataset allowed for the examination of apathy across multiple timepoints and facilitated statistical adjustment for a wide range of covariates, enhancing both internal validity and generalisability.

A central aim throughout the project was to ensure clinical relevance. Large-scale datasets like TRACK-TBI are particularly valuable in TBI research, where small, heterogeneous samples are common. The breadth of data enabled clinically meaningful subgroup analyses and the identification of early indicators of poorer long-term outcomes which are critical for informing prevention and service planning. This is particularly valuable, given that most clinical attention is focused on the acute phase of recovery, while access to longer-term support remains limited. Apathy, though under-recognised in clinical care, is associated with reduced rehabilitation engagement, poorer functional outcomes, and lower quality of life. The opportunity to explore this within a longitudinal framework was a major strength of the project.

Limitations of Secondary Data and the Need for a Proxy Measure

Secondary data analysis also presented notable trade-offs, particularly a lack of control over study design and variable inclusion. TRACK-TBI was not designed to assess

apathy, and no validated apathy measure was included. This reflects a broader gap in the field, despite its clinical relevance, apathy remains largely absent from standard post-TBI assessments (Starkstein & Leentjens, 2008; van Reekum et al., 2005).

To address this, I constructed a proxy apathy measure using theoretically relevant items from validated mental health tools. These items tapped core domains of apathy—diminished interest, reduced motivation, and impaired initiation— based on established theoretical models (Levy & Dubois, 2006; Marin, 1991). This approach enabled a pragmatic, theory-informed analysis, but it also introduced limitations. The items were not originally designed to assess apathy and may overlap with related constructs such as depression or fatigue, raising concerns about content and discriminant validity.

Measurement and Validity Considerations

Using an ad-hoc measure required careful conceptual grounding, but its psychometric properties were not formally tested. While face and preliminary construct validity were supported, a more rigorous validation process, such as comparison with an existing apathy scale in an external sample, would have enhanced confidence in the findings. Input from clinical experts or service users during development could also have improved the measure's relevance and content validity.

This process highlighted the broader challenge of measuring complex psychological constructs like apathy, especially when consensus definitions are lacking. It also highlighted the importance of triangulating multiple data sources, including behavioural observations, clinician ratings, and caregiver reports. In cases of more severe TBI, insight into apathy may be limited (Marin, 1991), making supplementary input beyond self-report particularly valuable.

In future research, I would advocate for the use of validated, multidimensional apathy measures that integrate subjective and informant input to better capture the nuanced presentation of apathy after TBI.

Ethical Considerations and Open Science

Working with secondary data raised important ethical considerations. Without direct participant interaction, I felt a responsibility to ensure that the analyses remained grounded in the lived experiences behind the data. My clinical background helped orient the research around outcomes that matter in everyday recovery, while a commitment to open science supported transparency and accessibility.

Ethical considerations extended beyond data protection to include the relevance, interpretation, and communication of findings in ways that could inform and benefit future care. Open science practices were central to this approach. To promote transparency, the analysis code was made publicly available, and a preprint of the systematic review was uploaded to ensure open access. These practices enable others to engage with, evaluate, and build upon the work.

Open science fosters equity in knowledge dissemination, enhances reproducibility, and encourages interdisciplinary collaboration (Nosek et al., 2015; Tennant et al., 2016). These benefits are particularly important in clinical research, where access barriers can slow the translation of evidence into practice. It also supports methodological scrutiny, a core component of scientific integrity (Munafò et al., 2017).

Importantly, open practices help make findings accessible not only to researchers but also to clinicians, service users, and policymakers, who are often excluded by paywalls or technical constraints. In this way, open science can help narrow the research–practice gap and support more timely, evidence-informed decision-making in real-world settings.

While open science practices promote transparency and accessibility for the research community, they are unlikely to reach or be directly useful to individuals with TBI and their caregivers. To address this gap, research dissemination also needs to include service-user–focused approaches. For example, findings could be shared through collaboration with brain injury charities and information centres (e.g., Headway) in the form of psychoeducational resources, lay summaries, or infographics that explain apathy and its impact on recovery in accessible language. Providing clear information about apathy as a neuropsychological consequence of brain injury could help validate the experiences of families, reduce stigma, and support more adaptive coping. Embedding findings into clinical training and MDT discussions would further ensure that research knowledge is translated into practice, making apathy more visible as a clinical target.

Generalisability

While there are important limitations to generalising these findings, the TRACK-TBI cohort remains one of the largest prospective TBI datasets available. It includes participants from multiple U.S. sites and encompasses a wide range of injury severities and clinical presentations, enhancing the external validity of findings within high-income healthcare settings.

However, the sample was drawn exclusively from the United States, with 79% of participants identifying as White, limiting the representativeness of the data in relation to global population diversity. Cultural, structural, and healthcare system differences are likely to influence how apathy is experienced, expressed, and interpreted. For instance, access to rehabilitation services, models of trauma care, and societal attitudes toward motivation and mental health vary across countries, which may shape the identification and reporting of

apathy symptoms. These factors warrant caution when applying findings beyond North America or similarly structured healthcare contexts.

More broadly, there is a persistent geographical imbalance in TBI research. Although over 80% of TBI cases occur in low- and middle-income countries (LMICs), most clinical and epidemiological studies are conducted in high-income Western countries (Dewan et al., 2018; Maas et al., 2017). This has led to a limited and potentially skewed understanding of global TBI outcomes. While RCTs in LMICs are increasing, they remain largely focused on acute care (Teasell et al., 2024), with far fewer studies exploring long-term or neuropsychiatric outcomes. Patients in LMICs are also more than twice as likely to die following severe TBI compared to those in high-income countries, reflecting significant disparities in trauma care and rehabilitation infrastructure (De Silva et al., 2009).

In this context, the current findings, though clinically relevant, should be interpreted within the confines of a high-income, predominantly White U.S. sample. Future research must prioritise more globally inclusive datasets to ensure that models of recovery and intervention strategies are applicable across diverse populations and healthcare systems.

Contributions and Clinical Relevance

This research makes several key contributions to the understanding of apathy following TBI. The study identified that apathy prevalence after TBI is over one third, it often emerges early and persists over time, even after adjusting for confounders. However, this pattern appears more complex when considering co-occurring mood symptoms. This highlights the importance of early identification and repeated assessments, alongside monitoring mood symptoms.

Clinically, the findings support the integration of apathy into routine multidisciplinary team (MDT) formulations, particularly in the early stages post-injury. Introducing apathy-

specific prompts into psychological and neuropsychological assessments may help ensure that this often-overlooked symptom is detected and addressed. Enhanced training for clinicians across services could improve recognition of apathy, clarify its distinction from depression or low mood, and reinforce its significance in shaping engagement with rehabilitation.

The results also have implications for caregiver support and psychoeducation. Apathy is associated with increased caregiver burden (Marsh et al., 1998) and is frequently described by family members as one of the most difficult symptoms to manage (Kelly et al., 2008). Framing apathy as a neuropsychological consequence of brain injury, rather than a sign of lack of effort, may help to reduce blame, increase understanding, and support more adaptive coping strategies. Psychoeducational materials and family-focused interventions could play an important role in validating caregiver experiences and promoting constructive responses to apathy-related behaviours. Finally, this research contributes to the growing recognition of apathy as a clinically meaningful outcome in neurorehabilitation.

Future Directions and Implications for Intervention

This project identified several priority areas for future research and clinical development. Although the study found small but consistent associations between early apathy and later functional outcomes, these findings are preliminary. Further research is needed to evaluate whether apathy can serve as a clinically useful early marker of recovery trajectories following TBI. Replication using validated, multidimensional apathy measures will be essential.

A foundational next step is reaching a consensus definition of apathy. This will require interdisciplinary collaboration to develop a conceptually robust and clinically meaningful framework that distinguishes apathy from related constructs such as depression or

fatigue (Worthington & Wood, 2018). At present, definitional ambiguity continues to limit both measurement and intervention development.

Most large-scale TBI datasets do not include dedicated apathy measures. Future cohort studies should incorporate psychometrically validated, theoretically grounded apathy assessments to enable nuanced examination of apathy's trajectory over time and its interplay with factors such as mood, executive functioning, and social support. Notably, many existing apathy scales were developed for neurodegenerative conditions and require validation in TBI populations (Arnould et al., 2013).

In clinical settings, apathy remains under-identified. Existing screening tools rarely assess motivational deficits explicitly, and few are designed for use in early or acute phases of recovery. Future studies should develop and evaluate brief, behaviourally anchored tools suitable for integration into acute care or early rehabilitation settings.

Treatment research is sparse. Few targeted interventions exist, though a single-case study suggests that motivation-based behaviour therapy may be beneficial (Lane-Brown & Tate, 2010). Interventions such as multisensory stimulation and music therapy have shown benefits in dementia populations (Holmes et al., 2006; Verkaik et al., 2005). Pharmacological approaches, including acetylcholinesterase inhibitors, have shown modest benefits in other neurological conditions (Berman et al., 2012), but their effectiveness in TBI remains unclear. Psychological strategies such as behavioural activation and goal management training, already used in acquired brain injury, also warrant further investigation.

There is a clear need for well-designed randomised controlled trials to test the feasibility, acceptability, and efficacy of interventions targeting apathy after TBI. Given the condition's multifactorial nature and the heterogeneity of TBI, future studies should explore subgroup-specific adaptations. Interdisciplinary collaboration will be vital to ensure

interventions are conceptually grounded, clinically feasible, and relevant to real-world contexts.

Conclusions

This project deepened my understanding of apathy as a multidimensional and clinically significant outcome of TBI, with wide-reaching implications for everyday functioning and long-term recovery. Conducting both a systematic review and secondary data analysis highlighted the conceptual and methodological challenges that arise from the absence of a consensus definition and a validated apathy measure specific to TBI. These limitations complicated efforts to compare findings across studies. Despite these challenges, the research illustrates that apathy is a meaningful and often under-recognised outcome of TBI. It can emerge early in recovery, during a window when individuals are more likely to receive clinical support, underscoring the importance of timely identification and intervention.

Through this process, I also developed skills in conducting large-scale research that is transparent, reproducible, and aligned with open science principles. It was important to me that this work not only met scientific standards but was also generalisable and clinically meaningful, particularly given the broader context of TBI as an enduring condition, and apathy as a frequently overlooked yet impactful symptom within it.

Looking ahead, addressing apathy in the context of TBI will require interdisciplinary collaboration, clearer conceptual frameworks, and further development of valid, clinically appropriate interventions. By increasing the visibility of apathy as a core outcome, we can work toward a more comprehensive understanding of recovery, one that prioritises not only survival and physical function, but also psychological wellbeing and autonomy.

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The Appendices

Appendix A: Search terms

"apathy" OR "abulia" OR "amotivation" OR "avolition" OR "indifference" OR "emotional indifferen*" OR "disinterest" OR "neuropsychiatric inventory" OR "frontal lobe personality scale" OR "Lille apathy rating scale" OR "frontal system behavior scale" OR "frontal system behaviour scale" OR "key behavior change inventory" OR "key behaviour change inventory" OR "apathy evaluation scale" OR "apathy scale" OR "irritability-apathy scale" OR "irritability apathy scale" OR "dimensional apathy scale" OR "apathy motivation index" OR "reduced interest" OR "reduced drive" OR "reduced volition" OR "reduced motivation" OR "diminished interest" OR "diminished drive" OR "diminished volition" OR "diminished motivation" OR "loss of interest" OR "loss of drive" OR "loss of volition" OR "loss of motivation"

AND
"traumatic brain injur*" OR TBI OR concussion OR "craniocerebral trauma" OR "head injury" OR "Craniocerebral Trauma" [Mesh]

Appendix B: JBI Critical Appraisal Checklist for studies reporting prevalence data

Item	*Elaboration*
1. Was the sample frame appropriate to address the target population?	This item considers whether the study sample adequately reflected the characteristics of the wider target population, including factors such as age, gender, diagnosis, and relevant medical history.
2. Were study participants recruited in an appropriate way?	This item assesses whether the recruitment method was suitable for producing a representative sample. Acceptable approaches include random sampling or other systematic methods (e.g. census, stratified, or cluster sampling). Less appropriate approaches are non-probability methods such as convenience or volunteer sampling, which may introduce bias.
3. Was the sample size adequate?	This item considers whether the study included enough participants to provide reliable prevalence estimates. Larger samples reduce uncertainty around estimates by producing narrower confidence intervals. Ideally, studies report a sample size calculation to demonstrate adequacy (Munn et al., 2015). In this review, we judged samples as sufficiently large where at least 30 participants per group were included, in line with the Central Limit Theorem, which holds that samples of ≥30 can approximate a normal distribution (Hogg, Tanis, & Zimmerman, 2015).
4. Were the study subjects and setting described in detail?	This item assesses whether the study provided sufficient information about participants and the study context to judge whether the sample was comparable to the target population. Clear descriptions of demographic characteristics and setting are important for evaluating generalisability.
5. Was data analysis conducted with sufficient coverage of the identified sample?	This question assesses coverage bias, which indicates whether the sample is representative in that all subgroups have comparable response rates for the study.
6. Were valid methods used for the identification of the condition?	This item assesses whether apathy was measured using valid and reliable tools. Use of validated scales reduces the risk of classification bias, whereas reliance on unvalidated self- or observer-reports may compromise internal validity.
7. Was the condition measured in a standard, reliable way for all participants?	This item considers whether apathy was measured consistently across participants. Reliability is supported when raters are trained, apply the same validated scale in the same way, and demonstrate agreement in their ratings.

8. Was there appropriate statistical analysis?	This item assesses whether statistical methods were clearly reported and suitable for estimating prevalence. Appropriate analysis requires transparent reporting of numerators and denominators, prevalence percentages, and confidence intervals.
9. Are all important confounding factors/sub-groups/ differences identified and accounted for?	This item evaluates whether studies considered variables that could influence prevalence estimates, such as age, gender, injury severity, time since injury, or co-occurring mental health conditions. Accounting for these factors helps reduce bias from spurious associations.
10. Were sub-populations identified using objective criteria?	This question refers to whether sub-populations are identified using valid, reliable and thus, reproducible criteria. For example, patient sub-populations should be created through validated measures conducted by qualified clinicians or credible clinical records.

Table B1. *JBI Critical Appraisal Checklist for studies reporting prevalence data*

Appendix C: Study quality assessment

Year	Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Summary score
2024	Venkatesan & Rabinowitz	1	1	1	1	1	1	1	1	1	1	**10**
2023	Nguyen et al.	1	1	1	1	1	1	1	1	1	1	**10**
2023	Quang et al.	1	1	1	1	1	0	1	1	1	1	**9**
2022	Ubukata et al.	1	1	1	1	1	0	1	1	1	1	**9**
2021	Balan et al.	1	1	1	0	1	1	1	1	0	1	**8**
2020	Devi et al.	1	1	1	1	1	1	1	1	1	1	**10**
2020	Huang et al.	1	1	1	1	1	0	1	1	1	1	**9**
2017	Nygren DeBoussard et al.	1	1	1	1	0	0	00	1	1	00	**6**
2015	Arnould et al.	1	1	1	1	1	0	1	1	1	1	**9**
2015	Lengenfelder et al.	1	00	1	0	1	1	1	1	0	1	**7**
2014	Knutson et al.	1	1	1	0	1	1	1	1	0	000	**7**
2012	Wiart et al.	1	1	1	1	1	0	0	1	1	1	**8**
2009	Lane-Brown & Tate	1	1	1	1	1	1	1	1	1	1	**10**
2006	Kilmer et al.	1	1	1	1	1	1	1	1	1	1	**10**
2004	Al-Adawi et al.	1	1	1	1	1	1	1	1	1	1	**10**
2002	Cantagallo & Dimarco	1	1	1	1	1	1	1	1	0	1	**9**
2001	Pachalska et al.	1	1	0	0	1	0	1	1	0	000	**5**
1991	Dunlop et al.	1	0	1	0	1	00	0	1	00	00	**4**

Table C1. *Study quality assessment using JBI Checklist for prevalence studies*
Notes: 1 = Yes, 0 = No, 00 = Unclear, 000 = NA.

Appendix D: Full data extraction of all included studies

Authors, year	*Country*	*Population*	*Setting*	*TBI N*	*Mean age*	*Male (%)*	*Apathy measure*	*TBI validated measure (Y/N)*	*Rater*	*Apathy N*
Venkatesan & Rabinowitz, 2024	USA	Public	Outpatient	106	63.9	72%	Frontal Systems Behaviour Scale	Y	Self-report	53
Nguyen et al., 2023	Vietnam	Public	Outpatient	75	33.9	88%	Neuropsychiatric Inventory	Y	Caregiver	46
Quang et al.,2023	Vietnam	Public	Outpatient	45	33.4	87%	Dimensional Apathy Scale	N	Caregiver	20
Ubukata et al.,2022	Japan	Public	Outpatient	88	41.9	73%	Apathy Scale	N	Self-report	51
Balan et al., 2021	Brazil	Public	Inpatient	41	32.0	83%	Apathy Evaluation Scale	Y	Caregiver	12
Devi et al., 2020	India	Public	Outpatient	50	36.2	76%	Neuropsychiatric Inventory	Y	Caregiver	5
Huang et al., 2020	USA	Veterans	NA	25	28.0	100%	Head Injury Symptom Checklist – adapted	N	Self-report	1

Nygren DeBoussard et al. , 2017	Sweden	Public	Inpatient	81	NA	NA	Clinical interview	N	Clinician	26
Arnould et al., 2015	France	Public	Inpatient	68	35.6	84%	Apathy Inventory	N	Caregiver	14
Lengenfelder et al., 2015	USA	Public	NA	33	40.9	NA	Frontal Systems Behaviour Scale	Y	Caregiver	11.55
Knutson et al., 2014	USA	Veterans	Study registry database	176	58.4	100%	Neuropsychiatric Inventory	Y	Caregiver	28
Wiart et al., 2012	France	Public	Outpatient	47	33.4	74%	Clinical interview	N	Clinician	20
Lane-Brown & Tate, 2009	Australia	Public	Outpatient	34	34.4	88%	Apathy Evaluation Scale	Y	Caregiver	23.46
Kilmer et al., 2006	USA	Public	Study registry database	51	38.1	72%	Neuropsychiatric Inventory	Y	Caregiver	19
Al-Adawi et al., 2004	Oman	Public	Outpatient	80	30.9	66%	Apathy Evaluation Scale	Y	Self-report	16
Cantagallo & Dimarco, 2002	Italy	Public	Inpatient	53	32.9	76%	Neuropsychiatric Inventory	Y	Caregiver	25

Pąchalska et al., 2001	Poland	Public	Inpatient	15	34.4	47%	Frontal Behavioural Inventory	N	Caregiver	13
Dunlop et al., 1991	USA	Public	Study registry database	68	34.6	87%	Neuropsychiatric scale devised for the study	N	Clinician	28.56

Table D1. *Data extraction: population and apathy measure details*

Authors, year	*Months since TBI*	*Severity categorisation method*	*TBI severity (%)*			*Cause of TBI (%)*				
			Mild TBI	*Moderate – severe*	*Severe*	*Transport accident*	*Fall*	*Assault*	*Combat*	*Other*
Venkatesan & Rabinowitz, 2024	126	GCS + other factors	16	23	61	NA	NA	NA	NA	NA
Nguyen et al., 2023	27.2	GCS	0	52	48	92	4	1	NA	3
Quang et al.,2023	25.4	GCS	0	100	0	91	7	2	0	0
Ubukata et al.,2022	97.4	GCS	20	14	66	86	10	NA	NA	4
Balan et al., 2021	28.0	NA	0	0	100	NA	NA	NA	NA	NA
Devi et al., 2020	4.5	GCS	16	36	48	86	10	4	0	0
Huang et al., 2020	19.5	GCS + other factors	100	0	0	0	0	0	100	0
Nygren DeBoussard et al. , 2017	3.0	GCS	0	0	100	NA	NA	NA	NA	NA
Arnould et al., 2015	38.8	NA	0	0	100	72	24	4	0	0
Lengenfelder et al., 2015	93.5	NA	0	100	0	NA	NA	NA	NA	NA
Knutson et al., 2014	NA	NA	NA	NA	NA	0	0	0	100	0
Wiart et al., 2012	133.2	Glasgow Outcome Scale	28	49	23	NA	NA	NA	NA	NA
Lane-Brown & Tate, 2009	80.6	NA	0	0	100	76	6	6	NA	12

Kilmer et al., 2006	12.0	Other factors	0	100	0	68	16	8	NA	8
Al-Adawi et al., 2004	8.4	GCS	8	3	41	76	13	NA	NA	11
Cantagallo & Dimarco, 2002	24.9	GCS	0	8	64	NA	NA	NA	NA	NA
Pąchalska et al., 2001	11.3	NA	NA	NA	NA	NA	NA	NA	NA	NA
Dunlop et al., 1991	4.0	NA	NA	NA	NA	53	15	20	0	2

Table D2. *Data extraction: TBI details.*
GCS = Glasgow Coma Scale; NA = Not reported; Other factors = Length of post traumatic amnesia, length of loss of consciousness, trauma-related intracranial neuroimaging abnormalities

Appendix E: Influence analysis

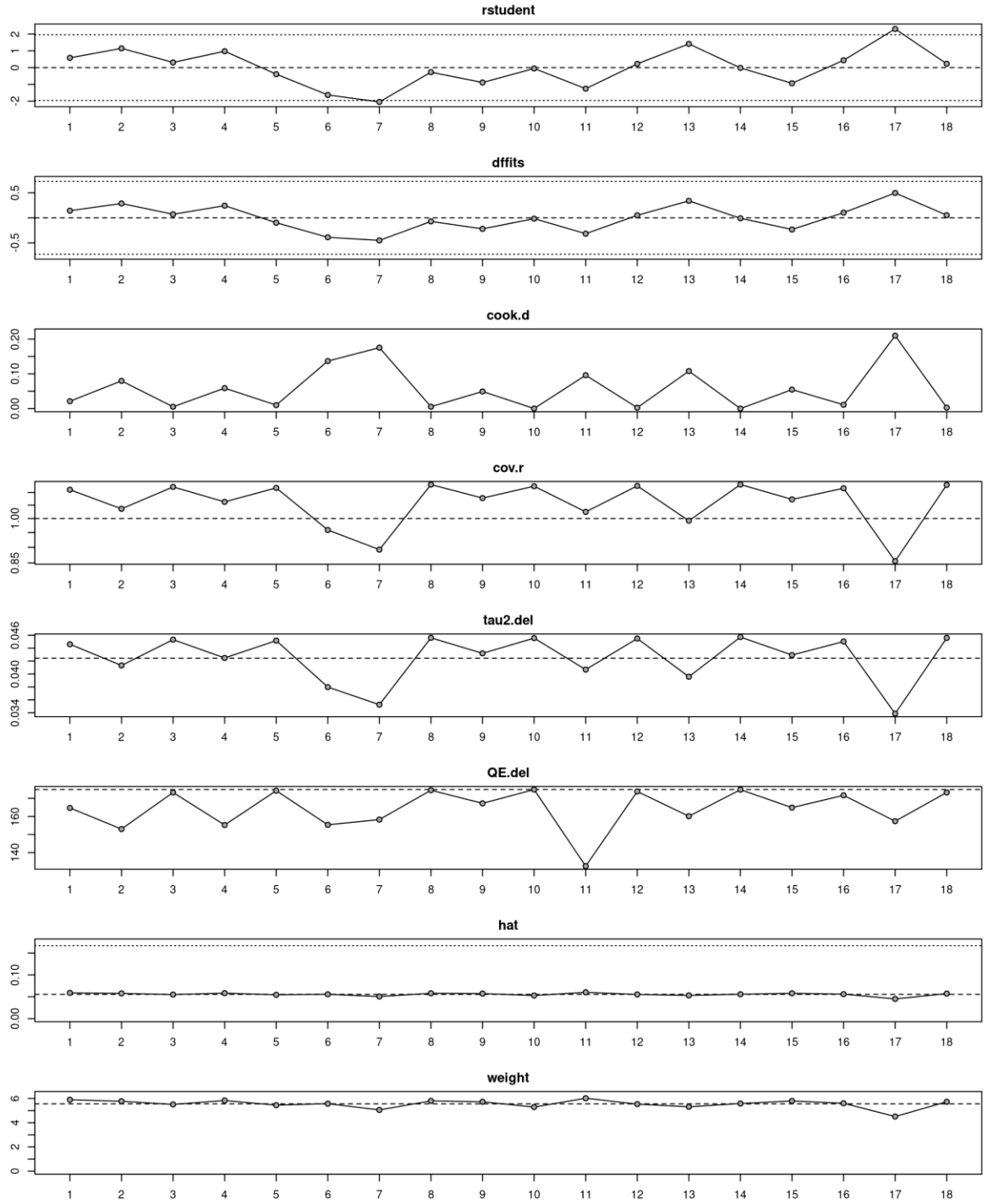

Figure E1*: Influence Analysis*

Appendix F: Baujat Diagnostics Plot

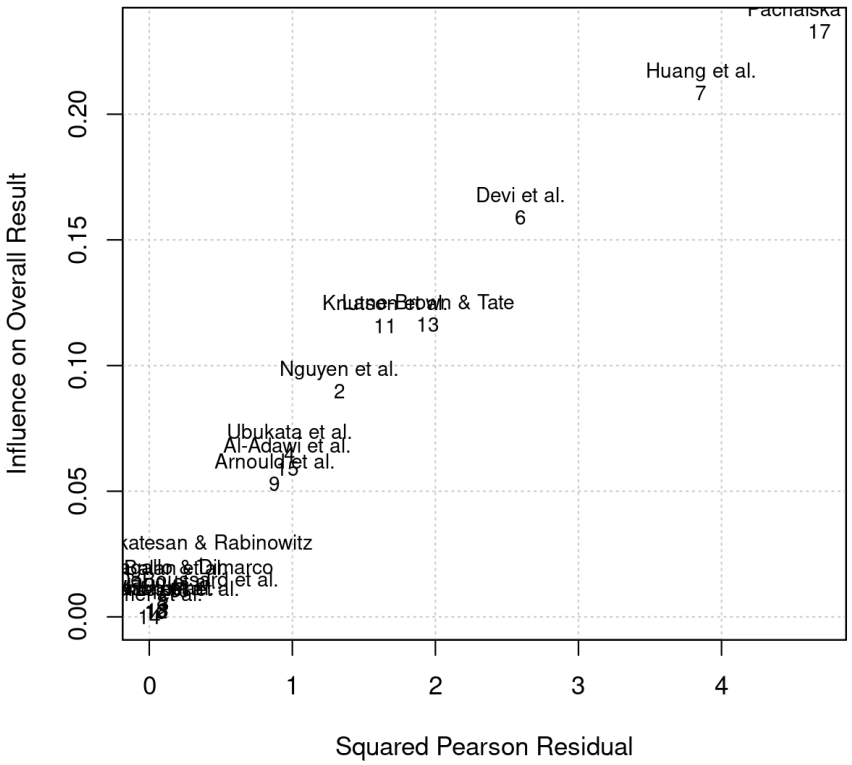

Figure F1. F: *Baujat Diagnostics Plot*

Appendix G: Content Validity Matrix for the Proxy Apathy Index

Proxy item	Primary apathy facet (best fit)	Closest AES facet	Closest NPI–Apathy facet	Anhedonia overlap
PHQ-9: "Little interest or pleasure in doing things"	Interest / anticipatory motivation (mixed)	Cognitive/behavioural interest–engagement	Diminished interest/enthusiasm in usual activities	High (explicit 'pleasure')
BSI-18: "Feeling no interest in things"	Interest / activation (anticipatory)	Interest–engagement (loss of curiosity/concern)	Reduced interest in surroundings/activities	Low–Moderate
MPAI-4: "Problems initiating activities without being prompted"	Initiation / auto-activation	Behavioural initiation (difficulty starting without cues)	Reduced initiative / spontaneous activity	Low
PCL-5: "Loss of interest in activities that were previously enjoyable"	Sustained engagement / maintenance (mixed)	Interest–engagement (maintenance of activity set)	Less interest in usual/recreational activities	Moderate–High (references 'enjoyable')
PCL-5: "Feeling emotionally numb or unable to have loving feelings"	Affective / relational motivation	Emotional responsivity/concern (blunted affect)	Indifference / reduced emotional reactivity	Low

G1 Table: *Content-Validity Matrix for the Proxy Apathy Index*

Note: *AES = Apathy Evaluation Scale; NPI = Neuropsychiatric Inventory. Anticipatory vs. consummatory coding: 'Anticipatory' indexes interest/drive/energisation to act, while 'consummatory' indexes hedonic pleasure during/after reward; 'mixed' indicates both signals are present. Mappings to AES and NPI–Apathy are content-based and do not imply psychometric equivalence or factor alignment.*

Appendix H: Missing data pattern for core variables included in analyses

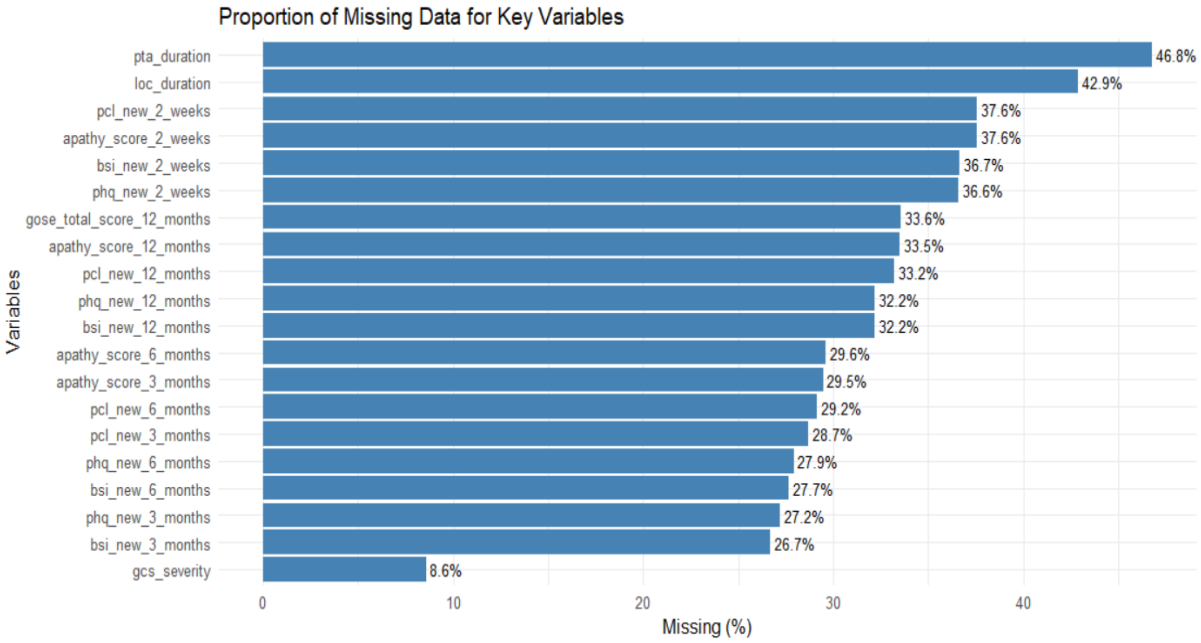

Figure H1. *Missing data pattern for core variables included in analyses*