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HS&DR Evidence Synthesis Centre Topic Report

Evidence for specialist treatment of people with acquired brain injury in secure psychiatric services: systematic review and narrative synthesis

Liz Shaw[1†*], Michael Nunns[1†], Simon Briscoe[1], Amelia Mosley[2], Daniel Dalton[3,4], Rob Anderson[1], Jo Thompson Coon[1]

[1]Exeter HS&DR Evidence Synthesis Centre, Institute of Health Research, University of Exeter Medical School, University of Exeter, Devon, Exeter, EX1 2LU, UK
[2]NHS England Specialised Commissioning Mental Health, Skipton House, 80 London Road, London, SE1 6LH, UK
[3]NHS England, Skipton House, 80 London Road, London, SE1 6LH, UK
[4]Norfolk & Suffolk NHS Foundation Trust, Trust Headquarters, Hellesdon Hospital, Drayton High Road, Norwich, NR6 5BE, UK

*Corresponding author: E.H.Shaw@exeter.ac.uk
†Joint first author

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This report

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Abstract

Patients with acquired brain injury (ABI) may experience various physical, cognitive or emotional sequelae and are at increased risk of mental health difficulties. They may display aggressive, sexually inappropriate or disinhibited behaviour which challenges those supporting them and poses a risk to themselves or others. Such individuals may need assessment, care and/or treatment within secure settings. There is limited availability of secure placements and referral must be based on the patient meeting certain criteria.

Objectives

To systematically review evidence that can inform the arrangements for the specialist care of adults with ABI who may require secure psychiatric services.

Data sources

Seven bibliographic databases (CINAHL, HMIC, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, PsycINFO, Social Policy & Practice, ASSIA) were searched on 27th June 2019, date-limited to 2000. Database searches were supplemented with citation searching; inspecting relevant reviews; searching ClinicalTrials.gov and WHO International Clinical Trials Registry Platform, searching relevant websites; liaising with clinical experts and affiliation searches.

Review methods

We sought evidence about adults with non-degenerative ABI placed in, eligible for referral to, or being assessed for eligibility for referral to secure psychiatric services in any high-income country. Eligibility for referral to secure services was based on assessment or observation of challenging behaviours. Psychometric studies of tools used in assessments were eligible for inclusion. Study selection, data extraction and quality assessment were completed independently by two reviewers. Given the heterogeneity of studies, outcomes and data, a narrative synthesis approach was used. We were interested in identifying patient, diagnostic or symptom characteristics associated with requiring care in secure settings.

Findings

6297 unique titles and abstracts were screened against inclusion criteria, leading to full-text screening of 325 papers. Forty-six observational and case-control studies and one systematic review were included; however none were set in, or referred explicitly to secure settings. Thirty-eight of the primary studies evaluated patient characteristics associated with challenging behaviour. Eight primary studies and the systematic review evaluated the psychometric properties of measures used to assess challenging behaviour. Narrative synthesis indicated a highly heterogeneous set of studies providing uncertain evidence about patient characteristics which may be associated with challenging behaviours. Whilst tentative associations were found between certain patient characteristics and occurrence of challenging behaviour, the conflicting nature of this evidence reduces confidence in these findings. There was no strong evidence to recommend the use of specific patient assessment tools.

Limitations

We found no evidence regarding referrals to secure treatment settings and thus were not able to directly answer our research questions. Studies investigating associations between patient characteristics and challenging behaviours varied in methodological rigour and evidence was highly heterogeneous.

Conclusions

There is no direct evidence to support decisions about the suitable setting for the care of adults with ABI who display challenging behaviour. There is tentative evidence about patient characteristics associated with risk of challenging behaviour.

Future work

Primary research is needed to inform evidence-based decisions on the appropriate setting for the care of people with ABI who display challenging behaviour.

Study registration Open Research Exeter: **http://hdl.handle.net/10871/40286**

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Contents

List of Tables

List of Figures

List of Supplementary Material

Table S1. Studies excluded following full-text screening: Report Supplementary Material File 1

Supplementary material can be found on the NIHR Funding and Awards report topic page (https://doi.org/10.3310/hsdr-tr-130320).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

Abbreviations

AMSTAR-2	A Measurement Tool to Assess Systematic Reviews (2nd Version)
ANOVA	Analysis of Variance
BIRT	Brain Injury Rehabilitation Trust
COSMIN	Consensus-based Standards for the Selection of Health Status Measurement Instruments
	EL Emotional Lability
GCS	Glasgow Coma Scale
GRADE	The Grading of Recommendations Assessment, Development and Evaluation of systematic reviews
KSMS	The Sister Kenny Symptom Management Scale
MBPC	Memory and Behaviour Problems Checklist
MHA	Mental Health Act
MSCEIT	Mayer-Salovey-Caruso Emotional Intelligence Test;
NIH	United States National Institute of Health
NR	Not Reported
PICO	Population, Intervention, Comparator, Outcome
PTA	Post-Traumatic Amnesia
PTSD	Post-Traumatic Stress Disorder
SASNOS	St Andrews Swansea Neurobehavioral Outcome ScaleTBI Traumatic Brain Injury
UK	United Kingdom

Glossary

Note: Definitions are with respect to the use of these terms in this review, but other definitions exist.

Acquired Brain Injury

A brain injury sustained after birth. Acquired brain injuries are categorised as either traumatic (i.e. sustained as a result of impact to the head) or non-traumatic (i.e. resulting from a medical condition that affects the brain, e.g. stroke or brain tumour).

Affiliation searches

Searching for evidence from authors affiliated with institutions known to be relevant to the topic of the review.

Anoxia

An absence or severe reduction of oxygen reaching bodily tissues.

Axis I disorder

All psychological diagnoses, e.g. depression, obsessive-compulsive disorder, anxiety, except intellectual disability (an IQ $\leq$ 70) and 'personality disorder' labels.

Axis II disorder

'Personality disorders' and intellectual disability.

Behaviour which challenges or 'Challenging Behaviour'

Behaviours such as aggression, self-harm, destructiveness and disruptiveness, which are of an intensity, frequency or duration as to threaten the quality of life and/or the physical safety of the individual or others and may lead to responses that are restrictive, aversive or result in exclusion.

Cerebrovascular accident

Otherwise known as a stroke. Interruption of blood flow within the brain caused by blockage of arteries leading to the brain or bleeding within brain tissue.

Content validity

Extent to which content of the outcome measure reflects the construct being evaluated

Construct validity

Degree to which the scores of the outcome measure are consistent with the hypotheses, assuming that the outcome measure is a valid measure of the construct under consideration.

Criterion validity

Extent to which scores on the outcome measure reflect a 'gold standard' measurement of the construct.

Disinhibition

Manifestations of behaviour, speech or emotions which are characterised by a lack of restraint and impulsivity and are thus outside of those expected by social norms.

Emotional lability

Rapid, often exaggerated changes in mood in response to strong emotions or feelings such as laughing, crying or increased irritability or anger.

Executive functioning

A set of mental skills supported by the functioning of the frontal lobe of the brain. These skills can include working memory, ability to plan ahead, flexible thinking and self-control.

Locked rehabilitation services

Rehabilitation services which provide assessment, treatment and support to stabilise the person's symptoms and help them gain/regain the skills and confidence to live successfully in the community. Symptoms may relate to a person's physical, cognitive and emotional needs, directly or indirectly arising from an acquired brain injury, which cannot be supported by mainstream health or social care services. Such services may also support a range of individuals (for example, learning disability and brain injury) with complex needs and/or offending history, where current risk does not meet criteria for secure services.

Mental Health Act 1983

A UK Act of Parliament that applies in England and Wales and gives approved mental health professionals the power to detain people who have a mental health disorder in a hospital setting.

Non-Traumatic Brain Injury

A brain injury resulting from a medical condition that affects the brain, e.g. stroke or brain tumour.

Perseveration

Repetition of particular word, phrase or gesture without prior stimulus or beyond what is required within given situation or context. Associated with dysexecutive syndrome.

Rehabilitation

Restorative treatment that aims to reduce the long-terms effects of brain injury. Brain injury rehabilitation takes place in inpatient, outpatient and community settings depending on the stage and severity of the injury.

Reliability

Extent to which scores for an individual patient on the same outcome measure remain the same across different conditions; including different reviewers on the same occasion (inter-rater reliability), same persons on different occasions (intra-rater reliability), across a period of time (test-retest reliability) and using different sets of items from the same outcome measure (internal consistency).

Response suppression

A person's ability to inhibit speech or behaviour, which may be impaired as a result of brain injury resulting in socially inappropriate actions or responses.

Secure services

Provide assessment, care and treatment to adults who represent a risk to the public in an inpatient setting which provides a range of physical, procedural and relational security measures. Three levels of security currently exist for adults who present a grave and

immediate risk of harm (high secure), serious risk of harm (medium secure) or significant risk of harm (low secure) to the public

Structural validity

Extent to which scores on outcome measure reflect the dimensionality of the construct being evaluated.

Traumatic Brain Injury

A brain injury sustained as a result of impact to the head. Can result in a 'penetrating' injury which damages the skull, or 'closed head' injury, where the skull remains intact.

Validity

Extent to which outcome measure evaluates the construct it states it intends to measure.

Plain English Summary

The problem and why it is important

Many people have brain injuries that they acquired since birth following, for example, an accident, fall or serious illness. As a result, some patients may act in a way that threatens or endangers the safety or quality of life of themselves or others. It may be appropriate for these patients to receive treatment in a 'secure' facility, which specialises in caring for patients whose behaviour can make them dangerous to members of the public. Secure settings are restrictive and therefore only appropriate for people that really need them, so the decision to refer a patient to a secure service must be fully supported by evidence.

What we aimed to achieve

We wanted to find out whether there was evidence to help clinicians decide which patients are most likely to need to receive care in secure services.

What we did

We looked for research published from 2000 onwards, studying adults with brain injuries, to see whether their background, injury diagnosis or symptoms influenced whether they needed secure care. We wanted evidence from the UK and other high-income countries. We looked for patient characteristics linked with the need for referral to secure care or the likelihood of behaviour others find challenging.

Main Messages

We couldn't find any studies that looked directly at secure settings. We did find 38 studies that considered whether patient characteristics were linked with challenging behaviour and 8 studies looking at the accuracy of tools for measuring different types of behaviour. The findings were so varied that only a few tentative suggestions about what might be relevant in patient assessments could be made.

What should happen next?

There needs to be a lot more research about how and why patients with brain injury are referred to secure care or not.

Scientific summary

Background

An estimated 1.5 million people in the UK have an acquired brain injury (ABI). ABI can lead to various physical, cognitive or emotional symptoms, with patients also being at increased risk of mental health difficulties. One possible consequence of ABI is the presence of behaviour that threatens the quality of life or safety of the patient or others. Such 'challenging behaviour' includes displays of aggression, sexually inappropriate behaviour or disinhibition. Individuals who display challenging behaviour that endangers their safety or that of others may need to receive their treatment in a secure setting. The availability of secure ABI rehabilitation setting is limited in the UK as the restrictiveness of the setting could constitute an infringement of the human rights of the patient if the referral is not appropriately justified. Therefore decisions about referral need to be rigorous and evidence-based.

Objectives

This review aims to summarise and synthesise evidence that can inform the arrangements for the specialist care of adults with ABI who may require secure psychiatric services. This overarching interest can be broken down into three specific research questions:

1) Is there evidence to support the differentiation between different groups of adult patients with ABI as a criterion influencing the most appropriate care setting for treatment of adults with ABI?

2) Is there evidence to support the use of diagnostic, disease- or symptom-severity assessment criteria in influencing the most appropriate setting for care and treatment of adults with ABI?

3) Is there evidence to support the use of risk assessment tools in influencing the most appropriate setting for care and treatment of adults with ABI?

Methods

Data sources

We searched seven bibliographic databases (CINAHL, HMIC, MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, PsycINFO, Social Policy & Practice, ASSIA) on 27th June 2019 and date-limited to 2000. Database searches were supplemented with citation searching; inspecting relevant reviews; searching ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform, searching relevant websites; liaising with clinical experts and affiliation searches.

Study selection

The following inclusion criteria were applied to records identified by the search strategy:

Population:

Adults aged 18 or over, or 16 and over but receiving adult services; diagnosed with an ABI of any type, except for progressive, degenerative diseases; participants were placed in, eligible for referral to, or being assessed for eligibility for referral to secure psychiatric services. We determined eligibility for referral to secure services based on the presence or assessment of challenging behaviours or difficulties that may warrant treatment in a secure setting.

Phenomenon of Interest

Evidence relevant to the at least one of the three research questions, including any evidence about testing, assessment or patient classification to determine whether patients may require secure care.

Geographical context

Research from any high-income country.

Study Design

Any study design containing relevant evidence, including: systematic reviews, randomised and non-randomised controlled trials, observational cohort, cross-sectional and case control studies and psychometric evaluations of relevant assessment tools.

Study selection

After an initial calibration exercise, inclusion criteria were independently applied to the title and abstract of each citation by two reviewers, with disagreement resolved through

discussion. This process was repeated for the full text of each paper provisionally meeting the inclusion criteria. Expert stakeholders helped to resolve disagreements at full text screening.

Data extraction

Data extraction was performed by one reviewer and checked by a second, with disagreements settled through discussion. Extracted data included relevant details about the study, sample, setting, measured patient characteristics, outcomes of interest and study findings.

Critical appraisal strategy

Appraisal for observational cohort, cross-sectional and case-control studies was undertaken using the relevant NIH study quality assessment tool. Systematic reviews were appraised using AMSTAR-2. Studies developing or evaluating psychometric tools were evaluated using the COSMIN Risk of Bias Checklist

Synthesis methods

After identifying no studies based in secure settings, we focused our synthesis on the indirect evidence which sought to identify patient characteristics associated with challenging behaviour, and thus could influence the decision about referral to secure settings.

Sample characteristics and outcomes of critical appraisal were initially displayed and described. Given the heterogeneity of evidence, we performed a narrative synthesis, involving the following key stages

- Studies were grouped according to the outcome of interest (aggression, sexually inappropriate behaviour, other difficulties of emotional and/or behavioural regulation) and tabulated
- Within each outcome group described above, we clustered independent variables by groups based on the research questions: demographic, diagnostic and injury type, symptoms, other
- We described and narratively interpreted the findings of studies, identifying trends within each outcome group and explaining any inconsistencies where possible

- We provide an overall interpretation of findings from the three subgroups, identifying any common threads or observations across studies.

The narrative synthesis was led by one reviewer and checked for sense and consistency by a second. Stakeholders reviewed the synthesis to check interpretation.

Psychometric studies and systematic reviews were described in terms of the quality of their analyses and the weight of evidence provided.

Expert clinical advisors and patient and public involvement

We consulted with representatives from the National Specialised Mental Health Commissioning Team, NHS England during the development of the research protocol, study selection and when forming the discussion. Stakeholders critically reviewed all sections of the report. Unfortunately it proved too challenging to recruit patients or members of the public with relevant experience, due to the timeline of the review and the later change in its focus and the impact these issues had on our ability to approach candidates from such a vulnerable population.

Findings

Bibliographic database searches identified 6692 records and supplementary searches identified 1312 records. Following de-duplication there were 6279 unique records which were screened against our inclusion and exclusion criteria. The full texts of 328 articles were sought for further consideration.

None of these studies were based in secure settings, or evaluated referral pathways to secure settings, meaning there was no evidence to directly answer the research questions. However, 38 primary studies sought to identify predictors of, or variables associated with challenging behaviours which may warrant secure treatment. Eight primary studies and one systematic review evaluated the validity and reliability of tools used in the assessment of challenging behaviours. Following discussion with our stakeholders, we decided that synthesis of these 47 studies would enable us to indirectly address our research questions.

The evidence based upon the 38 observational and case-control studies examining variables associated with challenging behaviours was highly heterogeneous with some important

methodological flaws. However, there is evidence to support the inclusion of ABI symptoms and mental health assessments in particular during the evaluation of patient needs and when determining the likelihood of challenging behaviours. Tentative associations were found between lower patient age, male gender and lower-levels of communication and aggressive behaviour, but there is little evidence to suggest they have a bearing on likelihood of sexually inappropriate behaviour or other difficulties of emotional or behavioural regulation. Aggressive behaviour was found to be related to poorer physical functioning in 56% of the analyses evaluating this association. There is some evidence to suggest that the aetiology of ABI, location or type of brain damage, and injury severity may be possible factors affecting the likelihood of challenging behaviours, along with executive dysfunction. Whilst cognitive function appeared not to be relevant to the risk of sexually inappropriate behaviour, it appears to be a relevant consideration for other types of challenging behaviour. There were associations between mental health outcomes and risk of challenging behaviour and whilst no association was found between substance abuse and challenging behaviour, the number of studies conducting these analyses were small (n=12). Overall, whilst tentative associations were found between certain patient characteristics and the occurrence of certain types of challenging behaviour, the conflicting nature of this evidence reduces confidence in these findings and any associations should be interpreted with caution, within the context of the body of evidence included in this report.

Finally, the evidence focusing on the validity and reliability of tools used to assess challenging behaviours indicated that use of these tools was not supported by robust evidence about their psychometric properties.

Strengths and limitations

The evidence available did not directly address the research questions. In addressing the question of variables associated with challenging behaviour, it must be noted that evidence came from observational, cross-sectional and case-control studies and that almost all failed to detail power requirements, but stated associations based on correlational analyses.

This systematic review took a broad and thorough approach to seeking evidence, providing a much-needed statement of the state of the evidence in this area. However, this resulted in a

heterogeneous sample of studies, precluding detailed synthesis of evidence, and permitting only observation of trends and patterns within the data. A set of narrower inclusion criteria might have increased the homogeneity of the sample, yet our synthesis suggests that findings would still be equivocal.

Assessment tools used to observe challenging behaviours in ABI patients have not been supported by sufficient evaluations of their psychometric properties.

Conclusions

There is no direct evidence to support decisions about referral to secure services for people with ABI who display challenging behaviours. There is tentative evidence to suggest that certain patient characteristics, including demographic, symptom and mental health status, may be associated with risk of challenging behaviours, and should form part of future patient assessments. However, urgent primary research is needed in this field to support evidence-based practice.

Study registration

The protocol is registered at Open Research Exeter: **http://hdl.handle.net/10871/40286**

Funding

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1 Background

1.1 Adult secure services in the UK

Adult medium and low secure services provide care and treatment for people with mental and/or neurodevelopment disorders who may be detained under the Mental Health Act (MHA) 1983, whose risk of harm to others and of escape from hospital cannot be managed safely within other mental health settings.[1]

The secure psychiatric care pathway can be complex and there are many interdependencies with other services and organisations. Patients will typically have complex chronic mental illnesses and/or disorders, including neurodevelopmental disorders, which are linked to offending or seriously harmful behaviour. Some patients will be involved with the criminal justice system, courts and prison, and may have Ministry of Justice restrictions imposed.

Secure services provide a comprehensive range of evidence-based care and treatment provided by practitioners, expert in the field of forensic mental health. A range of specialist treatment programmes are available, delivered either individually or within groups. However, the specific needs or diagnoses catered for by different services or centres varies considerably. The aim of treatment for each individual will be to safely return to either (a) the community, (b) to a lower level of security or into non-secure services, or (c) to prison.

1.2 Acquired brain injury

An acquired brain injury (ABI) is a form of brain injury sustained after birth, i.e. individuals are not born with the injury as a result of congenital or genetic disorders.[2] Acquired brain injuries can be broadly categorised as traumatic or non-traumatic in aetiology. Traumatic brain injuries (TBI) are those sustained as a result of some form of impact to the head, whilst non-traumatic brain injuries are of internal causation, including stroke, brain tumour, or meningitis.[2]

An estimated 1.5 million people in the UK are currently living with a disability resulting from a brain injury.[3] Depending on the location and severity of the injury, people living with an ABI can experience a variety of difficulties, which can be divided into four broad categories;

physical, communicative, cognitive and behavioural/emotional.[4] People living with an ABI are more likely to experience mental health difficulties,[5] are at increased risk of engaging in offending behaviour or drug use and present a higher risk of harm to others and/or themselves.[3] One study estimates that over 60 per cent of the UK prison population have a brain injury.[6]

1.3 Provision of specialist acquired brain injury services

Delivering services for people with an ABI can be complex as differences in the aetiology and severity of the injury can lead to variations in level of functioning and range of potential needs across different individuals.[7]

Recovery from an ABI can occur over many months or even years. The 'slinky model' of rehabilitation indicates that patients require different services and levels of support depending on the stage of their recovery.[8] This support ranges from specialist rehabilitation as a post-acute inpatient, stepping down to services provided by community-based rehabilitation services then on to longer-term community support, including specialist case management.

The level of support available from families and the structure of local service provision can vary considerably. This may mean that whilst the longer-term needs of people living with ABI can be met through community-based, residential or general inpatient services, the needs of individuals with severe difficulties may mean secure inpatient services are best equipped to care for them. Secure services specialise in reducing the risk of harm the patient presents to themselves and/or others, whilst supporting them to achieve their treatment goals. However, the availability of secure ABI rehabilitation settings is limited in the UK, as the restrictiveness of the setting could constitute an infringement of the human rights of the patient if the referral is not appropriately justified (Human Rights Act, 1998).[9] It may also be the case that demand for secure services exceeds supply,[10] thus, it is important that the assessment, care and/or treatment needs of the patient, match with the availability and referral to an appropriate service.

1.4 Secure acquired brain injury services in the UK

To support this review, NHS England provided information (personal communication) about the Specialised Adult Secure Mental Health Services which are commissioned directly by NHS England Specialised Commissioning. NHS England currently commissions an approximate total of 75 adult medium and low secure ABI across 3 hospital sites in the North West and Midlands regions in England. All of the commissioned services are for men and currently there is no ABI-specialist high secure provision.

A 2017 service audit undertaken by NHS England in collaboration with the providers of commissioned adult low and medium secure ABI services found significant differences in the diagnostic groupings and sections of detention under the Mental Health Act for patients using these services over a 30-month period. Referral acceptance rates, source of admission, and rate of patient movement through services also varied significantly across the services.[11]

These findings suggested differences in the access assessment process across secure ABI services, regional differences in patient pathway planning, and possible differences in the type of provision and interventions being offered across the different hospital sites.[11]

1.5 Context of this review

The implementation plan for NHS England's Five Year Forward View for Mental Health seeks to ensure that individuals who require support from secure services can do so close to home, in the least restrictive environment appropriate to their needs.[12] It is intended that the provision of secure services will be also be aligned with non-secure inpatient services, community services and prison mental health services.

NHS England commissions adult secure services in line with the Manual for Prescribed Specialised Services. National specifications for specialised services are developed by relevant Clinical Reference Groups.[13] For adult secure services, there are distinct service specifications for high, medium and low secure services which include clearly defined clinical outcomes and quality standards.[14] These service specifications apply equally to all sub-specialisms of secure services, but as there is currently there is no distinct specification for adult secure ABI services, likewise there are no nationally indicated clinical outcomes or quality measures which are specifically related to secure ABI services.

To deliver the ambitions of the Five Year Forward View for Mental Health with respect to adult secure services, the Adult Secure Clinical Reference Group recommended that a targeted piece of work focusing on the evidence-base for the provision of adult secure specialist ABI services be undertaken, in order to inform future national work to agree the appropriate referral, assessment and treatment pathways, patient clinical outcomes, and quality indicators for these services.[12]

1.6 Aims and objectives of the review

This review aims to summarise and synthesise evidence that can inform the arrangements for the specialist care of adults with ABI who may require secure psychiatric services. This overarching interest can be broken down into three specific research questions:

1. Is there evidence to support the differentiation between different groups of adult patients with ABI as a criterion influencing the most appropriate care setting for treatment of adults with ABI?
2. Is there evidence to support the use of diagnostic, disease- or symptom-severity assessment criteria in influencing the most appropriate setting for care and treatment of adults with ABI?
3. Is there evidence to support the use of risk assessment tools in influencing the most appropriate setting for care and treatment of adults with ABI?

By seeking to identify evidence relating to these specific research questions, the review can directly inform service development and commissioning in the NHS within England and determine the need for further research.

2 Methods

The protocol for this review was registered on the Open Repository for Exeter on 6th January 2020 prior to commencing data extraction.[15] The methods used to identify and select evidence followed best practice guidance.[16-18]

2.1 Search strategy

We identified studies by searching bibliographic databases, checking the reference lists of included studies and topically relevant systematic reviews, searching clinical trials registries, liaising with stakeholders and searching websites. We also used forward citation searching and author citation searching to carry out targeted searches for studies conducted at or associated with UK low and medium secure ABI services.

The bibliographic database search strategy was developed using MEDLINE (via Ovid) by an information specialist (SB) in consultation with the review team and stakeholders. Search terms were derived from the titles, abstracts and indexing terms (e.g. MeSH in MEDLINE) of relevant studies identified in the topic brief and background searches. In addition, search terms were derived from the search strategies of topically similar systematic reviews and websites. Careful attention was given to ensuring an appropriate balance of specificity (i.e. minimising the retrieval of irrelevant studies) and sensitivity (i.e. retrieval of all relevant studies). A draft search strategy was sense checked by stakeholders with expert knowledge of the topic; in particular, the stakeholders commented on the exhaustiveness of terminology used in the search strategy to describe relevant acquired brain injuries and care settings.

The final search strategy consisted of two strands. The first strand combined search terms for acquired brain injuries with search terms for secure settings. The second strand combined search terms for acquired brain injuries, search terms for screening, assessment or referral, and search terms for challenging behaviours associated with acquired brain injuries. The first strand aimed to retrieve studies that discussed the use of secure settings for people with acquired brain injuries. The second strand aimed to retrieve studies that discussed the assessment of people with acquired brain injuries who display challenging behaviours but did not explicitly mention secure settings in the titles, abstracts or indexing terms.

The final search strategy was translated for use in an appropriate selection of medical and health care bibliographic databases including:

- CINAHL (via EBSCO)
- Health Management Information Consortium (HMIC) (via Ovid)
- MEDLINE (via Ovid)
- MEDLINE In-Process & Other Non-Indexed Citations (via Ovid)
- PsycINFO (via Ovid)
- Social Policy and Practice (via Ovid)
- ASSIA (via ProQuest)

All searches were carried out on 27th June 2019 and date-limited from 2000 to date of search. English language only filters were used wherever available. No study type filter was used. The ASSIA search was split into two parts and conducted in two stages due to limitations of the search interface which prevented running the search in full. The search strategies and number of results retrieved for each bibliographic database are reported in Appendix 1. The search results were exported to Endnote X8 (Clarivate Analytics, Philadelphia, PA, USA) and de-duplicated using the automated de-duplication feature and manual checking.

The reference lists of all included studies and topically relevant systematic reviews were checked and any potentially relevant studies were retrieved and taken forward to full-text screening, as described in section 2.3.

We searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) to identify recently completed studies. The search strategies and number of results retrieved are reported in Appendix 1. We attempted to identify published or unpublished reports of any completed trials that contained potentially relevant results by inspecting the trial record for details of publications and emailing the principal investigators.

The websites of topically relevant websites were searched to identify published or unpublished studies not retrieved by other search methods. The full list of websites searched and the corresponding search strategies are reported in Appendix 1.

We conducted targeted searches for relevant studies conducted at or associated with UK low and medium secure ABI services, namely St Andrew's Healthcare Northampton hospital site, Elysium Healthcare (previously St George's Healthcare) and St Mary's Hospital site and Lancashire Care NHS Foundation Trust Guild Lodge hospital site. This involved using three approaches informed by Booth and colleagues' CLUSTER approach:[19]

- Using the 'Affiliations' search function in Scopus (Elsevier) to identify studies by authors affiliated with UK secure ABI services;
- Contacting the lead authors of relevant studies conducted at UK secure ABI services for details of any similar studies.
- Forward citation searches of relevant studies conducted at UK secure ABI services using Scopus (Elsevier).

We attempted to search the conference proceedings of the United Kingdom Acquired Brain Injury Form (UKABIF) but the proceedings could not be obtained. We were able to identify selected conference proceedings via CINAHL and forward citation searches using SCOPUS.

2.2 Inclusion and exclusion criteria

The inclusion criteria and exclusion criteria, according to the *PICoS* categories i.e. Patient/Population, phenomenon of Interest and Context applied to the studies identified through the search strategy are detailed below.[20]

Population:

Included if:

Participants were adults (aged 18 or over), including those aged 16+ receiving adult services. If participants below the age of 18 were included alongside users of adult secure services, the findings for those aged over 18 should be reported separately.

Participants had any diagnosed acquired brain injury, as defined above, which included injury acquired through any cause including, but not limited to:

- Trauma – head injury or surgical damage
- Vascular accident e.g. stroke

- Cerebral anoxia
- Other toxic or metabolic insult (e.g. hypoglycaemia)
- Infection (e.g. meningitis) or inflammation

Participants placed in, eligible for referral to, or being assessed for eligibility for referral to secure psychiatric services, even if the study does not explicitly look at where people are referred. Eligibility for referral to secure services was considered to be the presence (or assessment of the presence) of challenging behaviours that may warrant treatment in a secure setting, including:

- Aggression
- Antisocial behaviour
- Behavioural dysregulation
- Criminal behaviour
- Features associated with dysexecutive syndrome which could indicate a need for a secure service e.g. response suppression, inhibition, emotional lability, disinhibition
- Emotional dysfunction
- Emotional lability
- Difficulties with empathy
- Inappropriate sexual behaviour
- Inappropriate interpersonal behaviour
- Physical assault
- Suicidality
- Violence; including verbal or physical, against self, others or objects.

Participants could be in any setting, including within the community.

Where participants with an ABI were one subgroup within a study including participants with multiple diagnoses, but where the study's findings were reported separately for those with an ABI.

Excluded if:

- Participants without a diagnosis of ABI
- Participants aged under 18, or receiving support from adolescent services
- Participants with a diagnosis of a progressive, degenerative central nervous system disease such as multiple sclerosis, Parkinson's disease or a dementia (e.g. Alzheimer's disease)
- Participants living with an intellectual or learning disability/difficulty without clear indication that these difficulties arose from an ABI.

Phenomenon of Interest:

Evidence must be relevant to at least one of the three research questions. This encompassed evidence seeking to establish the value of testing, assessment or patient classification procedures (e.g. psychometric, scans, risk assessments etc.) for predicting the needs of people with an ABI who may require support within a secure setting.

Psychometric evaluations of assessment tools must consider some aspects of both reliability and validity in order to be included.

Geographical context

We were primarily interested in research conducted within the UK. We also included studies that were conducted in other high-income countries. High-income countries were identified from the World Bank list of high-income economies[21] and stakeholders were consulted regarding the relevance of health systems in included studies.

Study design

Included if:

Any study design containing evidence relevant to review questions 1 to 3. This included, but was not limited to:

- Systematic reviews of quantitative evidence.
- Empirical studies that have collected quantitative data (e.g. about tests, assessments, classification systems).

Excluded if:

- Studies described as "Systematic Reviews" which did not have all of the following: a) a clearly stated research question, b) clearly stated inclusion criteria c) method for critically appraising quality of included primary studies
- Commentaries, opinion pieces and editorials
- Case studies of individual patients
- Epidemiological studies e.g. studies that take an epidemiological approach to understand comorbidities associated with an ABI
- Studies collecting only qualitative data.

Date of publication

From 2000.

2.3 Study selection

As an initial calibration exercise of inclusion judgments and the clarity of our inclusion criteria, reviewers applied the inclusion and exclusion criteria to a sample (e.g. n=100) of studies identified by the database searches. Decisions were discussed in a face to face meeting to ensure consistent application of criteria and the wording of draft inclusion and exclusion criteria was revised to reflect reviewer interpretation and judgement where necessary.

The revised inclusion and exclusion criteria were then independently applied to the title and abstract of each identified citation by two of three reviewers (MN, LS, SB). Disagreements were resolved through discussion. The full text of each source included after this stage was

retrieved where possible, and assessed using the same process. Items without an abstract were included for full text screening. Where full texts were not obtainable, studies were excluded. EPPI Reviewer (V.4.11.1.1, EPPI-Centre, London, UK) and Endnote (X8) software was used to support study selection.

2.4 Data extraction

Study data was extracted for each study by one reviewer and checked by a second (LS, MN). The role of first reviewer was shared equally between the two reviewers. This data included: study first author, title and date of publication; country where the study was conducted; study design; aims; research question(s) to which the study relates; relevant sample characteristics such as sample size, age, gender and level of education; ABI type, severity and participant recruitment methods and setting; details of any interventions and comparator, if relevant; details of independent variables, outcome measures and results obtained.

Given the heterogeneity expected in included studies, the results that were abstracted from papers included statements of which independent variables (e.g. patient characteristics, diagnostic characteristics or risk factors) were found to be associated with challenging behaviours and/or the potential need for treatment in a secure setting, as reported within the included studies. For studies evaluating the psychometric properties of tools to assess presence or risk of challenging behaviours, data were obtained that pertained to the psychometric properties of the tool, as highlighted in sample outcome tables in the COSMIN tool.[22]

Study design was categorised during data extraction. Where study design was unclear, we referred to guidance to aid our interpretation.[23]

2.5 Critical appraisal

Critical appraisal was undertaken alongside data extraction by one review and checked by a second (LS, MN), with disagreements resolved through discussion. Critical appraisal was used to inform the confidence which could be placed in findings arising from the synthesis and not to exclude studies from the review or from analyses.

We anticipated the inclusion of multiple study designs, therefore critical appraisal for randomised controlled trials (RCTs), controlled trials (CTs) observational cohort, cross-sectional and case-control studies was to use the relevant United States National Institute of Health (NIH) study quality assessment tool.[24] Studies were deemed to be of 'High' quality if they scored positively on 70% or above of items on the critical appraisal tool used. Studies were deemed to be of 'medium' quality if they scored positively on between 50% and 69% (inclusive) of critical appraisal items and of 'Low' quality if they scored positively on less than 50% of items on a critical appraisal measure. Systematic reviews were appraised using the AMSTAR-2 tool.[25]

Studies developing or evaluating psychometric tools were evaluated using the COSMIN Risk of Bias Checklist.[26, 27] Whilst this checklist is typically used for patient-reported outcome measures, it can be adapted for use with those rated by observers.[28] The COSMIN checklist was applied at the level of each individual study. The COSMIN tool allows the quality of evidence about psychometric studies to be summarised at a group level (i.e in the style of GRADE[29]) if enough tools measure the same constructs, or individually if not. We judged our approach based on the heterogeneity of included studies.

2.6 Synthesis methods

Observational cohort, cross-sectional and case-control studies

We tabulated sample characteristics and outcomes of critical appraisal of included studies and summarised narratively. Studies were then grouped according to the dependent variable being measured. These three groups were:

- Aggression
- Sexually Inappropriate Behaviour
- Other difficulties of emotional and/or behavioural regulation

Grouping was outcome-led, thus studies measuring multiple dependent variables could belong to more than one group. The purpose of these groupings was to facilitate the identification of independent variables associated with the occurrence of particular outcomes of interest.

The quality and findings of included systematic reviews were tabulated separately and described narratively.

A narrative synthesis was performed, consisting of the following stages:

- Forming groups of studies by outcome (aggression, sexually inappropriate behaviour, other difficulties)
- Tabulating studies within each group, identifying independent variables associated with increased risk of challenging behaviour/need for secure services
- Producing a description and narrative interpretation of the findings of studies, including identification of commonalities within each outcome group and explaining any inconsistencies where possible
- Producing overall interpretation of findings from the three subgroups, identifying any common threads or observations across studies.

The narrative synthesis was led by one reviewer and checked for sense and consistency by a second (MN, LS).

Psychometric studies and systematic reviews

Studies which focused on developing or evaluating the psychometric properties of measures of the outcome of interest were described narratively within the relevant group but the outcome of critical appraisal was summarised separately.

2.7 Stakeholder involvement

As an employee of NHS England and Improvement, AM has provided insight on the commissioning process and provided expertise ABI secure services. DD is a Consultant Forensic Psychiatrist and the Associate National Clinical Director Mental Health for NHS England.

We consulted with these two representatives from the National Specialised Mental Health Commissioning Team, NHS England (AM, DD) during the development of the research protocol, with particular input in identifying search terms for the bibliographic database search strategy and finalising inclusion criteria. They also supported the research team to

ensure that application of these inclusion criteria was consistent with their clinical and service delivery expertise, for example when clarifying study settings, and which studies measured behaviours that may indicate the need for secure services. These stakeholders provided comments on the background section of the draft report to ensure the context for this review was explained adequately, provided expert knowledge to help understand key concepts and terminology and supported the research team to group studies according to outcome prior to synthesis. AM also provided clinical context to the findings of this review, which informed the discussion section of this report.

2.8 Deviations from the protocol

'Dysexecutive Syndrome' was added to our outcomes of interest following discussion with stakeholders after registering our protocol. To clarify, the features of Dysexecutive Syndrome of interest to us, and thus those that have been included in our review, are disinhibition, lack of response suppression and emotional lability. Other features of dysexecutive syndrome were considered too far removed from challenging behaviours to be likely to influence the decision about need for treatment in a secure setting. Similarly, stakeholders also indicated that studies where the sole outcome was an Axis 1 or 2 disorder could be excluded from the review, as these needs would not necessarily indicate requirement for referral to specialist or secure services. Thus, we removed these constructs from the list of outcomes for inclusion in the review.

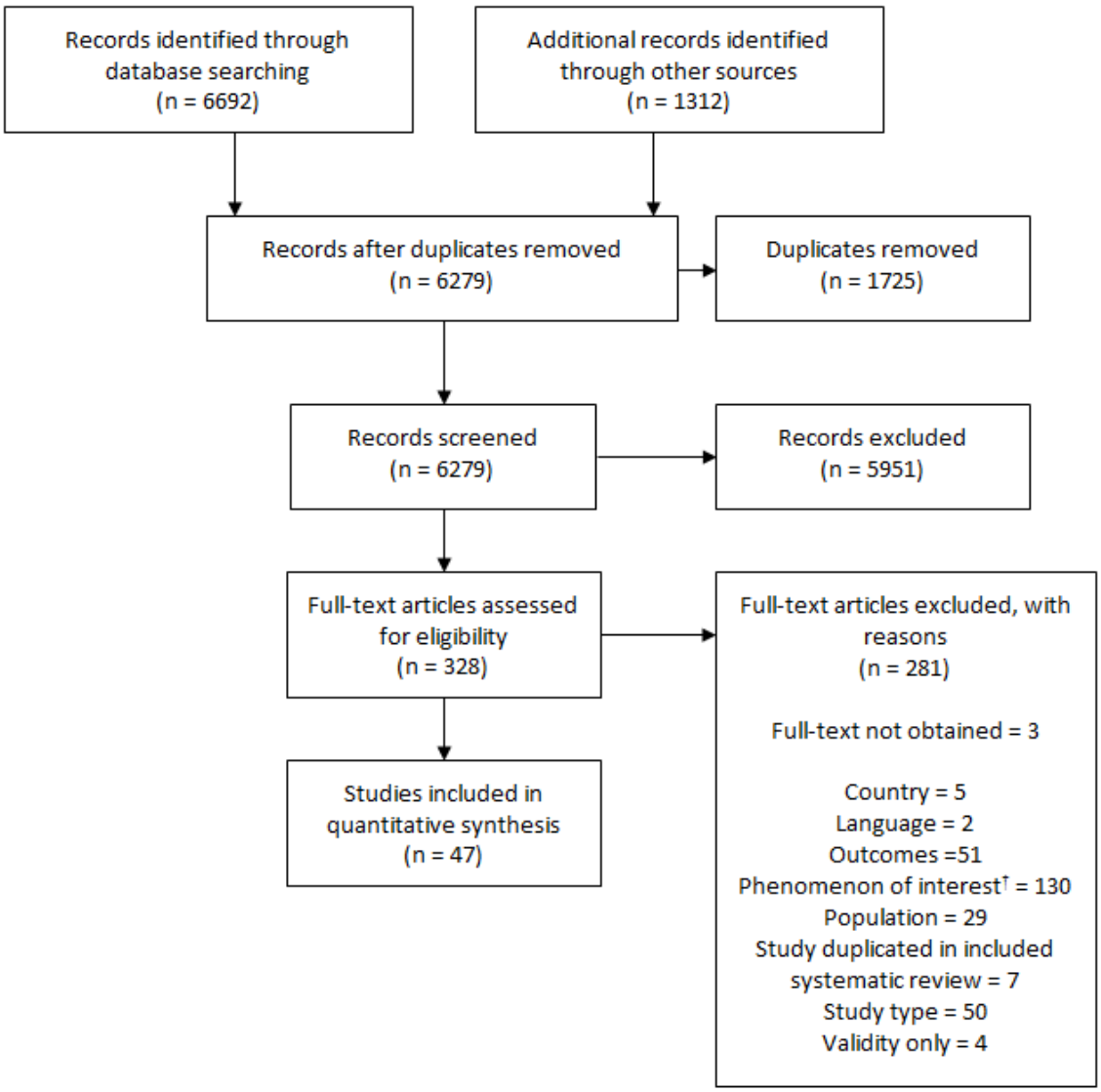
Completion of full text screening revealed that no studies had been located which were set in, or explicitly mentioned assessment for eligibility for treatment in a secure setting. After discussing with stakeholders the lack of includable studies that addressed our research questions directly, it was agreed that it would still be useful to synthesise studies which focused on identifying or assessing a diagnostic, symptom or risk characteristic which could be used to inform decisions about whether an individual with an ABI may benefit from secure services; that is, challenging behaviours. As such, our review focused solely on this indirect evidence, rather than evidence directly about referral pathways or decisions. The data extraction, critical appraisal and synthesis methods detailed in sections 2.4, 2.5 and 2.6 above reflect this decision.

3 Results

3.1 Study selection

The PRISMA diagram in Figure 1 summarises the study selection process. Bibliographic database searches identified 6692 records and supplementary searches identified 1312 records. Following the removal of duplicates there were a total of 6279 unique records (titles and abstracts) which were screened against our inclusion and exclusion criteria. The full texts of 328 articles were sought for further consideration. Of these, 325 full texts were successfully retrieved (99%). Following full text screening, 281 articles were excluded for the reasons specified in Figure 1. Almost half of the excluded papers were excluded due to criteria relating to the phenomenon of interest (n=130). Other common reasons for exclusion included outcomes not of interest (n=51), population not of interest (n=29) and study design (n=50). A smaller number of articles were excluded due to taking place in a non-high income country (n=5), non-English language publication (n=2) and psychometric studies which measured the validity of tools but not their reliability properties (n=4). The complete record of reasons for exclusion at full text screening is reported in Table S1 (See Report Supplementary Material File 1).

In total 47 studies were identified that met our inclusion criteria including 46 primary studies and one recent, high quality systematic review. No studies took place in secure settings, or explicitly evaluated a referral pathway that included a secure setting. Therefore all the remaining 47 studies were included on the basis of studying outcomes that may influence the decision about referring a patient to a secure rehabilitation setting, as outlined in section 2.2. The aforementioned recent, high quality systematic review that we identified was included alongside primary studies in our synthesis. This was a systematic review of psychometric studies evaluating tools assessing aggression.[28] We therefore excluded the individual studies they included which would have been otherwise duplicated in our review (n=7).



†Phenomenon of interest encompasses whether a study sought to establish the value of testing, assessment or patient classification procedures for predicting the needs of people with an ABI who may require support within a secure setting.

Figure 1. PRISMA flowchart

3.2 Sample characteristics

Country of publication and study design

The characteristics of the samples in the included primary studies are displayed in Table 1. Of the 46 articles included in the review, 14 were conducted in the USA,[30-43] 12 in the UK,[44-55] and 7 in Australia.[56-62] The remaining studies were conducted in Italy,[63-65] the Netherlands,[66-

[68] France,[69, 70] Norway,[71, 72] Canada,[73] Denmark[74] and Saudi Arabia.[75] All studies were published in peer-reviewed journals, except for the PhD theses by Kugel[38] and James.[47] Studies two and three (of four) in the PhD thesis by James were also later published in peer-reviewed journal articles.[48, 49]

There were more prospective studies than any other design (n=14),[44 41, 42, 47-49, 55, 56, 65, 68, 71, 72, 74, 75] with case control studies the next most common (n=12).[33-35, 43, 53, 54, 58, 61, 62, 64, 67, 73] There were 6 cross-sectional studies[37, 46, 57, 63, 69, 76] and 4 retrospective[30, 31, 40, 66] with one study described best as a retrospective cross-sectional study[45] and one a multi-group comparison.[36] There were 8 psychometric studies.[32, 38, 39, 50-52, 59, 70]

Recruitment method

Where reported, participants were most often recruited to studies through convenience sampling during a given time period as inpatients in hospitals or rehabilitation centres (n=27).[32, 34, 36, 38, 39, 41-45, 47-53, 56, 60, 61, 64, 67, 68, 70, 73 54, 55] Patient data were obtained through a national[30, 31, 40] or hospital[46, 57, 58, 62, 71, 72] database in 10 studies. It was unclear in 7 studies whether data were obtained contemporaneously or via database review.[46, 63, 65, 66, 69, 74, 75] The study by Chan et al was a post-hoc analysis of data from two previous studies.[33] In the studies by Francis et al[59] and Homaifar et al[35] outpatients were recruited following hospital database review and wider advertisement. Kois et al recruited through advertisement only.[37]

Population characteristics

Notable exclusion criteria were where included studies excluded patients with a history of psychiatric disorder or substance abuse (n=18),[57, 58, 63, 64, 71, 75 35, 36, 43, 53, 55, 66-70, 72, 73] or a significant level of neurocognitive or comprehension deficit (n=18).[33-36, 42, 43, 52-55, 57, 58, 63, 68, 69, 72, 73, 75]

In total, across the 46 studies, data for 6964 participants were presented, approximately 22% of whom were female, with a mean age of 38 years. Only one study, by Moreno et al, had more female than male participants.[73] Taking mean or median ages across individual studies, rather than the sample as a whole, age was approximately 40; the oldest sample had a mean age of 68,[33] and the youngest 24.[62] The median sample size was 104 (mean=153, range=14 to 1339); by far the largest sample was in Arango-Lasprilla et al, who accessed 1339 patient

records from a national database.[30] The smallest sample was the 14 participants recruited to the psychometric analysis by Simpson et al.[62] Study 4 within the thesis by James merged datasets from two previously reported studies (studies 2 & 3).[47]

Traumatic brain injury was the most common diagnosis of ABI, making up all (n=32)[30, 31, 34-43, 50, 51, 53-59, 62, 64-67, 70-75] or the majority (n=7)[44-49, 61] of the sample in 40 studies. Of the studies where TBI was not the dominant diagnosis, Kelly et al included a more mixed sample, 42% of whom had sustained a TBI, 22% suffering a cerebrovascular accident and 9% an alcohol-related brain injury;[60] Simblett et al recruited 94% of participants with non-traumatic brain injury;[52] Visscher et al included participants with TBI (18%), cerebrovascular accident (25%), hypoxia (16%) and other aetiologies;[68] and three studies focused on stroke patients.[33, 63, 69] Details of the sample were not presented by Bogner et al.[32] Time since injury was highly varied, ranging from within two weeks[41] to 24 years,[35] but was unreported in 11 studies.[31, 32, 37, 38, 50, 51, 56, 61, 67, 69, 75]

Table 1. Characteristics of the included sample

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
Alderman (2002);[44] UK; Prospective; JAP	**Aims**: Demonstrate contribution of the Overt Aggression Scale-Modified for Neurorehabilitation to clinical audit and applied research **Outcomes**: Aggression	**n**=47; **Female**=15.2%; **Age**=34.7(10.7)[17-60] years; **Time since injury**= 97 months (NR) [13 months-32 years]; **Education**: NR	**M**: Observation of inpatients; **L**: Inpatient neurobehavioral service; St Andrew's Hospital; **E**: *Include* severe ABI	**Type**: 67.4% closed injury; 13% anoxia; 10.9% CV accident; 4.3% herpes simplex encephalitis. **Severity**: All patients at least 'severe' on GCS (8 or less when first seen in hospital) or PTA (24hrs or more). **Comorbidities**: NR
Alderman (2007);[45] UK; Retrospective cross-sectional; JAP	**Aims**: Describe characteristics and determinants of observed aggressive behaviour **Outcomes**: Aggression	**n**=108; **Female**=18.0%; **Age**=37.7 (11.6) [17-64] years; **Time since injury**= 106.4 months (NR) [0.5 -38 years]; **Education**: NR	**M**: Routine data collected as part of normal clinical activity, combined with that from previous study by Alderman et al 2002; **L**: St Andrew's Hospitals; **E**: *Include* severe ABI	**Type**: 64.8% closed injury. Of the remainder, 12.4% anoxia; 8.3% CV accident;5.7% viral infection; n=4 unknown. **Severity**: All patients at least 'severe' on GCS (8 or less when first seen in hospital) or PTA (24hrs or more). **Comorbidities**: NR
Aldossary (2019);[75] Saudi Arabia; Prospective cohort; JAP	**Aims**: Identify radiological and clinical factors associated with functional capacity one year after traumatic brain injury **Outcomes**: Aggression, disinhibition	**n**=251; **Female**=23%; **Age**=40.0 (8.6) [NR] years; **Time since injury**= NR; **Education**: NR	**M**: Data from registered cohort of patients with severe head trauma from 01/01/2014 to 1 January 2018; **L**: Accident departments of three regional hospitals; **E**: *Include* patients aged 18-60 with severe head trauma; performance of an MRI in the first month after head injury. *Exclude* patients with: history of psychiatric disorders, drugs or substance abuse, neurocognitive deficits, prior head trauma, signs of brain death at admission, CT or MRI evidences of gross intracranial lesion, neurosurgical intervention	**Type**: TBI (Traffic: 74%, Fall: 17%, Other: 9%, Pupillary abnormality: 12%). **Severity**: GCS score 8=20%; 7=15%; 6=7%; 5=7.6%; 4=12%; 3=38%; Duration of loss of consciousness (hours)=46.7 (20), PTA (weeks)=5 (2.8). **Comorbidities**: NR
Angelelli (2004);[63] Italy;	**Aims:** Characterise neuropsychiatric symptomatology	**n**=124; **Female**=29.0%; **Age**=60.7 (11.9) years;	**M**: Consecutive admissions to various hospital units from May 1998 to December	**Type**: Stroke (right hemisphere lesion: 57%, left hemisphere lesion:

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
Cross-sectional; JAP	and its evolution in a large group of post-stroke patients during their first year **Outcomes**: Agitation, disinhibition	**Time since injury**= All patients were hospitalised at 2 months, 20% at 6 months, and 10% were in-patients 1 year post-stroke; **Education**: 8.9 (3.9) years[a]	2001; **L**: Multiple hospitals; **E**: *Include* Unilateral cerebral ischemic stroke. *Exclude* patients with bilateral lesions, previous stroke, non-cerebral involvement, surgical patients, chronic disabling pathologies or other central nervous system diseases, prior psychiatric/substance abuse histories, anosognosia, severe comprehension deficit and cognitive decline. Patients taking psychotropic drugs (antidepressants or tranquilisers) were not excluded	43%). **Severity**: NR. **Comorbidities**: NR
Arango-Lasprilla (2012);[30] USA; Retrospective; JAP	**Aims:** Investigate whether White, African American and Hispanic individuals with TBI express differences in neurobehavioral symptoms at 1 year post-injury **Outcomes**: Aggression	**n**=1339; **Female**=27.2%; **Age**=38.3 (15.8) [18-89] years; **Time since injury**=1 year; **Education**: Less than high school=24.3%, high school/GED/trade=38.3 %, more than high school=37.4%	**M**: national database of the National Institute on Disability and Rehabilitation Research-funded TBIMS programme; **L**: NR (nationwide); **E**: *Include:* Presence of TBI, race/ethnicity self-reported as White, African American or Hispanic; aged 18+ at injury; injured between 1996 and 2001; NFI information taken during 1-year follow-up	**Type**: TBI (non-violent=88.1%, violent=11.9%). **Severity**: Mild (GCS >12)=33.3%; moderate (GCS 9-12)=16.3%; severe (GCS 8 or below)=50.3%. **Comorbidities**: NR
Baguley (2006);[56] Australia; Prospective cohort; JAP	**Aims**: Assess prevalence and predictors of aggressive behaviour among TBI survivors **Outcomes**: Aggression	**n**=261; **Female**=21.5%; **Age**=34.3 (14) years; **Time since injury**=NR ; **Education**: 11 (2.5) years[b]	**M**: 261 of 319 consecutive admissions were approached; **L**: specialised brain injury rehabilitation service of a tertiary referral hospital; **E**: NR	**Type**: TBI (motor vehicle related=66%, falls=17%, assault=12%, sport/other=5%). **Severity**: GCS mild=15%, moderate=17%, severe=68%; PTA=46.8 (27) days; PTA severity=96.4% ≥7 days; Median discharge GOS=2. **Comorbidities**: 9.7% psychiatric history, 9.8% alcohol abuse history
Bertisch (2017);[31]	**Aims:** Characterise and compare	**n**=210; **Female**=20.1%;	**M**: Moderate or severe TBI, enrolled in the	**Type**: Firearm injury (assault=84%,

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
USA; Retrospective; JAP	subgroups of survivors with assault-related versus self-inflicted TBI via firearms at inpatient rehabilitation and at 1-, 2-, and 5-year follow-up **Outcomes**: Risk to self (e.g. suicidality) or others	**Age**=29.9 (12.2) years[c]; **Time since injury**= NR; **Education**: No education=54%, high school diploma=33%,[d] associate's degree=7.8%, bachelor's degree=4%	TBIMS national database; **L**: NR; **E**: Inclusion criteria for the TBIMS database include (1) the presence of TBI of at least moderate severity; (2) GCS score of <13 on emergency department admission; (3) aged 16 years at the time of injury; (4) admission to a TBIMS acute care hospital before 72 hours post-injury; (5) participation in comprehensive rehabilitation at a TBIMS-designated brain injury inpatient program; and (6) informed consent provided by the patient or legal guardian. Individuals were selected from the NDB for inclusion in the current study if (1) the aetiology for the index injury was secondary to a firearm; and (2) the data regarding the mechanism of the FI-related TBI (i.e., assault vs self-inflicted) was available.	self-inflicted=16%). **Severity**: GCS=9.3 (4.3). **Comorbidities**: Preinjury drinking: abstaining=41%, light=16%, moderate=22%, heavy=20%; Lifetime psychiatric hospitalisations (yes)=9.3%; Lifetime suicide attempts (yes)=14%
Bogner (2000);[32] USA; Psychometric; JAP	**Aims**: Evaluate measurement properties of the Agitated Behaviour Scale using rating scale analysis; **Outcomes**: Agitated behaviour	**n**=106; **Female**=NR; **Age**=NR; **Time since injury**=NR; **Education**: NR	**M**: Inpatients receiving rehabilitation; **L**: NR; **E**: NR	**Type**: NR. **Severity**: NR. **Comorbidities**: NR
Borek (2001);[46] UK; Cross sectional; JAP	**Aims**: Investigate if an association exists between evidence of laterality of brain injury and neuropsychiatric symptoms in patients with non-penetrating brain injuries **Outcomes**: Aggression	**n**=98[e]; **Female**=23%; **Age**=41 [17-70] years; **Time since injury**=44% six months or less; **Education**: 24% educated beyond 16	**M**: Reviewed records of all patients with a non-penetrating brain injury referred to, and seen at, the Lishman brain injury unit between 1 August 1997 and 1 August 1999; **L**: Lishman brain injury unit, Maudsley Hospital, London; **E**: Cases with diffuse or bilateral injury were excluded (n=31)	**Type**: TBI=67%, anoxic=14%, stroke=11%, infection=5%, post-surgery=3%; 35% right-sided injury, 34% left-sided injury, 32% diffuse or bilateral injury. **Severity**: 47% severe ABI; 58% GCS<9; 80% unconscious >24 hours; 80% PTA >1 week. **Comorbidities**: Family history of

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
				psychiatric illness=18%, history of alcohol misuse=34%, previous brain injury=10%
Chan (2006);[33] USA; Case control; JAP	**Aims**: Examine, in a post hoc analysis of an antidepressant treatment trial, correlates of irritability and aggression after stroke and changes in irritability scores associated with antidepressant treatment **Outcomes**: Aggression	**n**=104; **Female**=36%; **Age**=68 (12.1) [NR] years; **Time since injury**=44.7 (12.7) days; **Education**: 12 (2.6) years[f]	**M**: Post-hoc analysis of patients from 2 previous studies; **L**: Younkers Rehabilitation Centre of the Iowa Methodist Medical Centre in Des Moines (n=89), the University of Iowa Hospitals and Clinics in Iowa City (n=1), and the Veterans Affairs Medical Centre in Iowa City (n=2). **E**: *Include* aged 18-85, with acute stroke within past 6 months. *Exclude* if: medical condition that was life-threatening or would interfere with recovery; severe comprehension deficit resulting from decreased consciousness, dementia, or aphasia; history of previous head injury or previously diagnosed brain disease other than stroke	**Type**: Stroke; infarction=88.1%, haemorrhage=11.9%; Left hemisphere=34.8%, right hemisphere=58.7%, brainstem/other=6.5%. **Severity**: NR. **Comorbidities**: History of alcohol abuse=8.7%, psychiatric history=15.2%, family psychiatric history=22%, major depression=28.3%, minor depression=11%, general anxiety disorder=14%
Ciurli (2011);[64] Italy; Case control; JAP	**Aims**: Quantify and characterise neuropsychiatric disorders following severe TBI using the Neuropsychiatric Inventory: (a) to obtain a comprehensive description of psychiatric disorders and (b) to study the clinical variables that predict the development of emotional and behavioural disorders after severe TBI **Outcomes**: Agitation, aggression, disinhibition	**n**=120; **Female**=25.8%; **Age**=31.3 (12.7) [15-64] years; **Time since injury**= Chronicity (months): 10.6 (15.1) [1-73], Time from injury (days): 22.4(17.0)[0-80]; **Education**: 11 (3.5) [3-18] years	**M**: patients in rehabilitation programs; **L**: Santa Lucia Foundation (Rome, Italy) and the Department of Neuroscience, Rehabilitation Hospital (Ferrara, Italy); **E**: *Include* if diagnosis of severe TBI, medically documented by CT or MRI data; Levels of Cognitive Functioning Scale score of 4 or more; age 15+ at time of injury; >30 days since injury; provision of informed consent. *Exclude* if a history of alcohol or drug abuse, psychiatric or neurological diseases prior to the severe TBI; taking antipsychotic, antidepressant, or anxiolytic	**Type**: TBI; n=46 pure diffuse axonal injury, n=38 focal unilateral or bilateral lesions, n=36 diffuse axonal injury with unilateral or bilateral focal lesions. **Severity**: NR. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
			drugs	
Draper (2007);[57] Australia; Cross-sectional; JAP	**Aims**: Investigate the association of psychosocial outcome 10 years following traumatic brain injury with demographic variables, injury severity, current cognitive functioning, emotional state, aggression, alcohol use and fatigue **Outcomes**: Aggression	**n**=53; **Female**=45%; **Age**=41.6 (13) [26-74] years; **Time since injury**= 10.6 (0.7) [10-12] years; **Education**: NR	**M**: Head injury database of Epworth Hospital where they had received rehabilitation between 1992 and 1995; **L**: Community based; **E**: *Exclude* if <16 at time of injury, sustained a subsequent head injury, hospitalised for psychiatric illness, hearing, vision or physical impairments that interfered with testing, insufficient English. Had to nominate an appropriate significant other to participate in the study	**Type**: TBI, 96% motor vehicle accidents. **Severity**: GCS (based on n=39)=7.54 (4.33) [3-15], 20% scoring 13-15, 13% scoring 9-12, 67% scoring 3-8; PTA=26.8 (24.8) [0.1-99) days. **Comorbidities**: NR
Draper (2008);[58] Australia; Case control; JAP	**Aims**: Investigate cognitive impairment 10 years following TBI. Examine which cognitive measures most accurately differentiate TBI individuals from controls. Examine association of specific cognitive impairments with injury severity **Outcomes**: Disinhibition	**n**=60; **Female**=45%; **Age**=42.0 (13.1) years; **Time since injury**= 10.6 (0.7) [10-12] years; **Education**: 12.1 (2.8) years	**M**: Head injury database of the hospital where they had received rehabilitation between 1992 and 1995; **L**: NR; **E**: *Exclude* if <16 at time of injury, sustained a subsequent head injury, hospitalised for psychiatric illness, hearing, vision, or physical impairments that interfered with testing, insufficient English.	**Type**: TBI, CT scans: n=10 normal, n=3 skull fracture only, n=2 diffuse axonal injury, n=1 subarachnoid haemorrhage, n=42 multiple focal lesions. Of those with focal lesions, 34 had frontal lesions on the right (n=10), left (n=5), and bilaterally (n=19); some also had lesions extending posteriorly (n=7), medially (n=4), and temporally (n=5), and evidence of skull fracture (n=16). Focal lesions were confined to the temporal, parietal, or occipital regions only for 8 participants, some with evidence of skull fracture (n=4). **Severity**: GCS (based on n=45)=7.4 (4.3) [3-15], 20% scoring 13-15, 13% scoring 9-12, 67% scoring 3-8. PTA=26.3 (24.7) [0.1-99] days, 36% having PTA <7 days, 22% PTA 1 to 4

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
				weeks, 42% PTA >4 weeks. **Comorbidities**: NR
Finnanger (2015);[71] Norway; Prospective; JAP	**Aims:** Investigate long-term executive, emotional, and behavioural function after moderate-to-severe TBI. Explore association between demographic, injury-related, psychological, global outcome, and neuropsychological factors and later problems **Outcomes**: Behavioural dysregulation, executive function, aggression	**n**=95; **Female**=28%; **Age**=29 (NR) [15-63] years[c]; **Time since injury**= 2.9 (0.9) [2-5] years[h]; **Education**: 12 (NR) [9-18] years	**M**: Members of database contacted between February 2009 and August 2010; **L**: Department of Neurosurgery at St. Olavs Hospital, Trondheim, Norway; **E**: Include if moderate and severe TBI, >one year after injury, 15-65 at time of injury, fluent in Norwegian, GOSE ≥5 at time of assessment. *Exclude* if ongoing or preinjury substance abuse, neurological or psychiatric conditions, previous moderate-to-severe TBI	**Type**: TBI; traffic accident=49%, fall=40%, ski accident=3%, other=9%. MRI findings: Extradural haematoma only=2%, pure TAI=25%, cortical contusions=24%, cortical contusions/TAI=45%. **Severity**: GCS median = 9 [IQR 7]; HISS grade, moderate TBI=58%; PTA <1 week=55%. **Comorbidities**: NR.
Francis (2017);[59] Australia; Psychometric; JAP	**Aims:** Describe the reliability and validity of the Social Skills Questionnaire for Traumatic Brain Injury **Outcomes**: Emotional dysregulation	**n**=51; **Female**=19.6%; **Age**=47.2 (14.0) [18-70] years; **Time since injury**= 12.4 (10.0) [1-46]; **Education**: 12.9 (2.41)[i] [9-22] years	**M**: Recruited from the outpatient records of three Sydney metropolitan brain injury units, as well as advertisements through acquired brain injury units and online brain injury associations; **L**: Sydney, Australia; **E**: Relatives of adults who had sustained severe TBI. Family members had to have had a severe TBI, be discharged from hospital and living in the community and be proficient in English.	**Type**: TBI; car accidents=50%, falls=26%, motor bike accidents=8%, assault=6%, other=12%. **Severity**: PTA 69.5 (54.7) [2-279] days. **Comorbidities**: NR.
Greve (2001);[34] USA; Case control; JAP	**Aims:** Characterise demographic, injury-related, and pre-morbid behavioural characteristics in TBI patients who are an aggression risk. Determine if TBI patients who display impulsive aggression demonstrate personality style and patterns of neurocognitive deficits	**n**=45; **Female**=8.9%; **Age**=36.0 (9.5) years; **Time since injury**= 11.2 (6.3) years; **Education**: 12.0 (1.8) years	**M**: Cases identified through interviews with the client, staff, and a review of records; **L**: Multidisciplinary residential brain injury rehabilitation facility; **E**: *Include* in impulsive aggressive group if persistent, uncontrolled loss of temper (impulsive aggression) within 3 months of evaluation. The non-aggressive control group had never	**Type**: TBI. **Severity**: Severe. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
	similar to those seen in other impulsive aggressive groups **Outcomes**: Aggression		had any episodes of aggression whilst resident at the facility. All clients were in the chronic phase (minimum time post-injury >20 months) and had been in the programme at least 6 months. *Excluded* if problems with temper control existed had resolved more than 3 months prior to study onset; severe language or motor deficits; non-native English speaker. No clients excluded for being too volatile	
Harmsen (2004);[66] Netherlands; Retrospective; JAP	**Aims:** Investigate the association of post-traumatic amnesia with positive behavioural disturbances in an historic cohort of patients with severe TBI **Outcomes**: Positive behavioural disturbances	**n**=60; **Female**=20%; **Age**=37 (NR) [21-70] years; **Time since injury**=7 (NR) [4-20] weeks; **Education**: NR	**M**: Adult TBI inpatients admitted September 1996 to January 2002 were identified by consultation of the hospital registration system; **L**: Rehabilitation centre, Nijmegen, Netherlands; **E**: *Include* if age >20 at time of admission for severe TBI. *Exclude* if history of psychiatric or behavioural problems prior to brain injury or not in stable medical condition	**Type**: TBI. **Severity**: Severe; GCS=6 [3-13], PTA 10 [5-24] weeks. **Comorbidities**: NR
Homaifar (2012);[35] USA; Case control; JAP	**Aims:** Explore the relationship between executive dysfunction and suicidal behaviour in two groups of participants: veterans with TBI and a history of suicide attempt; veterans with TBI and no history of suicide attempt **Outcomes**: Executive functioning	**n**=47; **Female**=6%; **Age**=51.2 (9.8) [29-75] years; **Time since injury**=23.5 (14.9) [1-63] years; **Education**: NR	**M**: Identified on database, contacted via letter. Also recruited from inpatient and outpatient mental health clinics via flyers and presentations; **L**: Mountain state VA Medical Centre; **E**: *Include* if age 18–74, diagnosis of TBI. *Exclude* if diagnosis of schizophrenia; history of neurologic disease other than TBI; current substance abuse; inability to provide informed consent; significant hearing impairment; Computerized Assessment of Response Bias, Type III/IV or Test of Memory	**Type**: TBI. **Severity**: Mild=23%, mild-moderate=9%, moderate=11%, moderate-severe=4%, severe=53%. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
			Malingering score of lower than 50%; guardianship within the past 6 months	
James (2012, study 2/2013);[47, 49] UK; Prospective; D, JAP	**Aims:** Explore relationship between aggression and inappropriate sexual behaviour following ABI. Investigate predictive nature of clinical variables for each category of behavioural disturbance **Outcomes**: Aggression, inappropriate sexual behaviour	**n**=152; **Female**=25%; **Age**=Median: 39 (NR) [16-72] years; **Time since injury**=Median: 12 (NR) [2-468] months; **Education**: Median 10 (NR) [8-15] years	**M**: Clinical records scrutinised for routine observations; **L**: Post-acute neuro neurobehavioral brain injury rehabilitation centre during 2004-2009; **E**: *Include* if able to complete full six factor structure of Wechsler adult intelligence scale and Wechsler Memory scale. *Exclude* if too severely physically, cognitively or language-impaired testing, recently assessed prior to admission, ongoing civil litigation assessments taking priority, test results unable to be located, not fluent in English	**Type**: TBI=66%, of which road traffic accidents=53%, falls=28%, assaults=15%, combat-related injuries=3%; Non-traumatic=34%, of which cerebrovascular=16% (16% of which haemorrhagic in nature, 29% occlusive, 4% radiation-induced vasculitis), cerebral anoxia=9% (50% cardiac arrest, 21% drug overdose, 14% hypoglycaemic coma, 7% attempted hanging), 9% other (tumour, encephalitis, Wernicke's encephalopathy, 8% toxic solvent abuse, 8% acute pontine myelinolysis). **Severity:** For TBI patients (for n=60 with GCS data): severe=78%, moderate=10%, mild=12%; (for n=70 with PTA data) extremely severe=76%, very severe=21.4%, severe=2.9%, moderate and mild=0%. **Comorbidities**: NR
James (2012, study 3/2015);[47, 48] UK; Prospective; D, JAP	**Aims:** Replicate the statistical distinctions between verbal aggression, physical aggression and inappropriate sexual behaviour with the BARS and a newly available observational tool designed for recording inappropriate sexual	**n**=301; **Female**=22%; **Age**=42.7 (14.6) [16-76] years (age at time of injury=39.7 (16.8) [1-75] years); **Time since injury**=3 years; **Education**: Median 10	**M**: Recruited from admissions during January 2010-June 2012; **L**: Seven organisational residential rehabilitation programmes across UK, two specialised in challenging behaviour, five classed as community reintegration; **E**: Completed at least 9 weeks of residential neurobehavioral	**Type**: TBI=56% (road traffic accident=26%, falls=16%, assaults: n=34, combat-related=1%, other=2%); cerebrovascular accidents=22% (occlusive=11%, haemorrhagic-type=10%); anoxia=11% (cardiac arrest most

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
	behaviour after brain injury **Outcomes**: Aggression, inappropriate sexual behaviour	(NR) [6-18] years	assessment, which included continuous behavioural observation and recording, needed to have had each of the specified psychometric measures completed on admission	common=5%); other=11% (infectious diseases=5%, cerebral tumour=2%, alcohol-related brain damage=1%). **Severity**: Lowest GCS prior to sedation (n=126): median=5 [3-15]; PTA(days) median=70 [1-500]; abnormal neuroimaging reported in (96.3%); neurosurgery in the acute stage required for 43.5%. **Comorbidities**: Prior significant brain injury=13%; previous psychiatric illness=19%; history of aggression leading to a criminal conviction=9%; convicted of a sexual offence=1%;.pre-injury substance misuse=38%. 72.7% were taking at least one medication (anti-depressants=38%, anti-convulsants=46%, anti-psychotics=20%, anxiolytics=9%)
James (2012, study 4);[47] UK; Prospective; D	**Aims**: To explore if additional neuropsychological tests of executive function account for additional variance in the probability of having exhibited verbal or physical aggression or inappropriate sexual behaviour in patients included in studies 2 and 3 **Outcomes:** Aggression, inappropriate sexual behaviour	**n**=86; **Female**=19%; **Age**=Median: 35 years (at time of injury=34 years); **Time since injury**= NR; **Education**: Median 10 years	**M**: Subset of 453 participants from combined data sets from studies 2 and 3 (James); **L**: [As above]: **E**: [As above]	**Type**: TBI: 66%, non-TBI: 34%. **Severity**: Median GCS (for n=43) =5; median PTA (for n=37)=70. **Comorbidities**: NR
Johansson	**Aims:** Determine: frequency and	**n**=67; **Female**=40.3%;	**M**: Case review of consecutively evaluated	**Type**: TBI; 54% primarily right

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
(2008);[36] USA; Multiple group comparison; JAP	severity of aggressive behaviours in TBI outpatients; whether the clinical rating of anger severity was valid and consistent with a psychometrically-based anger scale; what pre-morbid factors potentially contribute to the emergence of anger and aggression in TBI patients; what comorbid emotional, physical, cognitive and quality-of-life factors negatively impact TBI patients **Outcomes**: Aggression	**Age**=40 (15.6) years; **Time since injury**= 25.1 (18.8) months; **Education**: 14.5 (3.0) years	TBI patients; **L**: Neuropsychology office in San Francisco; **E**: *Exclude* if age <16; testing not administered in English due to disputed proficiency; questionable effort on the Test of Memory Malingering; significant pre-morbid neurological history; pre-morbid psychiatric hospitalisation history; history of a pre-morbid TBI; atypical responses on RNBI validity scales; presence of severe sensory limitations; excessive time interval between injury and evaluation	hemisphere, 23% left hemisphere, 23% bilateral damage. Temporal and frontal regions most often compromised (81%). No penetrating brain injuries. **Severity**: 73% mild TBI; 27% moderate to severe TBI. **Comorbidities**: NR
Kelly (2008);[60] Australia; Cross sectional; JAP	**Aims:** Examine behaviour profiles of clients with ABI referred to a community-based behaviour management service. Determine whether behavioural profiles are related to aetiology of ABI **Outcomes**: Aggression, inappropriate sexual behaviour	**n**=190; **Female**=20.5%; **Age**=36.5 (14.3) [0-63.6] years; **Time since injury**= 8.7 (9.6) [0.1-41.3] years; **Education**: NR	**M**: Review of cases referred to an ABI Behaviour Consultancy for assessment and treatment of challenging behaviours; **L**: ABI Behaviour Consultancy, Victoria, Australia; **E**: *Include* non-degenerative brain injury, overt challenging behaviours, aged 18-65	**Type**: TB=41.6%, CV accident=21.6%, alcohol related=8.9%, hypoxic=12.1%, tumour=7.9%, other=7.9%. **Severity**: NR. **Comorbidities**: NR
Kerr (2011);[61] Australia; Case control; JAP	**Aims:** To obtain a profile of those patients with ABI who were aggressive, compared to those with ABI who were not aggressive and clarify the factors which are associated with aggression **Outcomes**: Aggression	**n**=64; **Female**=16%; **Age**=34.0 (16.8) [17-75] years; **Time since injury**= NR; **Education**: NR	**M**: Aggressive group: identified by reports by nursing and ward staff to the researchers. Non-aggressive group identified by review of admission lists; **L**: Two neuroscience wards of a metropolitan tertiary hospital in Brisbane, Australia; **E**: Aggressive group: aggressive once or more during hospitalisation. Non-aggressive group: absence of aggression during admission. *Exclude* patients without brain injury	**Type**: TBI=67.2%, non-TBI=32.8%. **Severity**: NR. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
Kois (2018);[37] USA; Cross-sectional; JAP	**Aims:** Explore neuropsychological correlates of self-reported impulsivity and maladaptive behaviour among Iraq/Afghanistan-era veterans with TBI and PTSD **Outcomes**: Impulsiveness	**n**=116; **Female**=12%; **Age**=37.7 (11.5) [18-71] years[j]; **Time since injury**= NR; **Education**: 14.7 (1.8) [12-20] years	**M**: Recruitment via email, listserves, flyers, and conference tables from January 2012 to February 2016; **L**: VA and non-VA medical centres and clinics, Vet Centres, veterans' organisations at local universities and colleges, state-wide organisations serving military families and veterans in the Southeast USA; **E**: *Include* if aged 18-65, served in the military after October 2001, diagnosed with TBI and PTSD	**Type**: TBI; mean number of TBIs 2.6 (1.2) per person. **Severity**: NR. **Comorbidities**: PTSD
Kugel (2015);[38] USA; Psychometric; D	**Aims:** Investigate the benefit of using the Mayer Salovey Caruso Emotional Intelligence Test to assess emotional processing deficits in adults with moderate to severe TBI **Outcomes**: Emotional regulation	**n**=22; **Female**=23%; **Age**=45.2 (10.3) [18-55] years; **Time since injury**=NR; **Education**: 10.9 (2.1) years	**M**: NR; **L**: Outpatient substance abuse unit in Blue Hills Substance Service (BHSS), Connecticut Department of Mental Health & Addiction Services' inpatient TBI unit, Connecticut Valley Hospital; **E**: *Excluded* Participant exclusion criteria included: court-mandated clients and non-English speakers	**Type**: TBI; 59% right hemisphere, 41% left hemisphere. **Severity**: Moderate to severe. **Comorbidities**: NR
McKeon (2017);[39] USA; Psychometric; JAP	**Aims:** Develop a novel tool for measuring behavioural dysregulation in adults with TBI using objective data sources and real-world application and provide preliminary evidence for its psychometric properties **Outcomes**: Behavioural dysregulation	**n**=14; **Female**=28.6%; **Age**=40.5 (3.3) [NR] years; **Time since injury**=19.7 (9.3) [NR] months; **Education**: NR	**M**: Non-experimental convenience sampling; **L**: Local brain injury rehabilitation centre; **E**: *Include* if receiving rehabilitation services, experienced behavioural challenges during daily living, not receiving treatment for a primary psychiatry condition.	**Type**: TBI; motor vehicle accident as pedestrian=28.6%, motor vehicle accident as driver=50%, fall=21.4%. **Severity**: NR. **Comorbidities**: NR
Mazzini (2003);[65] Italy; Prospective; JAP	**Aims:** Detect the incidence and risk factors for posttraumatic epilepsy (PTE) in rehabilitation patients; to define the influence of PTE for late	**n**=143; **Female**=17.5%; **Age**=32.3 (15) [11-79] years[c]; **Time since injury**=55.5 (33.5) [11-	**M**: Consecutive admissions between January 1994 and January 2000 for post-injury rehabilitation; **L**: Inpatient Rehabilitation Clinic of Veruno, Italy; **E**: *Exclude* if had	**Type**: TBI; mainly traffic accidents, penetrating injury=3%. **Severity**: Severe TBI; coma of 6 hours or more, GCS at injury=5.5 (2.5) [3-10],

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	clinical and functional outcome; to assess the cognitive and behavioural features of patients with PTE **Outcomes**: Disinhibited behaviour, agitation, aggression	180] days; **Education**: NR	neurologic deficits before trauma	duration of coma=32.2 (37) [1-180] days. **Comorbidities**: Drug abuse: 9%, alcohol abuse: 10%
Miles (2020);[40] USA; Retrospective; JAP	**Aims:** Examine the relationship between staff perceived irritability, anger, and aggression and PTSD in veterans with TBI **Outcomes**: Aggression	**n**=240; **Female**=6%; **Age**=(quartiles) 23; 29; 43 years; **Time since injury**= (quartiles) 58; 84; 135 days [k]; **Education**: High school diploma or less=38%, more than high school diploma=62%	**M**: Enrolled in VA TBIMS National Database; **L**: 1 of 5 VA Polytrauma Rehabilitation Centres (Richmond, VA; Tampa, FL; Minneapolis, MN; Palo Alto, CA; and San Antonio, TX); **E**: *Include* if 18 years or older, enrolled and discharged between 2010 and 2018. *Exclude* if not referred for polytrauma rehabilitation	**Type**: TBI; vehicular=54.3%, fall=17.6%, violence penetrating=5%, violence blast=0%, other=23.1%, injured during deployment=12.5%. **Severity**: Mild=9.9%, moderate=4.9%, severe=79%. **Comorbidities**: NR
Moreno (2018);[73] Canada; Case control; JAP	**Aims:** Explore the relationships between risky sexual behaviour, executive functions, and mental health in individuals with TBI **Outcomes**: Inappropriate sexual behaviour	**n**=42; **Female**=54.8%; **Age**=37.9 (9.7) years; **Time since injury**= 3.3 (4.3); **Education**: 12.8 (3.3) years	**M**: Recruited from a major rehabilitation centre; **L**: Rehabilitation centre in Montreal, Canada; **E**: *Include* individuals who have sustained a mild, moderate or severe TBI; who are six or more months post-injury; 18 years or older; fluent in French or English. *Exclude* if history of learning or language disability, including aphasia or communication disorders; pre-injury psychiatric, sexual or neurological disorders; diagnosis of substance abuse or substance dependence	**Type**: TBI, motor vehicle accident=42.9%, work and sports-related accidents=14.3%. **Severity**: mild=66.8%, 42% of which classified as "complex" mild TBI (e.g., with positive brain abnormality on CT scan). Loss of consciousness in 50%, PTA documented in 47.6%. GCS score at admission=12.5 (3.6), loss of consciousness= 5.8 (28.8) hours, PTA=80.8 (203.8) hours. **Comorbidities**: Recreational drug use=23.8%
Rao (2009);[41] USA; Prospective; JAP	**Aims:** Examine aggression in the first 3 months of TBI and characterise its severity and	**n**=107; **Female**=38.8%; **Age**=42.6 (17.7) [NR] years; **Time since**	**M**: NR; **L**: Acute trauma unit of Johns Hopkins Hospital and the Brain Injury (rehabilitation) unit of Kernan Hospital,	**Type**: Closed head injuries; motor vehicle accident=53.7%, falls=22.4%, assaults=22.4%. **Severity**: Mild TBI

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	association with psychiatric diagnoses in adults with first time closed-head injury **Outcomes**: Aggression	**injury**=First assessment within two weeks of trauma.; **Education**: 13.1 (2.9) [NR] years[l]	University of Maryland; **E**: *Include* if able to give informed consent; confirmed TBI; age ≥ 18, admission to the hospital for evaluation of head trauma. *Exclude* if prior TBI; open-head injury; history of any other type of brain illness	(GCS score of 13-15)=59.7%, moderate TBI (GCS score 9-12)=13.4%, severe TBI (GCS score <9)=26.9%. **Comorbidities**: 9% had a poor health (several unstable medical problems), 21% had fair health (more than one unstable medical conditions and/or several stable but chronic medical problems), 40% had good health (one unstable medical problem or few stable medical problems), 30% had excellent health (no current unstable medical problems)
Roussel (2016);[69] France; Cross sectional; JAP	**Aims:** Characterise the executive dysfunction profile in stroke. Examine the dysexecutive pattern according to stroke subtype. Examine the sensitivity of the harmonisation standards protocol **Outcomes**: Dysexecutive difficulties (Including Sexually Inappropriate Behaviour)	**n**=237; **Female**=48%; **Age**=48.7 (15.8) [NR] years; **Time since injury**= NR; **Education**: Education level primary=32%, secondary= 43%, higher=26%	**M**: Patients referred for cognitive complaints after stroke were recruited by 11 neurology and rehabilitation centres participating in the GREFEX study between 2003 and 2007; **L**: 11 neurology and rehabilitation centres in France; **E**: *Include* if aged 50 -90; Mini Mental State Examination score of 16 out of 30. *Exclude* if severe sensorimotor impairment; hemineglect or aphasia precluding cognitive assessment; illiteracy; alcoholism or a severe systemic comorbidity; previous neurologic and psychiatric diseases (other than depression or anxiety); recent introduction of psychoactive or antiepileptic medications; absence of informed consent.	**Type**: Stroke; arterial infarct=24.1%, haemorrhage=22.8%, subarachnoid haemorrhage=33.8%, CVT=19.4%. Lesion location (n=215); none n=42, posterior n=67, frontal n=61 (right-side n=78, left-sided n=61, bilateral n=34). **Severity**: NR. **Comorbidities**: NR
Sigurdardottir	**Aims:** Determine rates of cognitive	**n**=155; **Female**=24%;	**M**: Systematic review of hospital admission	**Type**: TBI; 47%=traffic accidents.

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(2015);[72] Norway; Prospective; JAP	impairment 1 year after severe TBI. Examine the influence of demographic, injury severity, rehabilitation and sub-acute functional outcomes on cognitive outcomes 1 year after severe TBI **Outcomes**: Disinhibition	**Age**=36.9 (16.7) years; **Time since injury**= NR (but assessed during admission); **Education**: 39% > 12 years	medical charts and clinical data from the acute hospital stay; **L**: Four health regions in Norway associated with four Trauma Referral Centres: the University Hospital of North Norway in the northern region, St. Olav's Hospital in the central region, Haukeland University Hospital in the western region, and Oslo University Hospital in the south-eastern region of Norway; **E**: *Inclusion* if Norwegian residents aged ≥16 years with severe TBI; GCS 3-8 during the first 24 hours after injury; admitted to a regional trauma centre within 72 hours of injury; Galveston Orientation and Amnesia Test score >75 at 1. *Excluded* if neurological diseases known to affect the central nervous system (progressive diseases, stroke, previous TBI, spinal cord injury, mental retardation, dementia); severe psychiatric diseases (psychosis, suicide); severe alcohol and/or intravenous drug abuse disorders; homeless	**Severity**: Severe; lowest GCS on admission 5.9 (1.8); PTA <7 days 22%, 7-13 14%, 14-20 8%, 21-27 11%, >27 days 47%. **Comorbidities**: NR
Simblett (2011);[51] UK; Psychometric; JAP	**Aims:** Report validation of the English version of the Dysexecutive Questionnaire using Rasch analysis **Outcomes**: Dysexecutive functioning	**n**=363; **Female**=30%; **Age**=47 (13) [18-75] years; **Age at injury**= 32 (14) [NR]; **Education** (for n=125); 16.0 (1.6) [NR] years	**M**: NR; **L**: Oliver Zangwill Centre for Neuropsychological Rehabilitation; **E**: Assessed within past 13 years	**Type**: TBI=68.3% (open and closed); non-traumatic=28.3%, including the presence of a tumour or cyst, exposure to toxins, a cerebrovascular accident, a diagnosis of epilepsy, infection and hydrocephalus). Unknown or unavailable information about cause=3.3%. **Severity**: (36.9% available data): 2.6 (0.7)[m].

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
				Comorbidities: NR
Simblett (2012);[50] UK; Psychometric; JAP	**Aims:** Explore if the Dysexecutive Questionnaire is a multidimensional measure of domains associated with poor executive functioning and explore psychometric properties **Outcomes**: Dysexecutive functioning	**n**=271; **Female**=NR; **Age**=NR; **Time since injury**= NR; **Education** NR (note: subset of 363 participants in Simblett 2011)	**M**: NR; **L**: Oliver Zangwill Centre for Neuropsychological Rehabilitation; **E**: Assessed within past 13 years	**Type**: TBI=66.8% (open and closed); non-traumatic=31%, majority being CV accident, hypoxia, infection or tumour or cyst. Also included exposure to toxins, or diagnosis with a condition such as epilepsy, Kosakoff's syndrome, leukodystrophy or hydrocephalus). 2.2%=unknown. **Severity**: NR. **Comorbidities**: NR
Simblett (2017);[52] UK; Psychometric; JAP	**Aims**: Evaluate the impact of changes to the Dysexecutive Questionnaire on psychometric properties and developing a more comprehensive tool for assessing problems with executive functioning following ABI. **Outcomes**: Dysexecutive functioning	**n**=208; **Female**=36.5%; **Age**=64.8 (16.7) [19-90] years; **Time since injury**=2.2 (2.3) [NR]; **Education** NR	**M**: NR; **L**: community neurorehabilitation services; **E**: *Include* if aged 18 years or older, diagnosed with a non-progressive brain injury, able to provide informed consent, adequate communication skills.	**Type**: TBI=5.8%, non-traumatic injury=94.2%. **Severity**: NR. **Comorbidities**: NR
Simpson (2001);[62] Australia; Case control; JAP	**Aims:** Identify social, neuro-radiological, medical and neuropsychological correlates of sexually aberrant behaviour after TBI **Outcomes**: Sexually aberrant behaviour	**n**=50; **Female**=NR; **Age at injury**=23.8 (9.6) [NR] years; **Time since injury**=10.8 (5.4) [NR] years; **Education**: NR	**M**: Database review; **L**: Brain-injury rehabilitation unit at Liverpool Hospital in Sydney, Australia; **E**: *Excluded* if injured pre-18, insufficient data available, sexual related criminal activity	**Type**: TBI; 84% road accidents, all closed-head injuries, 42% requiring neurosurgery. **Severity**: PTA 85.7(54) days. **Comorbidities**: NR
Spikman (2012);[67] Netherlands; Case control; JAP	**Aims:** Assess: social cognition impairment in moderately-to-severely injured TBI patients; whether different tests of social	**n**=28; **Female**=29%; **Age**=30.1 (12.9) [17-66] years; **Time since injury**= NR; **Education**:	**M**: The trauma neurologist referred a consecutive sample of patients when seen for clinical-neurological follow-up at home; **L**: University Medical Centre in Groningen,	**Type**: TBI. **Severity**: Moderate to severe. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
	cognition were interrelated; whether this relates to non-social cognition measures; whether social cognition tests were sensitive to injury severity and o the presence of prefrontal damage **Outcomes**: Empathy	4.9 (0.9) [3–7] *(on a 7-point scale ranging from 1 (primary school education only) up to 7 (university education))*	the Netherlands; **E**: *Include*: moderate or severe TBI. *Exclude*: more than one TBI, neurological conditions other than TBI (e.g., strokes, tumour, seizures, and neurodegenerative disorders), psychiatric conditions, substance abuse	
Tateno (2003);[42] USA; Prospective; JAP	**Aims:** Examine clinical correlates of aggressive behaviour occurring during early recovery from TBI **Outcomes**: Aggression	**n**=89; **Female**=40.4%; **Age**=36.1 (15.2) years; **Time since injury**= 30.2 (24.2) days; **Education**: 12.9 (2.6) years	**M**: Consecutive admissions; **L**: University of Iowa Hospitals and Clinics, Iowa Methodist Medical Centre, in Des Moines, Iowa; **E**: *Include* patients with TBI. *Exclude* patients with penetrating head injuries or associated spinal cord injury; severe comprehension deficits which precluded a thorough neuropsychiatric evaluation	**Type**: TBI; closed head injury; 75.3% injured in a motor vehicle accident. **Severity**: NR. **Comorbidities**: n=5 current alcohol and/or substance abuse.
Vanier (2000);[70] France; Psychometric; JAP	**Aims:** Proposes a set of factors to explain neuropsychological impairments after TBI. Conducts psychometric evaluation of the Neurobehavioral Rating Scale **Outcomes**: Agitation, hostility, disinhibition	**n**=286 (subset of 70 involved in reliability analysis); **Female**=21.5%; **Age**=29.5 (11.0) [16-70] years; **Time since injury**=71.1% <1year since injury; 14.8% 1-2years; 10.2% 2-5years; 3.9% >5years; **Education**: 23.3% 1-6 years; 59.7% 7-13 years; 17% >=14 years	**M**: NR; **L**: Majority from 13 rehabilitation units in France, plus a neurology hospital unit and a psychiatry hospital specifically devoted to traumatic head injury rehabilitation; **E**: *Include* if mild, moderate or severe TBI, whether closed or open. *Exclude* if history of hospitalisation for psychiatric disorder, brain disease or alcohol abuse before the injury, and patients whose injuries resulted from attempted suicide	**Type**: TBI. **Severity**: GCS (n=231 assessed within 12 hours of injury)=42.9% 3-5, 37.6% 6-8, 10% 9-12. 9.5% >=13. **Comorbidities**: NR
Visscher (2011);[68] Netherlands;	**Aims:** Study the prevalence, nature and determinants of aggression among inpatients with ABI	**n**=58; **Female**=28%; **Age**=49.2 (10.5) [24-73] years; **Time since**	**M**: Observation of inpatients; **L**: Specialised post-acute inpatient ABI treatment centre within general psychiatric hospital; **E**:	**Type**: TBI=18%; CV accident=25%; hypoxia=16%; alcohol or drugs related=11%; tumour=11%;

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
Prospective; JAP	**Outcomes**: Aggression	**injury**= 6.6 (7.1) [0-34] years; **Education**: NR	*Include* patients with severe neurobehavioral and/or neuropsychiatric disorders as a result of ABI. *Excluded* if neurodegenerative disorders, acute addiction, severe premorbid personality disorders, intellectual disabilities (IQ < 70), requiring complex somatic care, placed in seclusion because of severe acting-out behaviour	infection=9%; other=12%. **Severity**: NR. **Comorbidities**: NR
Weyer Jamora (2013);[43] USA; Case control; JAP	**Aims:** Examine effect of high chronic pain on neuropsychological test performance and self-reported emotional complaints in persons with post-concussion disorders after mild TBI **Outcomes**: Aggression	**n**=66; **Female**=40.9%; **Age**=42.9 (15.5) [NR] years; **Time since injury**=23.1 (15.3) months; **Education**: 14.9 (2.8) years	**M**: Case review of consecutively examined individuals; **L**: Outpatient neuropsychology office in San Francisco. **E**: *Include* patients with mild TBI. *Exclude* if <age 16; testing not administered in English due to disputed proficiency; questionable effort on at least two of: The Rey-15 Item Memory Test, the Dot Counting Test and the Test of Memory Malingering; atypical responses on Ruff Neurobehavioral Inventory validity scales; history of premorbid TBI; dual-diagnosis of mild TBI and PTSD or anxiety disorder; significant pre-morbid neurological history; pre-morbid psychiatric hospitalisation; excessive time interval between injury and evaluation; presence of severe sensory limitations. Two individuals excluded because their years of education were outliers	**Type**: TBI. **Severity**: Mild. **Comorbidities**: post-concussion disorder and chronic pain
Williams (2018);[53] UK; Case control; JAP	**Aims:** Explore the question of how alexithymia may predispose individuals to aggressive tendencies after head trauma	**n**=47; **Female**=27.7%; **Age**=38.9 (13.3) [20.2–72.0] years; **Time since injury**= 2.2 (1.6) [0.1–	**M**: Referral to university clinic and assessment at interview; **L**: University of Swansea Head Injury Clinic; **E**: *Exclude* if doubts about capacity to provide informed	**Type**: TBI. **Severity**: PTA=10.6 (19.0) [0-90] days; GCS at admission=11.2 (4.7) [3–15]. **Comorbidities**: NR

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
	Outcomes: Aggression	5.6] years; **Education**: 11.7 (1.3) [10-16] years	consent; history of pre-morbid psychiatric and/or personality disorder; previous head trauma or neurological disorder; history of learning disability, estimated pre-accident IQ < 70; dysphasia or any other neurological disorder that would compromise ability to complete the measures; age <20 at assessment	
Wolffbrandt (2013);[74] Denmark; Prospective; JAP	**Aims:** Investigate the occurrence and severity of agitation in patients after severe TBI; identify predictors of agitation and study interrater reliability for a translated version of the Agitated Behaviour Scale **Outcomes**: Agitation	**n**=46; **Female**=22%; **Age**=Median 47 [interquartile range 26 to 58] years; **Time since injury**= NR (enrolled when admitted to sub-acute care); **Education**: NR	**M**: Enrolled when admitted to unit between November 2006 and October 2007; **L**: Sub-acute rehabilitation unit, Denmark; **E**: *Include* if age 16+, TBI, GCS score 3-12 one day after cessation of sedation, patients with GCS 13-14 who had severe focal neurological deficits and/or severe agitation	**Type**: TBI; 46%=car accidents, 24%=motorbike and moped accidents, 13%=falls in public, 17%=industrial accidents or injuries related to accidents in spare time. **Severity**: Median PTA=72 days (IQR 34-154); 89% patients PTA >4 weeks; median injury severity score=29 (IQR 25-38), median GCS=12 (IQR 9-14). **Comorbidities**: NR
Wood (2006);[54] UK; Case control; JAP	**Aims:** Investigate the prevalence of mild developmental learning difficulties in patients who had sustained head trauma, to determine the impact on cognitive and neurobehavioral recovery **Outcomes**: Aggression, emotional lability, dysexecutive functioning	**n**=136; **Female**=17.6%; **Age at injury**=31.8 (9.7) [18-61] years; **Time since injury**= 34.6 (18.5) months; **Education**: None required special schooling, all completed secondary education, only 27 (54%) sat school-leaving examinations, the majority receiving low grades. 8% had special	**M**: Consecutive referrals for neuropsychological assessment over a 2 year interval; **L**: University Head Injury Clinic; **E**: *Include* if English is first language. *Exclude* if dysphasic or problems with vision or motor control that prevented neuropsychological examination	**Type**: All TBI due to road traffic accidents. **Severity**: GCS 10.5 (2.8) [4-15]; PTA=5.5 (14.1) [0-95] days. **Comorbidities**: n=55 reported mild developmental learning difficulties, 30% of whom had pre-injury history of affective disorder

Study (First author, year, country, design, status)	Main aim(s) and relevant outcomes	Sample (n; % female; age; time since index injury; education) (mean, (SD), [range])	Recruitment: Method (M), Location (L), Eligibility criteria (E)	ABI characteristics (type and severity), Comorbidities
		needs input on a peripatetic basis		
Wood (2006);[55] UK; Prospective; JAP	**Aims:** Compare neuropsychological and neurobehavioral profiles of individuals who display post-traumatic aggression with a non-aggressive brain-injured comparison group **Outcomes**: Aggression	**n**=287; **Female**=30.7%; **Age**=40.1 (13.0) [NR] years; **Time since injury**= 3.2 (2.3) [NR] years; **Education**: Mean school leaving age=16.7 (1.7) years	**M**: Patients recruited after referral for neuropsychological examination and rehabilitation advice; **L**: NR, Swansea, UK; **E**: *Exclude* if previous history of head injury, neurological or psychiatric disorder, alcohol or drug abuse, neurological or neuropsychological disability, a pre-accident history of aggressive behaviour	**Type**: All TBI; Cases with abnormal CT scans (n=168) had mainly suffered frontal haemorrhagic or contusion-like injuries. **Severity**: GCS=10.4 (4.3). **Comorbidities**: NR

Note: Age is at time of assessment in the study, unless stated. [a]For stroke group only, [b]All demographic data based upon n=228, [c]At time of injury, [d]Based upon whole potential sample n=399, [e]Final n=unknown. Assume report n=98 (Patients with traceable notes) here, [f]All demographic details based on n=92, [g]Mean age at diagnosis, [h]At follow up, [i]Sample was half informants and half informants with person with ABI present, [j]Based upon n=113, [k]Time from injury to admission, [l]All demographics based upon 67 participants not excluded from study; [m]A severity score of 1 indicating a GCS score within the range 13–15, PTA , 1 day or length of coma, 30 minutes; 2 indicating GCS score within the range 9–12, PTA within the range 1–7 days or length of coma 30 minutes; and 3 indicating a GCS score within the range 3–8, PTA 7 days or length of coma 24 hours.

ABI=Acquired brain injury; CV=Cerebrovascular accident; CT=Computerised tomography; CVT=Cerebral venous thrombosis; D=Dissertation; GCS=Glasgow Coma Scale; GREFEX=The Groupe de Reflexion pour l'Evaluation des Fonctions EXécutives; HISS=Head Injury Severity Scale; JAP=Article in peer-reviewed journal; MRI=Magnetic resonance imaging; NR=Not reported; PTA=Post-traumatic amnesia; PTSD=Post-traumatic stress disorder; SAB=Sexually aberrant behaviours; TAI=Traumatic diffuse axonal injury; TBI=Traumatic brain injury, VA=Veteran affairs.

3.3 Critical Appraisal

Critical appraisal required different tools for different study designs, therefore this section is organised according to which tool was used.

3.3.1 Observational cohort or cross-sectional studies

Twenty six studies were observational cohort or cross-sectional in design,[30, 31, 36, 37, 40-42, 44-49, 55-57, 60, 63, 65, 66, 68, 69, 71, 72, 74, 75] and thus critically appraised using the relevant NIH tool.[24] The results of this appraisal are displayed in Table 2.

Of these 26 studies, eight were of high quality, scoring positively on over 70% of critical appraisal items, and with no major flaws.[31, 40, 44, 55, 56, 68, 72, 74] These included six prospective studies[44, 55, 56, 68, 72, 74] and two retrospective studies.[31, 40] Fourteen studies were of moderate quality, having achieved positive ratings on 50-69% of items,[30, 45, 46, 63, 66, 71, 75, 36, 37, 41, 42, 47-49, 65] of which seven were prospective studies,[41, 42, 47-49, 65, 71, 75] two were retrospective,[30, 66] four were cross-sectional,[37, 45, 46, 63] and one was a multiple group comparison.[36] The remaining four studies achieved positive ratings in fewer than half of the critical appraisal items[47, 57,60, 69] and included three cross-sectional studies[57, 60, 69] and one study combining data from two other prospective studies in the same thesis.[47(study 4)]

Components on which studies consistently scored poorly included Item 5 regarding sample size justification or power description, with only three studies providing this information;[31, 55, 72] Item 6 on whether independent variables were measured prior to outcome of interest, with only seven studies fully providing this information;[30, 31, 44, 66, 68, 71, 72, 75] Item 10 on measurement of independent variables using only valid and reliable means for which only seven studies scored positively;[31, 36, 46, 65, 72, 74, 75] and only one study provided information on whether outcome assessors were blinded to participant's exposure status.[58]

All of the studies had a clearly stated research question and/or objectives, and only two did not clearly specify their study population.[31, 60] The majority of studies had a participation rate of at least 50% of eligible persons (n=19)[30, 36, 40-42, 44, 46-49, 55, 56, 65, 66, 68, 69, 71, 72, 74, 75] and only one study did not recruit subjects from a similar population using pre-specified inclusion criteria.[45]

Table 2. Critical appraisal for observational cohort and cross-sectional studies

Study (Author, Date)	1. Research question or objective in this paper clearly stated?	2. Study population clearly specified and defined?	3. Participation rate of eligible persons at least 50%?	4. Subjects recruited from similar population, including time period, using pre-specified and consistent criteria?	5. Sample size justification/power description/variance and effect estimates provided?	6. Independent variables of interest measured prior to the outcome(s) being measured?	7. Timeframe sufficient so one could see association between exposure-outcome if it existed?	8. Study examined different levels of exposure[a] as related to the outcome?	9. Exposure[a] measures clearly defined, valid, reliable, and implemented consistently across all participants?	10. Other Independent Variables measured in valid/reliable way?[b]	11.Was the exposure(s)[a] assessed more than once over time?	12. Outcome measures clearly defined/valid/reliable /implemented consistently across participants?	13. Outcome assessors blinded to participants exposure[a] status?	14. Loss to follow-up after baseline 20% or less?	15. Key potential confounding variables measured/adjusted for?
Alderman 2002[44]	Y	Y	Y	Y	N	Y	Y	Y	CD	NR	NA	Y	NA	Y	Y
Alderman 2007[45]	Y	Y	NA	N	N	N	Y	Y	CD	NA	NA	Y	NA	NA	NA
Aldossary 2019[75]	Y	Y	Y	Y	N	Y	N	Y	Y	Y	NA	CD	CD	Y	NA
Angelelli 2004[63]	Y	Y	CD	Y	N	N	N	Y	Y	N	NA	Y	NA	NA	Y
Arango-Lasprilla 2012[30]	Y	Y	Y	Y	N	Y	CD	Y	Y	N	NA	CD	NA	NA	Y
Baguley 2006[56]	Y	Y	Y	Y	N	N	Y	Y	Y	N	NA	Y	NA	Y	Y
Bertisch 2017[31]	Y	N	NA	Y	Y	Y	Y	Y	Y	Y	NA	Y	CD	NA	Y
Borek 2001[46]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	NA	N	Y	NA	N
Draper 2007[57]	Y	Y	N	Y	N	N	N	Y	Y	N	NA	NR	N	NA	NA
Finnanger 2015[71]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	NA	N	NA	N	Y
Harmsen 2004[66]	Y	Y	Y	Y	N	Y	Y	N	Y	NA	NA	Y	N	NA	CD
James, 2012: Study 2;	Y	Y	Y	Y	N	N	Y	Y	Y	N	NA	N	CD	NA	Y

Study (Author, Date)	1. Research question or objective in this paper clearly stated?	2. Study population clearly specified and defined?	3. Participation rate of eligible persons at least 50%?	4. Subjects recruited from similar population, including time period, using pre-specified and consistent criteria?	5. Sample size justification/power description/variance and effect estimates provided?	6. Independent variables of interest measured prior to the outcome(s) being measured?	7. Timeframe sufficient so one could see association between exposure-outcome if it existed?	8. Study examined different levels of exposure[a] as related to the outcome?	9. Exposure[a] measures clearly defined, valid, reliable, and implemented consistently across all participants?	10. Other Independent Variables measured in valid/reliable way?[b]	11.Was the exposure(s)[a] assessed more than once over time?	12. Outcome measures clearly defined/valid/reliable /implemented consistently across participants?	13. Outcome assessors blinded to participants exposure[a] status?	14. Loss to follow-up after baseline 20% or less?	15. Key potential confounding variables measured/adjusted for?
James 2013[47, 49]															
James, 2012: Study 3; James 2015[47, 48]	Y	Y	Y	Y	N	N	Y	Y	y	N	NA	Y	CD	NA	Y
James, 2012: Study 4[47]	Y	Y	N	Y	N	N	Y	N	Y	N	NA	N	CD	NA	N
Johansson 2008[36]	Y	Y	Y	Y	N	N	CD	N	Y	Y	NA	Y	NA	NA	NA
Kelly 2008[60]	Y	N	CD	Y	N	N	N	Y	Y	NA	NA	Y	NA	CD	NA
Kois 2018[37]	Y	Y	NA	Y	N	N	N	Y	Y	N	NA	NR	CD	NA	Y
Mazzini 2003[65]	Y	Y	Y	Y	N	CD	Y	Y	Y	Y	NA	N	N	CD	N
Miles 2020[40]	Y	Y	Y	Y	N	CD	Y	Y	Y	N	NA	Y	NA	NA	Y
Rao, 2009[41]	Y	Y	Y	Y	N	Y[c]	Y	Y	Y	N	NA	Y	CD	N	NA
Roussel, 2016[69]	Y	Y	Y	Y	N	N	N	Y	Y	NA	NA	NR	CD	NA	N
Sigurdardottir 2015[72]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	CD	NA	N	Y
Tateno 2003[42]	Y	Y	Y	Y	N	CD	Y	Y	Y	N	NA	Y	N	Y	N
Visscher 2011[68]	Y	Y	Y	Y	N	Y	Y	Y	CD	N	NA	Y	NA	Y	NA

Study (Author, Date)	1. Research question or objective in this paper clearly stated?	2. Study population clearly specified and defined?	3. Participation rate of eligible persons at least 50%?	4. Subjects recruited from similar population, including time period, using pre-specified and consistent criteria?	5. Sample size justification/power description/variance and effect estimates provided?	6. Independent variables of interest measured prior to the outcome(s) being measured?	7. Timeframe sufficient so one could see association between exposure-outcome if it existed?	8. Study examined different levels of exposure[a] as related to the outcome?	9. Exposure[a] measures clearly defined, valid, reliable, and implemented consistently across all participants?	10. Other Independent Variables measured in valid/reliable way?[b]	11.Was the exposure(s)[a] assessed more than once over time?	12. Outcome measures clearly defined/valid/reliable /implemented consistently across participants?	13. Outcome assessors blinded to participants exposure[a] status?	14. Loss to follow-up after baseline 20% or less?	15. Key potential confounding variables measured/adjusted for?
Wolffbrandt 2013[74]	Y	Y	Y	Y	N	CD	Y	Y	Y	Y	NA	Y	CD	Y	Y
Wood 2006[55]	Y	Y	Y	Y	Y	CD	Y	Y	Y	CD	NA	Y	NA	Y	Y

[a]For this item, exposure=ABI; [b]Additional item; [c]Partly; participants who were unable to give consent at baseline completed both independent and dependent variable measures at the assessment. CD=Cannot determine; N=No; NA=Not applicable; NR=Not reported; Y=Yes

3.3.2 Case control studies

Twelve studies[33-35, 43, 53, 54, 58, 61, 62, 64, 67, 73] were critically appraised using the NIH tool for case-control studies.[24] The results of this appraisal are displayed in Table 3.

One paper was judged to be of high quality,[43] five of moderate quality[33, 53, 54, 64, 73] and six papers of poor quality.[34, 35, 58, 61, 62, 67] Selection of participants was the most common source of potential bias, with none of the studies reporting random selection of cases and/or controls if selecting less than 100% of those available, although for one study this item was not applicable.[54] For the item on blinding of assessors, five studies did not report this information,[34, 43, 54, 58, 73] two studies did not blind assessors where possible[33, 35] and this information was unclear in one study.[62] Only one study provided a sample size justification[64] and only four studies reported the use of concurrent controls.[33, 34, 43, 54] Eight studies did not assess or control for key potential confounding variables.[33, 35, 43, 54, 58, 61, 62, 67]

All studies stated an appropriate research question, with the majority also clearly defining the study population (n=9)[33, 43, 53, 54, 58, 61, 64, 67, 73] and differentiating between cases and controls (n=11).[33, 35, 43, 53, 54, 58, 61, 62, 64, 67, 73]

Table 3. Critical appraisal for case control studies

Study (Author, date)	1. Research question /objective in this paper clearly stated and appropriate?	2. Study population clearly specified and defined?	3. Included a sample size justification?	4. Controls selected or recruited from similar population that gave rise to the cases (including the same timeframe)?	5. Inclusion criteria used to select cases and controls valid/reliable and implemented consistently?	6. Cases clearly defined and differentiated from controls?	7. If <100% of eligible cases and/or controls selected for the study, were they randomly selected?	8. Use of concurrent controls	9. Did the exposure/risk occur prior to development of the condition that defined a participant as a case?[a]	10. Are any other Independent Variables measured in a valid and reliable way?[b]	11. Measures of exposure /risk clearly defined/valid/reliable/ implemented consistently for all participants?	12. Assessors of exposure/risk blinded to participant case/ control status	13. Key potential confounding variables measured/adjusted for? Matching accounted for?	14.Were outcome measures clearly defined/valid/reliable/implemented consistently across participants?[b]
Chan 2006[33]	Y	Y	N	Y	Y	Y	CD	Y	N	Y	Y	N	N	Y
Ciurli 2011[64]	Y	Y	Y	N	Y	Y	N	CD	Y	N[c]	Y	NA	Y[d]	Y
Draper, 2008[58]	Y	Y	N	N	N	Y	N	N	Y	NR	NR	NR	N	NR
Greve 2001[34]	Y	N	N	Y	CD	CD	CD	Y	Y	N	N	NR	NA	Y
Homaifar 2012[35]	Y	N	N	Y	Y	Y	CD	N	CD	N	CD	N	N	NR
Kerr 2011[61]	Y	Y	N	CD	CD	Y	N	N	Y	N[e]	Y	NA	N	Y
Moreno 2018[73]	Y	Y	N	N	Y	Y	N	N	Y	Y	Y	NR	NA	Y
Simpson 2001[62]	Y	N	N	Y	CD	Y	CD	CD	CD	N	CD	CD	N	N
Spikman 2012	Y	Y	N	N	Y	Y	N	N	Y	N	Y	NA	N	NR
Weyer Jamora 2013[43]	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y	NR	N	Y
Wood 2006[54]	Y	Y	N	Y	N	Y	NA	Y	Y	Y	Y	NR	N	NR
Williams 2018[53]	Y	Y	N	CD	CD	Y	N	CD	Y	Y	Y	NA	Y	Y

[a]Exposure=ABI; [b]Additional item; [c]Partly: Demographic data gathered via file review and interview with relatives; [d]Y for case control analysis; [e]Partly: All independent variables Y, aside from one - activities of daily living - where measurement tool used was unclear; NA for analysis of interest; CD=Cannot Determine; N=No; NA=Not Applicable; NR=Not Reported; Y=Yes

3.3.3 Systematic reviews

The single systematic review included in this review[28] was critically appraised using the AMSTAR-2 tool,[25] (Table 4). The systematic review was of high quality, only scoring negatively on two of the relevant items; Item 1 which requires the research question and inclusion criteria to incorporate PICO components (although search terms were based on PICO), and Item 11 regarding an explicit statement of funding for the review. The study also scored a 'Partial Yes' on Item 4, regarding the use of a comprehensive literature search strategy, because they did not provide evidence of consulting with topic experts or searching trial registries.

Table 4. Critical appraisal for the systematic review

Study	Research questions/inclusion criteria included PICO components?	Did the report contain explicit statement that review methods were established prior to the conduct of the review and justify any significant deviations from the protocol?	Did the review authors explain their selection of the study designs for inclusion in the review?	Did the review authors use a comprehensive literature search strategy?	Did the review authors perform study selection in duplicate?	Did the review authors perform data extraction in duplicate?	Did the review authors provide a list of excluded studies and justify the exclusions?	Did the review authors describe the included studies in adequate detail?	RCTs only: Did the review authors use a satisfactory technique for assessing the ROB in individual studies that were included in the review?	NSRI only: Did review authors use satisfactory technique for assessing the ROB in individual studies included in the review?	Did the review authors report on the sources of funding for the studies included in the review?	RCTs: If meta-analysis performed did review authors use appropriate methods for statistical combination of results?	For NSRI only: If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	If meta-analysis was performed, did the review authors assess the potential impact of ROB in individual studies on the results of the meta-analysis or other evidence synthesis?	Did the review authors account for ROB in individual studies when interpreting/discussing the results of the review?	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Did the review authors report potential sources of conflict of interest, including funding received for conducting the review?
Whitwham, 2019[28]	N	Y	Y	PY	Y	NR	Y	Y	Includes only NRS	Y	N	Includes only NRS	No meta-analysis	No meta-analysis	Y	Y	No meta-analysis	Y

Table format based upon AMSTAR-2[25]; N=No; NR=Not Reported; NRS=Non-randomised studies; PY=Partial Yes; Y=Yes

3.3.4 Psychometric studies

The results of critical appraisal using the COSMIN tool are available in Table 5. Each of the eight studies in this section evaluated the psychometric properties of a different scale,[32, 38, 39, 50-52, 59, 70] although the three studies by Simblett et al[50-52] evaluated different versions of the Dysexecutive Questionnaire. Two studies considered the psychometric properties when self-rated[51] or informant-rated,[50] and one developed a revised version of the tool.[52] Two studies evaluated four domains,[39, 70] three evaluated three domains,[32, 50, 51] with three studies evaluating only two.[38, 52, 59]

The studies by Bogner et al,[32] McKeon et al,[39] and Francis et al[59] achieved mainly 'Inadequate' and 'Doubtful' ratings, reducing confidence in findings. The evaluation of the Neurobehavioral Rating Scale by Vanier et al achieved scores of 'Very Good' for three domains and 'Adequate' for its evaluation of structural validity, and was the strongest paper.[70]

Vanier's study[70] was the only one not to assess construct validity, however in the other studies there were doubts over the quality of the evaluation in all but the 2012 study by Simblett et al.[50] The most rigorously evaluated domain was that of internal consistency, which 7 studies conducted,[32, 38, 50-52, 59, 70] five performing an evaluation to a 'Very Good' standard.[38, 50-52, 70]

Overall, little confidence can be placed in the findings of psychometric studies as each tool has only been evaluated by a single study, none comprehensively (across all psychometric domains) and none to a consistently high standard.

Table 5. COSMIN Quality Assessment: Overall study quality

Measure (Study)	Development	Content Validity[a]	Structural Validity	Internal Consistency	Cross-cultural Validity/ Measurement Invariance	Reliability	Measurement Error	Criterion Validity	Hypothesis Testing for Construct Validity	Responsiveness
Agitated Behaviour Scale (Bogner 2000)[32]			InA	InA					InA	
Behavioural Dysregulation Rating Scale (McKeon 2017)[39]	InA	InD				InA			D	
The Dysexecutive Questionnaire: Self-rated (Simblett 2011)[51]			V	V					D	
The Dysexecutive Questionnaire: Informant (Simblett 2012)[50]				V	D				V	
The Dysexecutive Questionnaire-Revised (Simblett 2017)[52]				V					D	
Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015)[38]				V					D	
Neurobehavioural Rating Scale (Vanier 2000)[70]			A	V		V		V		
Social Skills Questionnaire for Traumatic Brain Injury (Francis 2017)[59]				InA					D	

[a] Calculated for studies which aimed to evaluate content validity; D=Doubtful; InA=Inadequate; InD=Indeterminate; V=Very good,

3.4 Synthesis of evidence

This section is divided into three main sections: evidence pertaining to aggression outcomes (section 3.4.1), evidence pertaining to sexually inappropriate behaviour outcomes (section 3.4.2) and evidence pertaining to other difficulties of emotional or behavioural regulation (section 3.4.3). Each main section begins with an overall summary of the findings, followed by a detailed description of the evidence related to that outcome and an appraisal of its quality. Each section ends with a table displaying which of the independent variables measured in the study are associated with an increased risk of the outcome of interest (denoted by '↑' and orange cell colour) or not ('↔' and green cell colour). Where an independent variable was measured, but the association with the outcome of interest was not reported, we have assumed no significant association between independent and dependent variables.

3.4.1 Outcome of interest: Aggression

3.4.1.1 Summary of evidence pertaining to aggression

A range of demographic variables were evaluated for their association with aggressive behaviour. Age, education and gender were most frequently explored, with studies most often finding no association between variables. However, significant associations between younger age (5 of 14 studies), fewer years in education (6 of 13 studies) and male gender (4 of 10 studies) were observed in several studies, suggesting that these variables are worthy of consideration for their potential relationship with aggression. Two thirds of the 18 studies exploring demographic variables were of moderate or high quality, providing confidence in the findings where consistent findings across studies have been demonstrated.

Regarding injury characteristics, 18 studies investigated their association with aggressive behaviour. The quality of these studies was again of moderate or high level in two thirds of the sample. There were a number of single studies finding significant associations, but there is a lack of conclusive evidence to support a hypothesis that any injury variables (e.g. location, aetiology, severity) are associated with increased aggression.

The association between symptoms arising from ABI and aggression was investigated in 18 studies, of which 14 were moderate or high quality. A number of physical symptoms were found to be linked with aggression, but only in individual studies. However, there were five studies (of ten) linking poorer physical status with increased aggression. Language and

communication difficulties were explored in four studies, with evidence overall suggestion a significant association between reduced communication ability and increased aggressive behaviour. Evidence evaluating the association between cognitive functioning and aggression presented inconsistent findings, preventing firm conclusions from being drawn.

Therefore while there was the greatest volume of studies exploring aggression outcomes, and these were generally of moderate or high quality, there was very little consistent evidence to support links between demographic, injury or symptom characteristics and increased risk of aggression. Overall, variations in study quality did not explain inconsistent findings across different studies. Although not unanimously supported, there are tentative suggestions that fewer years in education, the presence of communication difficulties and poorer physical status are linked with increased risk of aggression.

3.4.1.2 Description of evidence pertaining to aggression outcomes

Table 6 summarises the findings of the 26 studies which aimed to investigate the relationship between the characteristics of patients with ABI and the occurrence of aggressive behaviour.[30, 31, 33-36, 40-49, 53-57, 60, 61, 65, 68, 75] Three studies were reported within one thesis[47] and two associated papers.[48, 49] There were 11 prospective studies,[41, 42, 44, 47-49, 55, 56, 65, 68, 75] seven case-control,[33-35, 43, 53, 54, 61] three retrospective,[30, 31, 40] three cross-sectional[46, 57, 60] and one each of retrospective cross-sectional[45] and multiple group comparison studies.[36]

Studies were conducted in the UK (n=9),[44-49, 53-55] the USA (n=9),[31, 33-36, 40-43] Australia (n=4),[56, 57, 60, 61] Italy (n=2),[30, 65] Saudi Arabia (n=1)[75] and the Netherlands (n=1).[68] Patients were recruited from specialist brain injury unit/rehabilitation services (n=8),[34, 46-49, 56, 65, 68] inpatient neurobehavioral services (n=3),[44, 45, 61] multiple venues (n=3),[33, 41, 42], an ABI behaviour consultancy or neuropsychology office (n=3),[36, 43, 60] hospital clinic (n=2),[53, 54] accident and emergency department,[75] medical centre,[35] poly-trauma rehabilitation centre[40] or the community.[57] This information was not reported in three studies.[30, 31, 55] A total of 4510 participants were recruited, with sample sizes ranging from 45[34] to 1339.[30] The mean percentage of female participants included across the included studies was 25%, ranging from 6%[34, 35, 40] to 45%.[57] The aetiology of ABI in participants was exclusively traumatic in half of the studies,[30, 31, 34-36, 40, 43, 53, 56, 57, 65, 54, 55] mixed cause of injury in 10 studies,[44-49, 60, 61, 68, 75] closed head injury in 2[41, 42] and stroke in the study by Chan et al.[33] A mix of mean and median ages were reported, and are displayed in Table 1.

3.4.1.2.1 Critical appraisal

Of the nineteen studies studying aggression that were critically appraised using the NIH tool for observational cohort and cross-sectional studies,[24] 5 were of low quality,[47,34, 57, 60, 61] eleven were of moderate quality,[30, 45, 75;33, 36, 41, 42, 46-49, 65] and 6 were of high quality.[31, 40, 44, 55, 56, 68] Potential sources of bias included poor reporting of sample size justification, with only two studies reporting this information,[31, 55] independent variables not being measured prior to the outcome(s) of interest (n=10),[36, 42, 45-49, 56, 57, 60] and uncertainty as to whether non-ABI independent variables were measured using valid and reliable means (n=12).[30, 40-42, 44, 47-49, 55-57, 68] Only one study[46] out of ten where the item was relevant[31, 41, 42, 46-49, 57, 65, 75] reported that outcome assessors had been blinded to participants exposure status.

Of the seven studies critically appraised using the NIH tool for studies of case-control design, one was of high quality,[43] three were of moderate quality[33, 53, 54] and three were of poor quality.[34, 35, 61] None of the studies reported a sample size justification and only one[53] of seven studies demonstrated that potential key confounding variables had been controlled, where this item was relevant.

3.4.1.2.2 Demographic characteristics associated with aggression

Seventeen studies examined the association between patient demographic characteristics and the occurrence of aggressive behaviour.[30, 34, 36, 40-42, 44, 45, 47-49, 53-57, 61, 68] Five were of high quality,[40, 44, 55, 56, 68], nine of moderate quality[30, 36, 41, 42, 45, 47-49, 53, 55, 75] and three were poor quality.[34, 57, 61]

Age

Fourteen studies examined the relationship between patient age and aggression.[30, 34, 40-42, 44, 45, 47-49, 53, 55, 56, 61, 68] In five studies of moderate to high quality, younger patient age was associated with increased risk of aggression.[30, 45, 53, 55, 56] However, nine studies (two low, four moderate, three high quality) found no such significant relationship, including patients current age (n=5),[41, 42, 44, 61, 68] age at injury (n=2)[34, 40] and age at admission (n=2).[47-49] Two contradictory findings arose from one study which found that younger age was related to aggression severity, but not aggression frequency.[45] The weight of evidence overall suggests that there is no clear relationship between age and risk of aggression.

Education

The relationship between years in education and aggressive behaviour was explored in 13 studies.[30, 34, 36, 40-42, 47-49, 53, 55-57, 61] Six found a significant association between fewer years in education and increased aggression,[30, 34, 47, 48, 55, 57, 61] whilst seven found no association.[36, 40-42, 47, 49, 53, 56] There was little variation in study quality which could explain the difference in these findings between these two groups.

Gender

Ten studies of predominantly moderate to high quality studies investigated the relationship between gender and aggressive behaviour.[30, 44, 45, 47-49, 41, 42, 56, 61, 68] Four found that male gender was associated with increased risk of aggression,[30, 45, 49, 68] one with self-injury aspects of aggression only,[45] whilst six found no association.[41, 42, 44, 47, 48, 56, 61] Only 22% of the sample included in this systematic review was female, therefore most analysis of gender are likely underpowered. In the ten studies examining this association, those by Rao et al[41] and Kerr et al[61] contained the highest proportions of female participants (38% and 40% respectively) with the other samples including less than 25% females, which may have contributed to the non-significant association between gender and aggressive behaviour in some studies. However, the two studies with the highest proportion of females also demonstrated no significant association between gender and aggressive behaviour. Overall, the evidence regarding the association of gender with aggression is inconclusive.

Other variables

One study found a significant relationship with pre-morbid employment and aggression,[55] with one study finding no significant relationship with employment or living status.[41] This contradiction may reflect the different metrics of employment used in each study. One study judged to be of moderate quality proposed that a model consisting of lower age at injury, gender, level of education and employment status at injury was significantly associated with aggression.[30]

Characteristics which were found to be significantly associated with aggressive behaviour by single studies included higher levels of premorbid aggression,[34] being admitted to hospital involuntary,[68] and the presence of pre-morbid learning difficulties.[54]

Other patient characteristics which were found not to be significantly associated with brain injury included; history of brain injury (n=3),[47-49, 61] race (n=3),[30, 41, 42] current or premorbid marital status (n=2),[30, 41] socio-economic status (n=2),[40, 42] or legal status (n=2).[41, 47, 49]

3.4.1.2.3 **Diagnostic characteristics associated with aggression**

Eighteen studies examined the association between participants' ABI diagnostic characteristics and aggressive behaviour.[30, 31, 33, 34, 40-42, 44-49, 53, 60, 61, 65, 68, 75] Four of these studies were high quality;[31, 40, 44, 68] ten moderate quality[30, 33, 41, 42, 45, 47-49, 53, 65, 75] and four low quality.[34, 46, 60, 61]

Location of injury

Seven studies investigated the association between location and/or type of damage within the brain and aggressive behaviour.[33, 41, 42, 46, 47, 49, 65, 75] Presence of diffuse axonal injury and lesions in the corpus callosum and cerebral hemisphere (n=1),[75] lower frequency of diffuse injury (n=1),[42] and proximity of lesions to the frontal lobe (n=2)[33, 42] were associated with increased aggression. The contradictory results within the two moderate quality studies examining diffuse vs focal injury[42, 75] may be a reflection of the different aggression measures used or time-points at which aggressive behaviour was evaluated (1 year vs first six months after resolution of Post Traumatic Amnesia (PTA)), and the difference between the two studies of moderate quality by James[47] may be the result of one study[49] having a larger number of participants (n=301 vs n=152).

Seven studies of predominantly moderate quality found no significant association between the location and/or type of damage within the brain and aggressive behaviour,[33, 41, 42, 46, 47, 49, 61, 65] including intracranial abnormality (n=1),[47, 49] injury location (n=1),[61] hypoperfusion (n=1),[65] CTS abnormalities (n=1),[41] and laterality of lesion (n=3).[33, 42, 46] Overall, there is no clear evidence to support an association between location or site of injury and risk of aggression.

Aetiology

James' third study found a significant association between aetiology of brain injury and aggressive behaviour, indicating that TBIs were associated with increased risk of verbal, but not physical aggression.[47, 48] The low quality study conducted by Kelly et al, did not find traumatic aetiology to be associated with aggression, however they did observe an association with alcohol-related injury.[60] Just over 1% of the sample in the study by James[49] had suffered an alcohol-related injury, versus 9% of the sample in Kelly et al,[60] reducing comparability of these findings. The high quality study by Visscher et al[68] found an association between hypoxic aetiology and aggression, but there were six studies of predominantly of moderate

quality which found no association between aggression and aetiology,[30, 31, 33, 41, 47, 49, 61] although none of these aside from the study conducted by James included participants who had sustained an ABI through hypoxia.[47, 49] Within the study by James, only nine percent of the sample had sustained a hypoxic brain injury, which may have reduced the likelihood of finding a significant association between this type of brain injury and aggressive behaviour.

Injury severity

None of the studies found a significant association between various indicators of injury severity and aggressive behaviour (n=11),[30, 34, 40-42, 45, 47, 49, 53, 56, 65, 75] aside from two studies which found a significant association with longer duration of hospital admission.[61, 68] These findings were contradicted by findings from a low quality study by Kerr et al[61] who, despite finding a significant association between increased risk of aggression and longer duration of hospital stay, did not replicate the association with other metrics of injury severity such as Glasgow Coma Scale (GCS) and PTA duration, a finding consistent with other studies using one or both of these outcomes (n=6).[40-42, 47, 49, 53, 56] One study found a significant association in the opposite direction, indicating that reduced time in a residential brain injury rehabilitation facility was associated with increased aggressive behaviour.[34] This latter finding may reflect that individuals who had spent less time within the rehabilitation setting had had less opportunity to access and/or benefit from the therapeutic care and treatment on offer.

Six studies evaluated the association between injury chronicity and aggressive behaviour,[34, 44, 45, 47-49, 68] with only one[47, 48] demonstrating a significant association between longer chronicity and increased risk of aggression. One study found no relationship between aggression and existence of a prior brain injury occurring before index injury.[41]

3.4.1.2.4 Symptoms of ABI associated with aggression

Eighteen studies investigated the association between ABI related symptoms and aggressive behaviour.[33, 34, 36, 41-45, 47-49, 53, 55-57, 61, 65, 68] Four were high quality,[43, 44, 55, 56] ten were moderate quality[33, 36, 41, 42, 45, 47-49, 53, 65, 68] and four were low quality.[34, 47, 57, 61]

Physical symptoms

Aspects of physical health were found to be significantly associated with aggressive behaviour in seven studies.[36, 43, 47, 49, 55, 57, 61, 65] Physical health characteristics included fatigue/sleep difficulties,[55, 57] frequency and severity of post-traumatic epilepsy,[65] high levels

of pain post brain injury which impacts on daily functioning,[43] perceived decline in physical functioning[36] and absence of other medical conditions.[61] James[47(study 4)] demonstrated a significant association between aggression and score on the Mayo-Portland Adaptability Inventory-Version 4 (MPAI-4) Adjustment index, which combines items measuring physical and mental health, social behaviour and recreational activities. In contrast, one moderate quality study by Rao et al did not find any association between medical comorbidity or physical injury and aggression.[41] These contradictory findings may be partially explained by the difference in study quality. Alternatively, the amalgamation of items measuring different, but inter-related constructs within the Adjustment Index of the MPAI-4 used in the study by James may have made it more likely a significant association with aggressive behaviour was observed.[47]

Five studies indicated that patients with greater care and/or supervision needs (n=3)[41, 47, 48, 61] or poorer physical functioning (n=2)[44, 45] demonstrated increased levels of aggressive behaviour, although this association was not supported within one high quality study other than for severity of verbal aggression.[44] In addition, four studies indicated no association between level of independent functioning/functional impairment and aggression,[30, 42, 47, 48, 56] although one of these studies used the Ability Index of the MPAI-4, which measures aspects of both physical and cognitive functioning[47, 48] thus combining items measuring two different constructs which could have reduced the likelihood of finding an association.

Communication and language

Greater levels of language or communication difficulties were significantly associated with increased aggression in three moderate quality studies,[44, 45, 47] with Alderman et al[44] indicating that the severity of all aggression and frequency of aggression against the self and others were associated with poorer visual and auditory language comprehension and expression. A second paper by Alderman et al found that severity of all types of aggression was a function of poor communication, as indicated by speech production, written and oral expression, gestural communication, reading comprehension and auditory/visual comprehension, and high neurobehavioral disability (including level of disability, adjustment to rehabilitation setting, behavioural control, compliance and social interaction, amongst others).[45] No such association between aggression and language was found by a high quality study conducted by Wood,[55] although this study evaluated aggression at one time point, one to three years post-injury during a retrospective interview which may have reduced the

reliability of aggression ratings; whilst aggressive behaviour was measured during an inpatient stay following the occurrence of aggressive behaviour within the three studies demonstrating a positive association.[44, 45, 47(study 4)]

Cognitive impairment

A significant association between increased cognitive impairment and aggressive behaviour was found in five predominantly moderate to high quality studies.[33, 34, 47, 55, 68] Domains of cognitive impairment measured included multiple domains (n=3),[33, 55, 68] and impulsivity/disinhibition (n=3).[34, 47(study 4), 36] Two of the five studies which found a significant association used a shorter test of cognitive functioning - the Mini-Mental State Examination,[33, 68] one administered a full cognitive battery[55] and one a battery of specific tests of executive function.[34] In terms of executive functioning, the fourth study in the thesis by James[47] demonstrated a significant association between poorer inhibition, as measured by the Verbal Fluency and Tower tests, and aggression, and between physical aggression and better scores on one measure of inhibition (Verbal Fluency test) and poorer scores on Verbal Comprehension Index. However, the same study did not find any association between aggression and other tests of cognitive functioning. Within the study by Wood et al findings differed according to the type of analysis undertaken.[55] Profile analysis revealed significantly lower scores across all cognitive domains (language, visuo-spatial, mental speed, verbal and visual memory, working memory, executive function) for patients demonstrating aggressive behaviour, whereas one-way ANOVAs following this analysis indicated only differences in verbal memory and visuospatial abilities remained between aggressive and non-aggressive groups.[55]

Seven studies, again of predominantly moderate to high quality found no association between cognitive functioning and aggression,[36, 41, 44, 47-49, 53, 57] although one of these studies[48] used the MPAI-4 Ability index, which comprises items measuring both physical functioning and cognitive abilities such as memory, attention and concentration, and another study examined the association between premorbid intellectual functioning and aggression.[53] The majority of these studies assessed multiple cognitive domains (n=4)[41, 44, 47, 49, 57] and tended to use more complete batteries of cognitive functioning such as scales from the Wechsler Adult Intelligence Scale[47, 49] and the Doors and People tests.[57]

3.4.1.2.5 Other patient characteristics associated with aggression

Seventeen studies examined the association between other patient characteristics and aggressive behaviour.[33-36, 40-42, 44, 45, 47-49, 53, 55-57, 61, 68] Three of these were high quality,[44, 55, 56] ten of moderate quality[33, 36, 40-42, 47-49, 53, 61, 68] and four of poor quality.[34, 35, 44, 57]

Evidence regarding the potential relationship between mental health difficulties and aggression was mixed. Eight studies finding a statistically significant association between mental health difficulties and aggressive behaviour,[33, 41, 42, 44, 47, 49, 56, 57, 68] including current depression (n=5),[33, 41, 42, 56, 57] anxiety (n=4),[33, 41, 42, 57] PTSD symptoms (n=1)[40] and alexithymia (n=1)[53] Johansson et al found that perceived changes between pre-post morbid depression and PTSD were also associated with aggression.[36] Alderman et al found a significant association between frequency and severity of aggression against the self and a 'mood and self-esteem' factor, although this relationship was not replicated with other types of aggression[44] or within a later study.[45] Satisfaction with life and higher scores on a traumatic complaints list were found to be associated with aggression at 6 and 24 months post-discharge in one study.[56]

Whilst one study found a positive association between aggressive behaviour and pre-morbid mood disorder, the authors found this was not replicated with pre-morbid anxiety.[42] Four other studies found no association between prior history of mental health difficulties and aggression[35, 47, 48, 56, 61] and four studies found no relationship between aggressive behaviour and current mental health difficulties.[34, 40, 41, 55] One of these studies found a positive association between PTSD at admission to a polytrauma rehabilitations unit and aggression, however this relationship was not statistically significant at time of discharge.[40] Prescription of psychotropic medication was found to be associated with verbal aggression in one study.[47, 48] In addition, a low quality study by Greve et al found no difference between aggressive and non-aggressive groups on a scale of psychoticism, however individual subject analyses revealed a higher proportion of individuals with impulsive aggressive behaviour had clinically elevated levels of psychoticism.[34] Overall, differences in study quality did not explain the variation in findings across different studies regarding the association between mental health and aggressive behaviour.

Current[57] or pre-morbid[42] alcohol and/or substance use was found to be associated with aggressive behaviour within two studies. However, this relationship was found to be non-

significant within six studies, including alcohol/substance use in month prior to onset of aggression[42] or admission[68] and premorbid alcohol/substance abuse (n=5).[41, 47-49, 56, 61]

Poorer social functioning was found to be significantly associated with aggressive behaviour in five studies.[33, 41, 42, 47, 48, 57] One of these studies found a significant association on only one of the two measures of social functioning used[42]

History of aggression was found to be associated with current verbal aggression in one moderate quality study[47, 49] whereas no association between premorbid aggression was found in three studies, which were also of predominantly moderate quality (the exception being the low quality study by Kerr et al[61]).[42, 47, 48, 61] Pre-morbid neurological status[36] and medical history[61] were also not significantly associated with the occurrence of aggression.

Table 6. Findings of studies investigating factors associated with aggression. ↑denotes variables significantly associated with risk of aggression. ↔ denotes variables not associated with risk of aggression. Shading in study column indicates quality (green=high quality, white=moderate, orange=low)

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Alderman (2002);[44] UK	**Measure**: The Overt Aggression Scale-Modified for Neurorehabilitation; **Construct**: Aggression – verbal and physical (self, others and objects)	**Method**: Questionnaire; **Rater**: Observer (staff); **Time points**: As behaviour observed	**Design**: Prospective; **Analysis**: Tests of between group differences, correlations, factor analysis, regression [Examine correlates of, and predictors of aggression]	↑			Severity of all aggression, Frequency of aggression against self and others. Poorer visual/auditory language comprehension & expression. Severity of verbal: 'Independent functioning' factor. Frequency of aggression against objects: 'Adjustment/ behaviour' factor[a]	Frequency and severity of aggression against self: 'mood and self-esteem' factor
				↔	Age, gender	Chronicity, admission duration	(Other than where stated above) Cognition, insight, language, independent functioning, speech production	(Other than where stated above) Mood, adjustment and behaviour

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Alderman (2007);[45] UK	**Measure**: Overt Aggression Scale-Modified for Neurorehabilitation; **Construct**: Aggression: verbal and physical (self, others, objects)	**Method**: Observation; **Rater**: Staff; **Time points**: Two week period during admission	**Design**: Retrospective cross sectional; **Analysis**: Factor analysis, linear regression (stepwise) [Identify predictors of aggression]	↑	Severe aggression: younger age. Self-injury: male gender		Severity of all aggression: Poor Communication[b], high neuro-disability[c]. Frequency of all aggression: poor cognitive/ function[d], high levels of neurobehavioral disability. Frequency of aggression against others: poor communication, high neurobehavioral disability. Frequency and severity of aggression: Function of high cognitive impairment, functional handicap and high neurobehavioral disability	

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
				↔	Aggression frequency: Age; Aggression against others/objects; Gender	Time since injury, admission duration		Mood and self-esteem
Aldossary (2019);[75] Saudi Arabia	**Measure**: Schedules for Clinical Assessments of Neuropsychiatry; **Construct**: Aggression	**Method**: NR; **Rater**: Self; **Time points**: One year after head trauma	**Design**: Prospective; **Analysis**: Tests of between-group differences, ANOVA, correlations, logistic regression [Identify variables associated with aggression]	↑		Presence of DAI, cerebral hemisphere and corpus callosum lesions		
				↔		GCS, duration of unconsciousness, duration of PTA, pupil examination, mechanism of injury, length of hospitalisation		
Arango-Lasprilla (2012);[30] USA	**Measure**: The Neurobehavioral Functioning Inventory; **Construct**: Aggression	**Method**: Questionnaire; **Rater**: Self, informant, observer; **Time points**: One year after injury	**Design**: Retrospective; **Analysis**: Regression [Identify variables associated with aggression in different ethnic groups]	↑	Adjusted model: Lower age at injury, gender, level of education at injury and employment status at injury			
				↔	Race/ethnicity, marital status at injury	Cause of injury, length of stay	FIM at discharge, DRS at discharge,	

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Baguley (2006);[56] Australia	**Measure**: Overt Aggression Scale; **Construct**: Aggression: verbal and physical (self, others, objects)	**Method**: Observation scale; **Rater**: Observer: significant other, self; **Time points**: 6, 24 and 60 months after discharge	**Design**: Prospective; **Analysis**: Tests of between-group differences, correlations, regression [Identify predictors of aggression]	↑	Across all three time-points: Younger at time of injury.			Across all three time-points[e]: lower GHQ score, higher depression. At 6 and 24 months only: poorer satisfaction with life, higher score on traumatic complaints list
				↔	(Unless otherwise stated above) Gender, years in education	Best GCS, GCS category, PTA duration, PTA severity, discharge GOS	Injury-related impairment, functional limitations	Previous psychiatric history, current alcohol abuse
Bertisch (2017);[31] USA	**Measure**: Felony convictions; **Construct**: Possible risk to others	**Method**: Database review; **Rater**: NR; **Time points**: 1,2 and 5 year follow up	**Design**: Retrospective; **Analysis**: Tests of between group differences [Compare association of injury type with risk to self or others]	↑				
				↔		Nature of injury (assault vs self-inflicted)		
Borek (2001);[46] UK	**Measure**: Aggression incidence;	**Method**: Case notes; **Rater**: Researcher; **Time**	**Design**: Cross sectional; **Analysis**: Tests	↑				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
	Construct: Aggression	**points**: NR	of between group differences [Investigate association between injury laterality and aggression]	↔		Laterality of brain injury		
Chan (2006);[33] USA	**Measure**: Present State Exam[i]nation; **Construct**: Aggression	**Method**: Questionnaire; **Rater**: Patient, family or staff; **Time points**: NR	**Design**: Case control; **Analysis**: Test of between group differences, stepwise regression [Examine correlates of aggression]	↑		Anterior edge of lesion significantly closer to frontal pole of brain[f]	Greater cognitive impairment	Social functioning; Psychopathology (PSE, HAMD, HAMA) significantly greater
				↔		Type of stroke, side of lesion, degree of brain atrophy, lesion volume	Neurological deficit, impairment in ADL	
Draper (2007);[57] Australia	**Measure**: The Neurobehavioral Functioning Inventory: Aggression scale; **Construct**: Aggression	**Method**: Questionnaire; **Rater**: Self, relatives[g]; **Time points**: NR	**Design**: Cross sectional; **Analysis**: Correlations, regression [Examine variables associated with aggression]	↑	Lower education level		Fatigue	Poorer psychosocial functioning (occupational activity, interpersonal relationships, independent living skills, EGOS), anxiety, depression, alcohol use

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
				↔			Cognitive functioning[h]	
Greve (2001);[34] USA	**Measure**: Lifetime History of Aggression Questionnaire, **Construct**: Aggression	**Method**: Questionnaire in interview format; **Rater**: Self; **Time points**: NR	**Design**: Case control; **Analysis**: Tests of between-group differences [Examine variables related to aggression]	↑	Lower education level, higher incidence premorbid aggression	Less time in programme	Increased impulsiveness[i]	Psychotic symptoms, Feelings of anger, difficulties with aggression
				↔	Age at injury, age at admission	Time since injury, length of coma	Neuropsychological functioning[j]	EPQ: Neuroticism, Extraversion, Lie, Self-injury, BPAQ,
Homaifar (2012);[35] USA	**Measure**: Lifetime history of aggression scale; **Construct**: Aggression	**Method**: Psychometric test; **Rater**: NR; **Time points**: NR	**Design**: Case control; **Analysis**: Tests of between-group differences [Explore relationship between history of suicide attempt and aggression]	↑				
				↔				History of suicide attempt
James (2012, Study 2; 2013);[47, 49] UK	**Measure**: BIRT Aggression Rating Scale; **Construct**: Aggression (verbal and physical)	**Method**: Rating form; **Rater**: Staff; **Time points**: Over 9 weeks of assessment	**Design**: Prospective; **Analysis**: Tests of between-group	↑			Poor verbal comprehension	VA only: Taking psychotropic medication, history of aggression

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
			differences, logistic regression (backward stepwise) [Identify predictors of aggression]	↔	Age at admission/ injury, education, gender, history of prior brain injury requiring hospitalisation, medicolegal status	Chronicity, type of ABI, GCS, PTA duration, intracranial abnormality, requirement for neurosurgical intervention	Neurocognitive functioning (WAIS-III, WMS-III), handedness	Forensic history of aggression, forensic history of sexual offences, drug/alcohol history
James (2012, Study 3; 2015);[47, 48] UK	**Measure**: BIRT Aggression Rating Scale; **Construct**: Aggression (verbal and physical)	**Method**: Rating form; **Rater**: Staff; **Time points**: Over 9 weeks of assessment	**Design**: Prospective; **Analysis**: Principle component analysis, regression [Distinguish aggression and sexually inappropriate behaviour, identify predictors of aggression]	↑	Male gender; Lower education (VA only)	Chronicity 6 months+; TBI (VA only);	Higher MPAI-4 Adjustment score (poorer adjustment); greater supervision and care needs	Lower MPAI-4 Participation[k] (social participation)
				↔	Age at admission/ injury, prior brain injury	TBI (PA only)	MPAI-Ability Index	History of psychiatric illness, criminal convictions for aggression, premorbid substance misuse

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
James (2012, Study 4);[47] UK	**Measure**: BIRT Aggression Rating Scale; **Construct**: Aggression (verbal and physical)	**Method**: Rating form; **Rater**: Staff; **Time points**: Over 9 weeks of assessment	**Design**: Prospective (Combined sample study 2 & 3); **Analysis**: Regression (forced entry) [Additional analysis of combined study 2&3 data]	↑			Verbal fluency test (inhibition) and Tower test (inhibition) (VA only). Poorer scores on Verbal comprehension index and better scores on Verbal fluency test (PA only)	
				↔			(Unless stated above) Inhibition as measured by Trail making test, colour-word interference and Tower test; Neurocognitive functioning[l]	
Johansson (2008);[36] USA	**Measure**: Interview; **Construct**: Aggression (anger)[c]	**Method**: Clinical interview with reference to demographic questionnaire; **Rater**: NR; **Time**	**Design**: Multiple group (levels of anger) comparison; **Analysis**: Principle	↑			Perceived decline in pre–post-morbid 'physical' domain related to elevated post-morbid anger	Perceived decline on emotional scale: PTSD, depression

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
		points: NR	component analysis, MANOVA [Determine pre-morbid factors associated with aggression]	↔	Premorbid education		Premorbid neurological status Premorbid cognitive and physical functioning, perceived decline in cognitive functioning	Premorbid emotional functioning or quality of life; Premorbid neurological status
Kelly (2008);[60] Australia	**Measure**: Overt Behaviour Scale; **Construct**: Aggression, verbal and physical (objects, self, other people)	**Method**: Semi-structured interview: observation, questionnaire; **Rater**: Staff observer, family members, service providers working with client, friends; **Time points**: Once consented into study	**Design**: Cross sectional; **Analysis**: Profile analysis [Define behaviour profiles and link to aetiology of ABI]	↑		Aetiology: Alcohol-related brain injury (VA only)		
				↔		Aetiology: hypoxic (lower VA), traumatic, cerebrovascular accident, tumour, other		
Kerr (2011);[61] Australia	**Measure**: Aggression Study Incident Report Form; **Construct**: Aggression	**Method**: Incident report form; **Rater**: Staff; **Time points**: NR	**Design**: Retrospective; **Analysis**: Correlations, regression [Obtain profile of aggressive patients and	↑	10 years of education or less	Length of hospitalisation > 51 days	Absence of other medical conditions, dependency on staff for ADL	History of aggression
				Four factors significantly predicted membership to the aggressive group: Education ≤10 years or less, history of acting aggressively prior to hospitalization, dependence on staff for assistance with ADLs, inpatient admission of 51 days or more. Predicted 82.8% of cases into the correct group and explained 61.4% of variance				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
			determine predictors]	↔	Age, gender, history of brain injury	Nature, severity (GCS, PTA), type, location		Background history: Smoking, mental illness, medical diagnosis, history of drug use
Mazzini (2003);[65] Italy	**Measure**: Overt Aggression Scale; **Construct**: Aggression	**Method**: Questionnaire; **Rater**: NR (assumed clinical psychologist); **Time points**: 1 year after trauma	**Design**: Prospective; **Analysis**: Correlations, tests of between-group differences [Examine association between PTE and agitation]	↑			Frequency and duration of PTE	
				↔		Injury severity (hypoperfusion)		
Miles (2020);[40] USA	**Measure**: Mayo-Portland Adaptability Inventory-4; **Construct**: Irritability, anger, aggression	**Method**: Questionnaire; **Rater**: Staff; **Time points**: 2 time points: 2-3 weeks after start of treatment and 2-3 weeks prior to discharge	**Design**: Retrospective; **Analysis**: Regression [Examine relationship between PTSD and aggression]	↑				PTSD on admission (presence/ severity)
				↔	Age at TBI, gender, education, premorbid earnings	Injury severity (GCS, time to follow commands, duration of PTA/altered consciousness), time from injury to admission		PTSD at discharge

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Rao (2009);[41] USA	**Measure**: Overt Aggression Scale; **Construct**: Verbal aggression	**Method**: Observation; **Rater**: Staff; **Time points**: 3 months post TBI	**Design**: Prospective; **Analysis**: Tests of between-group differences, regression [Characterise aggression severity and relationship with psychiatric diagnoses]	↑			Increased dependence on personal and instrumental ADL	New-onset major depression, poorer social functioning
				↔	Age, gender, legal problems, education, race, living with others, marital status, employment status	Injury severity (GCS), duration of loss of consciousness, CTS abnormalities, aetiology, prior brain surgery, position of lesion	Cognitive tests,[m] medical comorbidity, physical injury	Pre or post injury history of alcohol/ substance abuse, or adult/child behaviour problems, other DSM-IV Axis 1 disorders
Tateno (2003);[42] USA	**Measure**: Overt Aggression Scale; **Construct**: Aggression, verbal and physical (against objects, self, others)	**Method**: Observation; **Rater**: Observer (NR); **Time points**: During first six months after clearing of posttraumatic amnesia	**Design**: Prospective; **Analysis**: Tests of between-group differences [Examine correlates of aggression]	↑		Focal lesions in frontal lobe vs other areas, lower frequency of diffuse injury		History of mood disorder and alcohol/ substance abuse, diagnosis of major depression, higher HAMD/HAMA scores, poorer social functioning (SFE)

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
				↔	Age, gender, race, years of education, socioeconomic status	Severity of injury (GCS, PTA), laterality of lesion	Frequency of hypoxia and hypotension, cognitive functioning (MMSE), functional independence (FIM)	History of anxiety disorder, frequency of minor depression, alcohol/ substance abuse in month prior to onset of aggression, legal intervention for aggression, social functioning (STC)
Visscher (2011);[68] Netherlands	**Measure**: Staff Observation Aggression Scale-Revised; **Construct**: Aggression	**Method**: Observation; **Rater**: Staff; **Time points**: As occurring during 17 week period	**Design**: Prospective; **Analysis**: Tests of between-group differences, logistic regression [Identify determinants of aggression]	↑	Male gender[n], involuntary admission	Longer duration of admission, hypoxia	Lower MMSE	Lower GAF scores (social, occupational and psychological functioning)
				↔	Age	Time since injury		Permission to leave clinic with no restrictions, substance/ alcohol abuse prior to admission
Weyer Jamora (2013);[43] USA	**Measure**: Ruff Neurobehavioral Inventory (emotional composite); **Construct**: Anger and aggression	**Method**: Questionnaire; **Rater**: Self; **Time points**: Single post-morbid interview	Case control, ; **Analysis**: Test of between-group differences [Examine effect of chronic pain level on aggression]	↑			High pain (vs Low pain)	
				↔				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Williams (2018);[53] UK	**Measure**: Buss Perry Aggression Questionnaire; **Construct**: Aggression: Total score and four subscales (physical, verbal, hostility, anger)	**Method**: Questionnaire; **Rater**: Self, proxy; **Time points**: Part of a routine clinical neuropsychological examination	**Design**: Case control; **Analysis**: Correlations, regression [Examine relationship of alexithymia with aggression]	↑	Younger age at injury			Higher alexithymia (except PA)[o]
				↔	Years in education, time since injury	Injury severity (PTA, GCS)	Premorbid intellectual functioning	
Wood (2006);[54] UK	**Measure**: Clinical interview; **Construct**: Impulsive aggression	**Method**: Clinical interview; **Rater**: Self, family member; **Time points**: NR	**Design**: Case control; **Analysis**: Test of between-group differences [Determine impact of MDLD on impulsive aggression]	↑	Presence of MDLD			
				↔				
Wood (2006);[55] UK	**Measure**: Incidence and nature of aggression; **Construct**: Aggression	**Method**: Semi structured interview, corroboration of records and reports; **Rater**: Self, family members, other patients; **Time points**: One point, 1 to 3 years post-injury	**Design**: Prospective; **Analysis**: MANOVA, profile analysis, one-way ANOVA [Compare profiles of aggressive patients with	↑	Lower reading test scores, lower education, premorbid employment status, younger age at injury		Lower cognitive functioning (including poorer verbal memory and visuospatial abilities)[p]; Increased impulsive and disinhibited behaviour, fatigue/ poor sleep, poor drive/ motivation	Social withdrawal

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; rater; measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
			non-aggressive patients]	↔			Language, mental speed, working memory, visual memory, executive function[p]; Headaches	Anxiety, depression

[a]Relationship between four factors (identified through factor analysis) and characteristics of aggression. Factor 1: Language (reading comprehension, written expression, auditory comprehension, auditory/visual comprehension, oral expression, vocal/non-vocal expression, communication, cognitive skills), Factor 2: Adjustment and Behaviour (compliance, adjustment to rehabilitation setting, interpersonal skills, social interaction, anxiety, insight/awareness of disability, behavioural control, Factor 3: Independent Functioning (memory, bathing, toileting, problem solving), Factor 4: Speech Production (motor aspects), Factor 5: Low Mood/Self-Esteem (depression, self-esteem); [b]Speech production (motor aspects), written expression, oral expression, vocal/non-vocal expression, gestural communication/pragmatics, reading comprehension, communication, auditory/visual comprehension; [c]Disability, adjustment to the rehabiliation setting, behavioural control, compliance, social interaction, interpersonal skills, insight/awareness of disability; [d]Memory for daily activities/tasks, cognitive skills, problem-solving for daily activities, bathing, toileting; [e]Multiple regression indicated at 6m depression most significant predictor, then age at injury, and traumatic complaints. At 24m depression and age at injury. At 60m depression and age at injury; [f]After a stepwise regression was completed, only 2 factors, HAMA and proximity of the lesion to the frontal pole of the brain, were significant in the final model; [g]Model using relative ratings provided weaker but still significant associations; [h]Information processing speed (Symbol Digit Modalities Test, Trail Making Test, Digit Symbol Coding), Auditory attention and working memory (Digit span test), Learning and memory (Rey Auditory Verbal Learning Test, Doors and People tests), executive function (Hayling and Brixton tests, controlled oral word association tests, Porteus Maze test-Vineland Revision, Sustained Attention to Response Task); [i]Main effects for total, aggression and Social Consequences/Antisocial Behaviour scores, which were all higher in the IA group; [j]Peabody Picture Vocabulary Test-III (standard score), Benton Facial Recognition Test (corrected raw score), Trail Making Test (total time for A and B), Controlled Oral Word Association Test (total correct for FAS and Animals), and Wisconsin Card Sorting Test (perseverative responses, perseverative errors, non-perseverative errors, per cent conceptual level responses (%CLR), categories completed, trials to complete the first category, and failure-to-maintain set (FMS)); [k]For VA only: participants who did not score on this item excluded from analysis; [l]Verbal Comprehension Index, Perceptual Organisation Index, Processing Speed Index, Working Memory (As measured on the WAIS-Third Edition) and Auditory Memory and Visual Memory (as measured on Wechsler Memory Scale Third Edition); [m]Mini Mental State Examination, National Adult Reading Test, verbal fluency (letter 's' and 'p') and category (animals & supermarket), Hopkins Verbal Learning Test-Revised, Brief Visuospatial Memory Test-Revised, Trail Making Test, Stroop Color and Word Test, Brief Test of Attention, and the Wisconsin Card Sorting Test, [n]Became insignificant following logistic regression; [o]Explains approximately 30% variance in BAPQ scores, and difficulty describing feelings seems to be the main protagonist; [p]Results from one-way ANOVA. Profile analysis indicates significant differences across domains of Language, visuospatial ability, mental speed, verbal memory, working memory, visual memory and executive function

ADL=Activities of Daily Living; ANOVA=Analysis of Variance; BPAQ=Buss-Perry Aggression Questionnaire; CTS=CT Scan; DAI=Diffuse Axonal Injury; DRS=Disability Rating Scale; EGOS=Extended Glasgow Outcomes Scale; EPQ=Eysenck Personality Questionnaire; FIM=Functional Independence Measure; GAF=Global Assessment of Functioning; GCS=Glasgow Coma Scale; GHQ=General Health Questionnaire; GOS=Glasgow Outcome Score; HAMD=Hamilton Depression Rating Scale; HAMA=Hamilton Anxiety Rating Scale; MANOVA=Multivariate Analysis of Variance; MPAI-4=Mayo-Portland Adaptability Inventory-Version 4; MMSE=Mini Mental State Examination; PA=Physical Aggression; PSE=Present State Examination; PTA=Post-Traumatic Amnesia; PTE=Post-Traumatic Epilepsy; STC=Social Ties Checklist; VA=Verbal Aggression

3.4.2 Outcome of interest: Sexually Inappropriate Behaviour

3.4.2.1 Summary of evidence pertaining to sexually inappropriate behaviour

There were seven studies which explored factors associated with presence of sexually inappropriate behaviour in patients with ABI.[47-49, 60, 62, 69, 73] The strongest evidence of positive associations came from two studies, of low to moderate quality, linking characteristics of executive functioning with sexually inappropriate behaviour, however there was also contradictory evidence from two low quality studies suggesting this relationship is unclear. The majority of evidence was for null relationships between independent variables and occurrence of sexually inappropriate behaviour. In particular, four studies explored whether aetiology was associated with such behaviour and found no relationship, except for one study tentatively linking alcohol-related injuries with increased occurrence.

The studies in this section were of varying quality, reporting generally conflicting results and dominated by four studies from one author. As such, no strong conclusions can be drawn about associations between risk of sexually inappropriate behaviour and any demographic, injury-related, symptom or other patient characteristics.

3.4.2.2 Description of evidence pertaining to sexually inappropriate behaviour

Seven studies aimed to investigate the relationship between the characteristics of patients with ABI and the occurrence of sexually inappropriate behaviour.[47-49, 60, 62, 69, 73] Three studies were reported within one thesis[47] and two associated journal articles[48, 49] and were based upon a retrospective file review of prospectively obtained data. Two studies were cross-sectional[60, 69] and two were case control studies.[62, 73] The findings of these studies are summarised in Table 7.

Three studies were conducted within the UK,[47-49] two in Australia,[60, 62] one in Canada[73] and one in France.[69] A total of 972 participants were recruited, ranging from 42 to 301. Participants were admitted to an ABI behaviour consultancy for assessment and treatment of challenging behaviours (n=1)[60] and neurology and/or rehabilitation centres (n=5).[47-49, 62, 69, 73] Included ABI subtypes were; Mixed including TBI (n=4),[47-49, 60] TBI alone(n=2)[62, 73] and Stroke (n=1).[69] The mean percentage of female participants across included studies was 34%, ranging from 19%[49] to 55%,[73] with one study not reporting this information.[62]

3.4.2.2.1 Critical appraisal

Study quality varied, with the percentage of positive scores on relevant appraisal items ranging from 23%[62] to 77%.[47, 48] Two studies were considered of low quality[47(study 4), 62] and the remaining five of moderate quality).[47-49, 60, 69, 73] Potential sources of bias included uncertainty whether independent variables were measured/recorded prior to dependent variables (n=5),[47-49, 60, 69] lack of sample size justification (n=5),[47-49, 60, 69] uncertainty over the validity and/or reliability of outcomes used to measure independent variables (n=4),[47-49, 62] and not assessing or controlling for key confounding variables (n=3).[47, 62, 69]

3.4.2.2.2 Demographic characteristics associated with sexually inappropriate behaviour

Four studies examined the influence of patient's demographic characteristics on the occurrence of sexually inappropriate behaviour.[47-49, 62, 73] Only younger age at injury and male gender was found to be associated with occurrence of this behaviour,[47, 48] albeit only observed in one of two studies to explore these associations.[47-49]. The conflicting findings in these two moderate quality studies within the same thesis could be explained by the larger sample in the third study (301 vs 152 patients), or by differences in measurement approaches. Staff within the two studies used different methods of recording occurrences of this challenging behaviour; staff in study 2 utilised a more generic monitoring system, whilst staff in study 3 used the purpose-made St Andrew's Sexual Behaviour Assessment (SASBA[77]). Although the occurrence of sexually inappropriate behaviour in study 3 as measured by the SASBA was re-coded to make the results consistent with those from the smaller study, there may have been differences in the accuracy and reliability of both the observation and recording of behaviour across different staff members over time. Whilst little information is provided regarding the method of behaviour recording used in study 2, the more formalised/detailed recording tool described in study 3 may have promoted the more accurate recording of behaviours of interest and resulted in the significant relationships observed between age and gender and sexually inappropriate behaviour.

None of the other included studies demonstrated a relationship between any of the demographic variables and the occurrence of sexually inappropriate behaviour. Given the limited number of studies, the variability in the type of demographic characteristic being measured and the nature of the potential sources of bias, the relationship between participant demographic characteristics and sexually inappropriate behaviour is unclear.

3.4.2.2.3 Diagnostic characteristics associated with sexually inappropriate behaviour

Six studies, two of low and four of moderate quality,[47, 62] looked for associations between diagnostic characteristics and the occurrence of sexually inappropriate behaviour.[47-49, 60, 62, 69, 73] Aetiology of ABI as a risk factor for sexually inappropriate behaviour was explored in four studies, with three studies of moderate quality showing no relationship.[47-49, 69] Three studies explored the link between whether the injury was traumatic, hypoxic or cerebrovascular in nature and this challenging behaviour, finding no relationship.[47-49, 60] Rousell et al looked for an association with different subtypes of stoke, finding no relationship.[69] The one study finding an association between aetiology of ABI and sexually inappropriate behaviour was that by Kelly et al.[60] However, the findings of this low quality study should be taken with caution. It was the only study examining whether alcohol-related injuries were linked with sexually inappropriate behaviour. Importantly, while their profile analysis indicated that the behavioural profile for the six types of brain injury included in the study were different from one another, the differences in the relative occurrence of sexually inappropriate behaviour between different aetiological groups was ascertained only through visual inspection of the data, rather than being supported by statistical analysis.[60]

The moderate quality study conducted Moreno et al indicated that the occurrence of sexually inappropriate behaviour may be related to greater injury severity, as defined by duration of loss of consciousness.[73] However, no association was found with other indicators of injury severity within the same study, including GCS, PTA duration and neuro-radiological abnormalities, consistent with two other studies.[47, 49, 62]

3.4.2.2.4 Symptoms of ABI associated with sexually inappropriate behaviour

Five studies evaluated the association between patients' ABI-related cognitive and behavioural symptoms and sexually inappropriate behaviour. Four studies,[47-49, 62] three by the same author[47-49] found no relationship between different aspects of cognitive functioning, which included verbal comprehension, perceptual organisation, processing speed and verbal and visual memory, and sexually inappropriate behaviour. Two of these four studies were judged to be of low quality, which limits the confidence which can be placed in this finding.[45, 60] One moderate quality study indicated that sexually inappropriate behaviour is associated with greater care needs.[47, 48]

Evidence regarding the relationship between aspects of executive functioning and sexually inappropriate behaviour was contradictory. One study demonstrated that more frequent and

severe problems with dysexecutive functioning, as measured across the behavioural, emotional and cognitive domains of the Dysexecutive Questionnaire,[73] were associated with higher levels of risky sexual behaviour. James found in the fourth study of their thesis, which combined data from studies two and three and was judged to be of low quality, that higher performance on test of Verbal Fluency and poorer performance on a test evaluating ability to plan ahead increased the risk of sexually inappropriate behaviour. [47] In contrast Simpson et al highlighted how impairments in planning/problem solving and concept formation were more common in patients who did not demonstrate such behaviour, although this latter finding may be influenced by the low number of participants and quality of this study.[62] Other aspects of executive functioning were also found to have no relationship with sexually inappropriate behaviour, including disorder of control, drive and impaired awareness[62] and inhibition,[47(study 4)] although these findings also stemmed from studies of low quality.

Overall, although a significant association between aspects of dysexecutive functioning and sexually inappropriate behaviour was reported in two papers (one of low and one of moderate quality),[47, 73] there were also conflicting findings from two other low quality papers,[47, 62] making this association unclear.

3.4.2.2.5 Other characteristics associated with sexually inappropriate behaviour

Four studies examined the association between other patient characteristics and sexually inappropriate behaviour.[47-49, 62, 73] Two studies, one of low and one of moderate quality, agreed that presence of current psychiatric difficulties was unrelated to occurrence of this behaviour.[62, 73] However this was contradicted by the third moderate quality study by James,[47, 48] which found an associated with higher scores on the MPAI-4 Adjustment Index. This discrepancy may be related to the constructs measured by Adjustment Index, as alongside difficulties with mental health it also incorporates items examining other social and physical health-related issues. Simpson found no association between psychosocial adjustment and sexually inappropriate behaviour, although this finding may be influenced by the study quality issues already highlighted above.[62] Two studies by the same author[47-49] indicated that a history of psychiatric symptoms was not related to the occurrence of sexually inappropriate behaviour.

The evidence regarding the association between history of substance misuse is also inconsistent, with one study indicating a significant association between the two variables[47, 48] and two studies indicating that past[47, 49] and current[62] substance misuse have no relationship

with sexually inappropriate behaviour. The former study includes a larger sample, uses a valid and reliable method of recording behaviour and was judged to be of higher overall quality than the latter two studies. The study conducted by Simpson et al suggested that sexually inappropriate behaviour was significantly associated with greater incidence of non-sexual criminal behaviour and lower return to work, although its low quality limits the confidence which can be placed in these findings.[62]

Table 7. Findings of studies investigating factors associated with sexually inappropriate behaviour. ↑denotes variables significantly associated with risk of sexually inappropriate behaviour. ↔ denotes variables not associated with risk of sexually inappropriate behaviour. Shading in study column indicates quality (green=high quality, white=moderate, orange=low)

Study (Author, Date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
James (2012, Study 2; James 2013);[47, 49] UK	**Measure**: Standardised organisation-wide system; **Construct**: Sexually inappropriate behaviour (spoken comments, inappropriate actions)	**Method**: Rating form; **Rater**: Staff; **Time points**: Observed over 9 weeks of assessment	**Design**: Prospective; **Analysis**: T-tests; backwards stepwise logistic regression [Identify predictors of SIB]	↑				
				↔	Age at admission, age at injury, chronicity, education, gender, prior brain injury requiring hospitalisation, forensic history of aggression, forensic history of sexual offences, and handedness	Type of ABI, severity of injury, intracranial abnormality, requirement for neurosurgical intervention	Neurocognitive/ behavioural functioning as measured by WAIS-III and WMS-III	Medicolegal status (none, settled or ongoing), psychiatric history, drug/alcohol history, prescribed psychotropic medication during assessment period
James (2012, Study 3; James 2015);[47, 48] UK	**Measure**: SASBA; **Construct**: Sexually inappropriate behaviour (spoken comments, inappropriate actions)	**Method**: Observation; **Rater**: Staff; **Time points**: Observed over 9 weeks of assessment	**Design**: Prospective; **Analysis**: Principle component analysis (promax rotation); logistic and linear regression analyses [Distinguish aggression and SIB, identify predictors of SIB]	↑	Male gender, younger age at injury		Higher Care and Needs Scale score[a]	Prior substance misuse, higher score (lower functioning) on MPAI-4 Adjustment Index (Mood, aggression social contact, leisure, pain/fatigue/ sensitivity to symptoms, family relationships), occurrence of challenging behaviour[b]

Study (Author, Date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
				↔	Age at admission, education, prior brain injury, criminal convictions for aggression	Whether traumatic injury or not	Score on MPAI-4 Ability Index (physical functioning/ symptoms memory, communication, attention, problem solving), supervision needs,	History of psychiatric illness, score on MPAI-4 Participation Index (Initiation, self-care, employment, social contact, residence, leisure)
James (2012, Study 4);[47] UK	**Measure**: SASBA; **Construct**: Sexually inappropriate behaviour (spoken comments, inappropriate actions)	**Method**: Rating form, **Rater**: Observer: staff; **Time points**: Observed over 9 weeks of assessment.	**Design**: Prospective [c]; **Analysis**: Logistic regression (forced entry)d [Additional analysis of combined study 2&3 data]	↑			Higher score on Verbal Fluency Test (executive function), Poorer scores on Tower Test (planning ability)[e]	
				↔			Performance on six neurocognitive tests: Verbal Comprehension Index, Perceptual Organisation Index, Processing Speed Index, Working Memory Index, Auditory Memory and Visual Memory and performance on tests measuring inhibition: Trail Making Test,	

Study (Author, Date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
							Colour-Word Interference Test	
Kelly(2008); [60] Australia	**Measure**: Overt Behaviour Scale; **Construct**: Inappropriate sexual behaviour	**Method**: Semi-structured interview **Rater**: Family members (49%), service providers working with client (48%), friends (3%) **Time points**: NR (once consented into study)	**Design**: Cross sectional; **Analysis**: Profile analysis [Define behaviour profiles and link to aetiology of ABI]	↑		Aetiology: Alcohol-related brain injury[f]		
				↔		Aetiology: Tumour (relatively low risk), traumatic, cerebrovascular, hypoxic, other		
Moreno (2018);[73] Canada	**Measure**: Sexual Risk Survey[g], **Construct**: Risky sexual behaviour	**Method**: Questionnaire; **Rater**: Self; **Time points**: One time point, retrospective recall of last 6 months	**Design**: Case control; **Analysis**: Correlations [Identify correlates of SIB]	↑		Total score: Loss of consciousness	Frequent and severe dysexecutive problems. Sexual risk taking with uncommitted partners predicted by DEX Behavioural, Cognitive and Emotion subscales,[h] Impulsive sexual acts predicted by DEX Behavioural and Cognitive subscales. Intent to engage in risky	

Study (Author, Date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
							sexual behaviour predicted by DEX Emotion and Cognitive subscales	
				↔	Time since injury	GCS; PTA; neuro-radiological abnormalities		Anxiety; depression
Roussel (2016);[69] France	**Measure**: Behavioral Dysexecutive Syndrome Inventory; **Construct**: Sexual conduct	**Method**: Interview; **Rater**: Informant (NR); **Time points**: NR	**Design**: Cross sectional; **Analysis**: Logistic regression [Examine relation of stroke subtype to SIB]	↑				
				↔		Stroke subtype		
Simpson (2001);[62] Australia	**Measure**: NR; **Construct**: Sexually aberrant behaviour	**Method**: NR (assumed review of patient records); **Rater**: NR; **Time points**: As occurring during stay in rehab centre	**Design**: Case control; **Analysis**: Assessed between-group differences; compared presence of 'global risk factor'[i] between groups [Identify correlates of SIB]	↑			Impairment in Planning/problem solving and concept formation more common in control group	Greater Incidence of nonsexual criminal behaviour, lower return to work
				↔	Employment status; living status	Neuro-radiological variables: type of abnormality, hemispheric lateralisation of greatest injury, site of injury; Medical variables: levels of follicle stimulating hormone, thyroid	Neuro-psychological variables: orientation, attention, cognitive speed, language, perception, constructional praxis, verbal and visual memory,	Psychosocial adjustment difficulties (both premorbid and post injury), substance abuse, psychiatric status/emotional disturbance

Study (Author, Date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
						stimulating hormone, luteinizing hormone, testosterone and incidence of epilepsy	generativity and behavioural aspects of executive abilities (disorder of control, drive and impaired awareness)	

[a]Not significant when participants who didn't score on this item were excluded; [b] When aggressive or sexually inappropriate behaviour recorded for a given patient, probability between 0.40 and 0.64 that any other aggressive or sexually inappropriate behaviour will be observed as well. Study found it difficult to predict SIB based on occurrence of verbal and physical aggression; [c]Participants in this study result of combined data sets from James (2012 study 2 and 3); [d]Criterion for inclusion in final set of predictor variables= significant correlations with any of three dependent variables ($p<.10$); [e]Null model successfully classified 77.9% cases. Logistic regression model was significant, although classification accuracy dropped to 76.7%; [f]Proportion of group displaying SIB, irrespective of number of levels; [g]Total score and sub-items: sexual risk taking with uncommitted partners, risky sexual acts, impulsive sexual acts, intent to engage in risky sexual behaviours and risky sexual behaviours; [h]Behavioural subscale measures impulsivity, lack of insight, disinhibition, and perseveration, cognitive subscale: self-monitoring, mental flexibility, distractibility, and decision-making, emotional subscale: difficulties in regulating/controlling emotions and apathy; [i]Any one of substance abuse, employment difficulties, nonsexual criminal behaviour, psychological/emotional difficulties qualified for group membership; ABI=Acquired Brain Injury; DEX=Dysexecutive Questionnaire; GCS=Glasgow Coma Scale; MPAI-4=Mayo-Portland Adaptability Inventory; PTA=Post-Traumatic Amnesia; SAB=Sexually Aberrant Behaviour; SASBA=St Andrew's Sexual Behaviour Assessment; SIB=Sexually inappropriate behaviour; TBI=Traumatic Brain Injury; WAIS-III=Wechsler Adult Intelligence Scale, Version 3; WMS-III=Wechsler Memory Scale Version 3

3.4.3 Outcome of interest: Other difficulties of emotional and/or behavioural regulation

3.4.3.1 Summary of evidence pertaining to other difficulties of emotional and/or behavioural regulation

Evidence in this section was grouped by outcomes relating to difficulties with emotional and behavioural regulation. These were agitation (n=5), disinhibition (n=8), emotional lability (n=3), maladaptive behaviour (n=3) and 'other' outcomes (n=1). In the largest sub-group, all 8 studies (two of low quality, five of moderate quality and one of high quality) seeking independent variables associated with disinhibition found that no demographic variables predicted risk of disinhibition. The evidence about injury severity was equivocal however, with half of the studies linking injury severity with disinhibition, although reasons for inconsistent findings were unclear There were also single studies each linking different dysexecutive symptoms with increased impulsivity, but overall the evidence was highly heterogeneous both in design and findings, providing little grounds for selecting any variables that could be linked with disinhibited behaviours.

The remaining categories of behaviour in this section had fewer than 5 studies each and were categorised by heterogeneity in terms of design and findings. While some single studies identified statistically significant associations between individual variables and difficulties with emotional and behavioural regulation, there was never enough agreement between studies to place confidence in these findings.

3.4.3.2 Description of evidence pertaining to other difficulties of emotional and/or behavioural regulation

Thirteen studies investigated the relationship between characteristics of people living with an ABI and difficulties with emotional and behavioural regulation.[35, 37, 54, 58, 63-67, 69, 71, 72, 74] Five studies were case-control,[35, 54, 58, 64, 67] four were prospective,[65, 71, 72, 74] three were cross-sectional,[37, 63, 69] and one was based on a retrospective file review.[66] Findings are displayed in Table 8.

Three studies were conducted in Italy,[63-65] two in the USA,[35 37] two in the Netherlands,[66 67] and Norway[71, 72] in addition to single studies from France,[69] Australia,[58] Denmark[74] and the UK.[54] A total of 1372 participants were recruited to these studies, ranging from 28[67] to 237.[69] Participants were recruited through neurology and/or rehabilitation departments (n=2),[69 , 71] rehabilitation programmes (n=4),[58, 64-66] and trauma centres in University hospital (n=3),[72 54,

[74] medical centres (n=3)[35, 37 67] and hospital units (n=1).[63] Subtype of ABI was predominantly TBI (n=10),[35, 37, 54, 58, 64-67, 71, 74] including two studies focusing on severe TBI only.[66, 72] The remaining two studies included participants who had suffered a stroke.[63, 69] The mean percentage of female participants across included studies was 25%, ranging from 6%[33] to 48%.[69] Ages were reported as median or means, see Table 1 for details.

3.4.3.2.1 Critical appraisal

The percentage of positive scores on critical appraisal ranged from 31%[35] to 92%.[54] Only one of the studies evaluating the association between patient characteristics and difficulties of behavioural/emotional regulation provided a sample size justification.[72] Other sources of bias included uncertainty over whether sufficient timeframe was available between measuring exposure and outcomes of interest (n=4)[37, 63, 64, 69] and whether independent (n=6)[35, 37, 58, 63, 67, 71] or dependent variables (n=9)[35, 37, 54, 58, 65, 67, 69, 71, 72]were measured using a valid and/or reliable method. None of the studies which were evaluated using the case-control NIH measure stipulated if they used concurrent controls.[35, 54, 58, 64, 67]

3.4.3.2.2 Agitation

Five studies examined the association between patient characteristics and agitation.[63-66, 74] One was of low quality,[63] three of moderate quality[64-66] and one of high quality.[74] Four examined associations with symptoms secondary to acquiring a brain injury[63-65, 74] and three examined associations with patient demographic characteristics.[63, 64, 74]

Demographic characteristics associated with agitation

Three studies, one of low,[63] one of moderate[64] and one of high quality,[74] examined the association between patient's demographic characteristics and agitation.[63, 64, 74] All of these studies examined the effect of patient age on occurrence of agitation[63, 64, 74] with only one finding a significant association.[74] This study was judged to be of high quality, although the low number of patients in this study (n=46) may limit the confidence which can be placed in this significant association.[74] Three studies of low to high quality examined the association between gender and agitation,[63, 64, 74] with none finding a significant relationship, similarly there was no relationship between level of education and agitation in two low-moderate quality studies.[63, 64]

Diagnostic characteristics associated with agitation

Five studies examined the association between different ABI aetiological characteristics and agitation.[63-66, 74] Three of these evaluated the association between features of the ABI and agitation.[63-65] The moderate quality study conducted by Mazzini et al found a significant association between the occurrence of left anterior temporal lobe hypoperfusion and agitation.[65] The remaining moderate quality studies found no association between injury features, which included severity of lesions,[63, 65] axonal damage, cortical atrophy, level of hydrocephalus/hypoperfusion[65] and extracranial injury.[63]

The only study which found an association between any measure of injury severity (e.g. GCS, duration of unconsciousness, days spent in ACU) and agitation was a moderate quality study by Harmsen et al, who found an association with increased duration of PTA.[66] This is in contrast to findings from two other studies,[63, 74] one of low[63] and one of high quality,[74] who found no significant association between PTA duration and agitation. The study by Harmsen et al included a relatively low number of participants (n=60) and only included individuals with severe TBI, which may reduce both the level of confidence in and generalisability of their findings.[66]

Symptoms of ABI associated with agitation

Four studies looked at the association between different symptoms secondary to sustaining an ABI and agitation[63-65, 74] but no two studies explored the same symptoms. Significant associations were found between the presence of aphasia,[63] lower FIM score on admission[74] and occurrence of post-traumatic epilepsy[65] and agitation. Ciurli et al did not find a significant association between the time from injury to follow commands or cognitive functioning and agitation.[64]

3.4.3.2.3 Disinhibition

Eight studies examined the association between different patient characteristics and disinhibition.[37, 54, 58, 63-65, 69, 72] Two of these were judged to be of low quality,[35, 56] five of moderate quality[52, 61, 62, 63, 67] and one of high quality.[70] Seven studies examined the association between disinhibition and ABI diagnostic characteristics,[37, 58, 63-65, 69, 72] four examined the association with patient demographics,[37, 63-65] four with ABI symptoms[37, 63-65] and two with other characteristics.[37, 54]

Demographic characteristics associated with disinhibition

All five studies which examined the association between patient age and level of education with disinhibition[37, 63-65, 72] did not find a significant relationship between these variables. The three studies (one of low and two of moderate quality) which looked at the association between patient gender and disinhibition also did not find a significant relationship.[37, 63, 64] The only other independent variable considered was injury chronicity in one study, where the relationship with disinhibition was also not statistically significant.[64] Overall, studies evaluating the association between patient characteristics and disinhibition were of variable quality, with the percentage of positive scores on relevant critical appraisal items ranging from 58%[37] to 75%.[64]

Diagnostic characteristics associated with disinhibition

The association between disinhibition and injury severity was investigated in six studies,[37, 58, 63-65, 72] three of which found a significant association.[58, 64, 72] In these studies, greater injury severity was associated with disinhibition. Whilst the quality of the studies supporting this association varied (one each were appraised as being of low, moderate and high quality), the studies which found no association were of low[35] or moderate quality.[61, 63] Thus, there is tentative evidence to support the association between greater injury severity and disinhibition

The relationship between injury characteristics and disinhibition was evaluated by two studies,[64, 65] with only the moderate quality study by Mazzini et al finding an association between left anterior temporal lobe hypoperfusion and disinhibition.[65] The impact of injury site was investigated by moderate quality study by Ciurli et al, who found no significant relationship with disinhibition.[64] Type of stroke subtype was also found to be unrelated to degree of disinhibition, although this finding was based upon a study which only scored positively on 58% on relevant critical appraisal items.[69]

Symptoms of ABI and other factors associated with disinhibition

Evidence about the association between ABI related symptoms and disinhibition was heterogeneous, with each of the four studies examining this association evaluating a different independent variable. There were significant associations between impulsivity and dysexecutive functioning as indicated by poorer performance on TMT letter sequencing and test of motor speed and better performance on Stroop task,[37] and association between

disinhibition and the presence of post-traumatic epilepsy.[65] No association was found between disinhibition and aphasia,[63] time to follow commands,[64] or functional status.[65]

Evidence evaluating the association between other patient characteristics and disinhibition was limited. In the only study evaluating this particular outcome, Kois et al found a significant association between PTSD symptom severity and impulsiveness.[37] The findings from the study by Kois et al also indicated a non-significant association of patient's current alcohol use with impulsivity.[37] The relatively poor quality of this study reduces confidence in its findings, and it should be noted that the measure of impulsiveness was dependent on patient self-ratings, which could be considered less reliable than ratings by a close-relative or independent observer. The study by Kois et al was the only one to use a self-rated outcome measure to record patient levels of disinhibition/impulsivity.[37]

3.4.3.2.4 Emotional lability

Three studies evaluated the association between patient characteristics and emotional lability (EL),[54, 64, 65] with two moderate quality studies focusing on the association between EL and patient demographics.[54, 64] Wood et al found a significant association between the presence of a mild learning difficulty and EL.[54] However, no significant association was found with patient age, level of education and gender.[64]

Two studies evaluated the association between different ABI diagnostic characteristics and EL.[64, 65] Ciurli et al[64] fund no significant relationship between injury chronicity and EL, and neither the moderate quality study conducted by Ciurli et al[64] or the moderate quality study conducted by Mazzini et al[65] found significant association between injury site or features and EL.

Evidence examining association between ABI related symptoms and EL was limited to two studies, with one moderate quality study finding no association with occurrence of post-traumatic epilepsy[65] and the other moderate quality study demonstrating no association with time taken to follow commands.[64]

3.4.3.2.5 Maladaptive Behaviour

Demographic and Diagnostic characteristics

Two studies examined the association between patient demographics and maladaptive behaviour.[37, 71] One moderate quality study examined association with externalising behavioural problems such as rule breaking and intrusive behaviour[71] and difficulties with

behavioural regulation,[71] and one low quality study examined the association with maladaptive behaviour.[37]

Finnanger et al found a significant association between a younger age at injury and occurrence of rule breaking behaviour and between fewer years of education and difficulties of behavioural regulation.[71] This latter finding contrasts with the only other study who evaluated the association with education and maladaptive behaviour.[37] No significant associations were found between age or gender and maladaptive behaviour.[37] In the study examining relationship with employment status, no significant relationship was found with any maladaptive behavioural outcome.[71]

The only ABI aetiological characteristic that was examined for its association with maladaptive behaviour was injury severity. Only one of the two studies evaluating this variable found any relationship between injury severity and occurrence of maladaptive behaviour. [71] This study found a significant relationship between one of its measures of injury severity, presence of Traumatic Axonal Injury, and greater rule breaking behaviour and behavioural dysregulation.

Due to the limited quantity of evidence and heterogeneous nature of the outcome variables considered, no firm conclusions can be drawn regarding the nature of the association between patient demographic or ABI aetiological characteristics and the occurrence of maladaptive behaviour.

ABI related symptoms and other characteristics

Three studies evaluated the relationship between ABI related symptoms and the occurrence of maladaptive behaviour.[35, 37, 71]

Evidence from the three studies examining the relationship between executive functioning and maladaptive behaviour provided mixed findings.[35, 37, 71] The moderate quality study by Finnanger et al[71] reported no significant relationship between executive functioning at three months post injury and externalising behaviour or behavioural regulation. Homaifar et al[35] indicate that participants with a history of a suicide attempt made more perseverative errors during the Wisconsin Card Sorting Task, but scores on other measures of executive functioning (Iowa gambling task) did not indicate greater likelihood of previous suicide attempt. One moderate quality study by Kois et al found a significant association between poorer scores on tests of visual attention and task switching and maladaptive behaviour.[35]

Finnanger found no other significant associations between tests of motor function, attention and visual or verbal memory and maladaptive behaviour.[71] The low quality study by Homaifar et al also found no relationship between Immediate or Delayed memory function and history of attempted suicide.[35]

One study found a significant association between depressive symptoms at twelve months post injury and difficulties with externalising behaviour/behavioural regulation.[71]

3.4.3.3 Other outcomes

Only one low quality study examined the association between ABI aetiological characteristics and other outcomes of interest.[67] Spikman et al examined the association between ABI characteristics and performance on two measures of empathy, finding that longer duration of post-traumatic amnesia was associated with lower empathy as measured by the Faux Past Test, but no association between PTA and level of empathy on Emotional Empathy questionnaire.[67] No association was found between injury chronicity or presence of non-frontal lesions and Empathy.[67] The quality of this study limits the confidence which can be placed in its findings.

Table 8. Findings of studies investigating factors associated with other difficulties of behavioural and emotional regulation (DEBR). ↑denotes variables significantly associated with risk of DEBR. ↔ denotes variables not associated with risk of DEBR. Shading in study column indicates quality (green=high quality, white=moderate, orange=low)

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Agitation								
Angelelli (2004);[63] Italy	**Measure**: Neuropsychiatric Inventory; **Construct**: Agitation	**Method**: Interview; **Rater**: Close relatives; **Time points**: 2 months (±10 days), 6 months (±20 days) and 1 year post-stroke (±30 days)	**Design**: Cross sectional; **Analysis**: Logistic regression [Identify predictors of agitation in stroke patients]	↑			Presence of aphasia	
				↔	Age, gender, education	Injury severity: GCS, duration of unconsciousness/ PTA, presence of severe extracranial injury, length of hospitalisation		
Ciurli (2011);[64] Italy	**Measure**: Neuropsychiatric Inventory; **Construct**: Agitation	**Method:** Interview; **Rater**: Informant (relative, carer); **Time points**: Once, in hospital	**Design**: Case control; **Analysis**: Logistic regression (forward stepwise) [Identify predictors of agitation]	↑				
				↔	Age, education, gender, injury chronicity	Injury site, injury features	Time from injury to able to consistently follow commands (TFC), Levels of Cognitive Functioning Scale	
Harmsen (2004);[66] Netherlands	**Measure**: File review; **Construct**: Positive behavioural disturbances (including agitation)[c]	**Method:** Database review; **Rater**: Researcher; **Time points**: Files examined at 1 time point from	**Design**: Retrospective **Analysis**: NR [Identify association between PTA and positive	↑		PTA duration		
				↔				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
		period from patient admission to follow up	behavioural disturbances]					
Mazzini (2003);[65] Italy	**Measure**: Neurobehavioural Rating Scale **Construct**: Agitation		**Design**: Prospective; **Analysis:** Correlations, tests of between-group differences [Examine association between PTE and agitation]	↑		Left anterior temporal lobe hypoperfusion	PTE[e]	
				↔		Posterior temporal lobe hypoperfusion; severity of lesions in frontal lobes; diffuse axonal damage; cortical atrophy; level of hydrocephalus; level of hypoperfusion		
Wolffbrandt (2013);[74] Denmark	**Measure**: Agitated Behaviour Scale; **Construct**: Agitated behaviour	**Method:** Observational; **Rater**: Observer; **Time points**: Initiated once out of coma or vegetative state, continuing until 7 consecutive days without three	**Design**: Prospective; **Analysis**: Logistic regression (backwards stepwise) [Identify predictors of agitation]	↑	Lower age		Lower FIM score on admission	
				↔	Gender	Injury Severity, GCS, PTA duration, days spent in ACU, days spent under sedation		

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
		Agitated behaviour scale scores >21 in 48 hours						
				Disinhibition				
Angelelli (2004);[63] Italy	**Measure**: Neuropsychiatric Inventory; **Construct**: Disinhibition	**Method**: Interview; **Rater**: Close relatives; **Time points**: 2 months (±10 days), 6 months (±20 days) and 1 year post-stroke (±30 days)	**Design**: Cross sectional; **Analysis**: Logistic regression [Identify predictors of disinhibition in stroke patients]	↑				
				↔	Age, gender, education	Injury severity, GCS, duration of unconsciousness/ PTA, presence of severe extracranial injury, length of hospitalisation	Aphasia	
Ciurli (2011);[64] Italy	**Measure**: Neuropsychiatric Inventory; **Construct**: Disinhibition	**Method:** Interview; **Rater**: Informant (relative, carer); **Time points**: Once, in hospital	**Design**: Case control; **Analysis**: Logistic regression (forward stepwise) [Identify predictors of disinhibition]	↑		GOS score of 3 associated with greater risk of disinhibition		
				↔	Age, education, gender, injury chronicity	Injury site, injury features	TFC	
Draper (2008);[58] Australia	**Measure**: Sustained Attention to Response Task; **Construct**: Executive control over attention or response inhibition	**Method:** Psychometric test **Rater**: Clinician; **Time points**: NR	**Design**: Case control; **Analysis**: Correlations, bivariate logistic regression [Identify	↑		Greater injury severity		
				↔				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
			association of cognitive impairments with injury severity]					
Draper (2008);[58] Australia	**Measure**: Controlled Oral Word Association Test; **Construct**: Impulsiveness	**Method:** Psychometric test **Rater**: Clinician; **Time points**: NR	**Design**: Case control; **Analysis**: Correlations, bivariate logistic regression [Identify association of cognitive impairments with injury severity]	↑		Greater injury severity		
				↔				
Kois (2018);[37] USA	**Measure**: The Barratt Impulsiveness Scale; **Construct**: Impulsiveness	**Method:** Questionnaire; **Rater**: Self; **Time points**: NR	**Design**: Cross sectional; **Analysis**: Correlations, regression [Identify correlates of impulsiveness]	↑			Poorer score on TMT letter sequencing. Negative association with sequencing; better score on Stroop task; poorer score on test of motor speed	Greater PTSD symptom severity
				↔	Age, gender, education	Injury severity	TMT motor speed	Alcohol use

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Mazzini (2003);[65] Italy	**Measure**: Neurobehavioural Rating Scale **Construct**: Disinhibited behaviour	**Method:** Questionnaire; **Rater**: Clinical psychologist; **Time points**: One year after trauma	**Design**: Prospective; **Analysis:** Correlations, tests of between-group differences [Examine association between PTE and disinhibition]	↑		Left anterior temporal lobe hypoperfusion	PTE[e]	
				↔		Severity of brain injury, axonal damage, cortical atrophy, level of hydrocephalus, level of hypoperfusion		
Roussel (2016);[69] France	**Measure**: GREFEX[f]; **Construct**: Dysexecutive difficulties: Inhibition	**Method:** Interview; **Rater**: Informant; **Time points**: NR	**Design**: Cross sectional; **Analysis:** Logistic regression [Examine relation of stroke subtype to inhibition]	↑				
				↔		Stroke subtype		
Sigurdardottir (2015);[72] Norway	**Measure**: Colour-Word Interference Test (conditions 1-4:	**Method:** Psychometric test; **Rater**: Observer;	**Design**: Prospective; **Analysis:**	↑		Total score DKEFS: Longer PTA duration[h]		

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
	subtest of DKEFS); **Construct** Response inhibition[g]	**Time points**: At 3 and 12 months post injury	Exploratory factor analysis; regression analysis; Receiver Operating Characteristic curve analysis [Examine influence of variables on response inhibition]	↔	Age, Education	GCS, CT classification scores, length of inpatient rehabilitation stay	Functional status (GOSE)	
Wood (2006);[54] UK	**Measure**: Hayling Test (A, B and C); **Construct**: Response suppression	**Method:** Psychometric test; **Rater**: Clinician; **Time points**: NR	**Design**: Case control; **Analysis**: Tests of between group differences [Determine impact of MDLD on response suppression]		Article does not make it clear which scales to report			
Emotional lability								
Ciurli (2011); [64] Italy	**Measure**: Neuropsychiatric Inventory; **Construct**: Irritability/Emotional	**Method:** Interview; **Rater**: Informant (relative, carer); **Time points**:	**Design**: Case control; **Analysis**: Logistic regression	↑	Irritability: Chronicity, TBI at 1 year from onset of severe TBI			

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
	lability	Once, in hospital	(forward stepwise) [Identify predictors of emotional lability]	↔	Age, education, gender, Emotional lability: chronicity	Injury site, injury features	TFC	
Mazzini (2003);[65] Italy	**Measure**: Neurobehavioral Rating Scale **Construct**: Mood swings	**Method:** Questionnaire; **Rater**: Clinical psychologist; **Time points**: One year after trauma	**Design**: Prospective; **Analysis:** Correlations, tests of between-group differences [Examine association between PTE and mood swings]	↑				
				↔		Severity of brain injury, axonal damage, cortical atrophy, level of hydrocephalus, level of hypoperfusion	PTE[e]	
Wood (2006);[54] UK	**Measure**: Clinical interview; **Construct**: Emotional lability	**Method:** Interview; **Rater**: Self, family member; **Time points**: NR	**Design**: Case control; **Analysis**: Tests of between group differences [Determine impact of MDLD on emotional lability]	↑	MDLD			
				↔				
Maladaptive Behaviour								

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
Finnanger (2015);[71] Norway	**Measure**: ASEBA: Adult Self Report Form; **Construct**: Behavioural problems, externalising problems: aggressive behaviour, rule-breaking behaviour, and intrusive behaviour	**Method:** Questionnaire **Rater**: Self; **Time points**: One time point, 2-5 years after injury	**Design**: Prospective, **Analysis**: Linear regression [Explore association between variables and maladaptive behaviour]	↑	Younger age at injury	Presence of TAI on early MRI predicted higher scores on ASR Total[b]		Depressive symptoms 12 months after injury
				↔	Composite score: Employment status, gender, education	GCS, duration PTA	Neuropsychological test performance at 3 months (Executive Functioning, motor function, attention, visual and verbal memory), GOS	
	Measure: Behaviour Rating Inventory of Executive Functioning-Adult Version; **Construct**: Executive functioning: behavioural regulation		**Design**: Prospective; **Analysis**: Linear regression [Explore association between variables and maladaptive behaviour]	↑	Fewer years of education	TAI on MRI[b]	Lower GOSE score at 12 months post injury	Depressive symptoms 12 months post-injury
				↔	Employment status, age, gender	GCS, PTA	Neuropsychological performance (Executive Functioning, motor function, attention, visual and verbal memory)	
Homaifar (2012);[35] USA	**Measure**: Columbia Suicide History Form; **Construct**:	**Method:** Questionnaire; **Rater**: NR; **Time**	**Design**: Case control; **Analysis**: Test	↑			More WCST perseverative errors	

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
	History of suicide attempt	**points**: NR	of between group differences and mixed effects modelling [Explore relationship between executive function and suicidal behaviour]	↔		Injury severity	Performance on Iowa Gambling task, Immediate Memory test or Delayed Memory tests	
Kois (2018);[37] USA	**Measure**: Head Injury Behaviour Scale; **Construct**: Maladaptive TBI-related behaviour	**Method:** Questionnaire; **Rater**: Informant; **Time points**: NR	**Design**: Cross sectional; **Analysis**: Correlations, regression [Identify correlates of maladaptive behaviour]	↑			Poorer score on test of visual attention/task switching	
				↔	Age, gender, education			
				Other				
Spikman (2012);[67] Netherlands	**Measure**: Emotional Empathy Questionnaire;	**Method:** Psychometric test; **Rater**: Clinician;	**Design**: Case control; **Analysis:**	↑				

Study (Author, date, country)	Outcome measure, construct of interest	Data collection method; Rater; Measurement time point(s)	Overview of study design and analysis	Risk	Demographic characteristics	Diagnostic characteristics	Symptom characteristics	Other characteristics
	Construct: Empathy	**Time points**: NR	Tests of between group differences [Explore relationship between social cognition and injury characteristics]	↔		Chronicity, PTA, position of lesions		
	Measure: Faux Pas test Empathy Score, **Construct**: Empathy	**Method:** Psychometric test; **Rater**: Clinician; **Time points**: NR	**Design**: Case control; **Analysis:** Tests of between group differences [Explore relationship between social cognition and injury characteristics]	↑		Longer PTA		
				↔		Chronicity; presence of non-frontal lesions		

[a]Mental health treatment utilisation: 4 questions (yes/no): 1) In past year have you received treatment for depression? 2) In past year have you received treatment for PTSD? 3) In past year have you had treatment for other MH problems? 4) In past year have you been hospitalised for psychiatric disorder?, [b]Not significant when adjusted for age and education, [c]Presence of 'restlessness' and/or 'agitation' documented in medical file in combination with the documented need of at least two of the following nursing measures in hierarchical order: A carefully structured one-person room with limited sensory stimulation; Continuous individual nursing and/or family guidance; Remote video control; Bed, chair or wheelchair adaptations to avoid risks of unsafe transfers or ambulation, [d](1) Hypo activity with apathy-abulia; (2) difficulties in anticipation, planning and initiation of activities; (3) disinterest and indifference to his/her own concern and others; (4) hyperactivity-distractibility-psychomotor instability; (5) irritability-impulsivity-aggressiveness; (6) euphoria, emotional lability and moria; (7) stereotyped and perseverative behaviour; (8) environmental dependency; (9) anosognosia-anosodiaphoria; (10) spontaneous confabulations; (11) social behaviour disorders; and (12) disorders of sexual, eating and urinary behaviour, [e]Frequency of seizures (year before last seizure), duration (subtracting the date of the first seizure from the date of the last seizure), [f]Adaption of seven tests: Trail Making Test, Stroop Test, Modified

Card Sorting Test, a verbal fluency test (naming animals/words beginning with letter F in two minutes, six elements test and the Brixton Test, a paper and pencil version of the dual task test, [g]Only total score for whole DKEFS provided, [h]after adjusting for age and education

ACU=Acute Care Unit; ANOVA=Analysis of Variance; DKEFS=Delis-Kaplan Executive Function System; GCS=Glasgow Coma Scale; GOS=Glasgow Outcomes Scale; GOSE=Glasgow Outcomes Scale-Extended; GREFEX=The Groupe de Reflexion pour l'Evaluation des Fonctions EXécutives; Levels of Cognitive Functioning Scale; MPAI-4=Mayo-Portland Adaptability Inventory 4; MRI=Magnetic Resonance Imaging; MDLD=Mild Developmental Learning Difficulties; MSCEIT= Mayer-Salovey-Caruso Emotional Intelligence Test; NR=Not reported; PTA=Duration of post-traumatic amnesia; PTE=Post-Traumatic Epilepsy; TAI=Traumatic Axonal Injury; TFC=Time to follow commands; TMT=Trail Making test;

3.5 Findings from psychometric studies

3.5.1.1 Summary

There were eight psychometric studies evaluating eight different tools to quantify outcomes relating to sexually inappropriate behaviour or difficulties with emotional and behavioural regulation.[32, 38, 39, 50-52, 59, 70] In addition, we identified a recent, high-quality systematic review of tools to assess aggression, which included seven studies that we would otherwise have included.[28] Of the primary studies included in the present review, internal consistency and structural validity were the most commonly evaluated psychometric constructs.

As described in section 3.3.4, the eight primary studies all evaluated different tools and they were often of low methodological quality. Therefore the evidence supporting measures to assess sexually inappropriate behaviour or difficulties with emotional and behavioural regulation is not robust. Findings are displayed in Table 9 and notable observations described below.

Structural validity was evaluated by three studies[32, 51, 70] with level of evidence indeterminate (n=2)[32, 70] or insufficient.[51] Internal consistency was assessed for all but one measure, the Behavioural Dysregulation Rating Scale.[39] All scales that were rated had good internal consistency, except for the MSCEIT, which performed poorly on the Emotion Management branch.[38] Some confidence can be placed in these ratings, as most studies performed evaluations to a 'very good' standard. Three versions of the Dysexecutive Questionnaire were evaluated across three studies by Simblett et al.[50-52] Structural validity was evaluated in the self-report study,[51] performing insufficiently. Internal consistency was rated within all three studies to be sufficient to a 'very good' standard, except an 'adequate' standard for structural validity in the revised version.[52]

Cross-cultural validity/measurement invariance was evaluated within Simblett et al, with the level of evidence deemed to be 'sufficient' for this item.[50] Reliability was assessed in two studies,[39, 70] with the level of evidence rated as insufficient for both. Hypothesis testing for construct validity was rated for seven of the eight studies.[32 38, 39, 50-52, 59] Level of evidence for this item was sufficient in two studies,[50, 52] indeterminate in two studies[32, 51] and insufficient in the remaining three studies.[38, 39, 59]

Systematic review findings

The only systematic review included in this review aimed to identify all measures used to assess aggression in adults with ABI, assess the reliability and validity of these measures and understand the characteristics of the sample each measure had been validated within.[28] The phenomenon of interest was the assessment of psychometric properties of measures of aggression, where aggression (verbal, physical, towards objects, towards self) was required to be a component of the assessment. Studies were excluded if the measure only included on item/question on aggression or only assessed violence towards self, sexual violence or intimate partner violence. Studies were published in English, with no date limits for publication. This review was judged to be of high-quality using the AMSTAR-2 appraisal tool.

Twenty five studies evaluating 17 measures were identified. These measures included the Neurobehavioral Functioning Inventory (NFI) (n=4), Agitated Behaviour Scale (n=3), Neuropsychiatric Inventory (n=2), St Andrews Swansea Neurobehavioral Outcome Scale (SASNOS) (n=3), and one study each evaluated the Attempted and Actual Assault Scale (Attacks), Behavioural assessment screening tool, BIRT Aggression Rating Scale, Challenging Behaviour Management tool, Checklist of Challenging Behaviour, Independent Living Scale, Memory and Behaviour Problems Checklist (MBPC), National Taiwan University Irritability Scale, Overt aggression scale - modified for Neurorehabilitation, Overt Behaviour Scale - Informant report, Overt Behaviour Scale-Self Report, and The Sister Kenny Symptom Management Scale (KSMS). Eleven studies evaluated some aspect of reliability, whilst measures of validity included content validity (n=4), structural validity (n=5), internal consistency (n=8), construct validity (n=12) and responsiveness (n=4). Six studies described the development of a new aggression measure. The Agitated Behaviour Scale was the only measure which was evaluated by three separate studies included within the systematic review by Whitwham et al[28] and an additional study located through our bibliographic data base searches.[32] Overall, the results of the additional study found through our bibliographic database searches did not add to the assessment of this measure's reliability and validity made by Whitwhatm et al.

The systematic review indicated that whilst some measures (e.g. the MBPC-1990R, NFI, SASNOS and KSMS) demonstrated positive psychometric properties based upon high quality research, these were based upon a limited number of studies, with a restricted range of psychometric properties evaluated within these.[28] Overall, Whitwham et al concluded due to

these limitations, and variable quality of the evidence available, that it was not appropriate to advise on the use of one tool across all settings.[28]

Table 9. Findings of psychometric studies. Text in cells represents both the rating (+, _ or ?) and the rationale for judgement.

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
Structural validity	+								
	?	Insufficient data reported						Relevant items (disinhibition, agitation) grouped in Factor 3 - survival oriented behaviour/ emotional state.	

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
	-			Only five out of the 18 subscales assessed (1) achieved satisfactory fit to the Rasch model, (2) met the assumption of unidimensionality, and (3) had a person separation index value which indicated suitability for at least group use (≥ .7).					

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
Internal consistency	+	TBI sample: person separation value=2.09; separation reliability=.81; item separation=16.01. Anoxia sample: person separation=1.80, item separation=6.63		PSI=.81	PSI=.91	PSI=.76 to .92		Cronbach's alpha ranged from .50 to .84. Cronbach's alpha for Factor 3=.728	Cronbach's alpha=.90
	?								
	-						Cronbach's alpha=.50 to .60 for the Emotion Management branch and its subtasks		

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
Cross-cultural validity/measurement invariance	+				DIF analysis: no differences found				
	?								
	-								
Reliability									
	?								
	-		Cohen's kappa κ= .60					Median kappa=.4. ICC values for factors ranged from .56 to .85	

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
Hypothesis testing for Construct validity	+				Hypotheses: Multidimensional measure of several domain specific functions associated with poor executive functioning; adequate psychometric properties; good inter-rater reliability	Hypothesis: adding items on activation to see if diving 'behavioural-emotional' scale into 'behavioural/ emotional' and 'activation' improved its psychometric properties			
	?	No hypothesis defined (by the review team)		No hypothesis defined (by the review team)					

Measurement Property	Rating	Study, validity and reliability constructs measured							
		Agitated Behaviour Scale (Bogner, 2000); [32] Construct/structural validity, separation reliability	Behavioural Dysregulation Rating Scale (McKeon, 2017); [39] Convergent/Divergent validity, Content and construct validity, inter-rater reliability	Dysexecutive Questionnaire: Self-rated (Simblett, 2011);[51] construct validity, internal consistency reliability	The Dysexecutive Questionnaire: Informant (Simblett, 2012);[50] construct validity, inter-rater reliability	The Dysexecutive Questionnaire-Revised (Simblett, 2017);[52] construct validity and internal consistency/ reliability of subscales	Mayer Salovey Caruso Emotional Intelligence Test (Kugel 2015); [38] construct and concurrent validity and internal consistency	Neurobehavioral Rating Scale (Vanier, 2000); [70] structural validity, inter-rater reliability	Social Skills Questionnaire for Traumatic Brain Injury (Francis, 2017); [59] construct and predictive validity, internal reliability
	-		Strong relationships with the DEX (r= .535) and the Go/No-Go Test (r=–.564), indicating convergence. Small negative relationship with SLS confirms divergent validity. Positive moderate correlation between BDRS and MAAS (r=.469) suggesting measures may be assessing related constructs.				Contrary to expectations, the MSCEIT does not measure emotional intelligence as a unified area of ability; does not demonstrate adequate convergent validity. No difference between RH/LH groups on performance on Emotional management branch		Convergent validity - failed to confirm hypotheses; divergent validity - confirmed hypothesis; predictive validity - confirmed hypothesis

Note: Rows for Measurement Error and Criterion Validity deleted, as no studies evaluated these domains. '+' rating denotes sufficient standard achieved; '?' denotes indeterminate standard achieved; '-' denotes insufficient standard achieved. BDRS= Behavioural Dysregulation Rating Scale, LH=Left Hemisphere, MAAS= Mindfulness Attention Awareness Scale, RH=Right Hemisphere, SLS= Satisfaction with Life Scale

3.6 Overview of key variables

Across the three outcome groups (aggression, sexually inappropriate behaviour, and other difficulties with emotional or behavioural regulation) a number of common independent variables were investigated. Within each outcome group there was little evidence to support strong statements about the association with any demographic, diagnostic, symptom or other patient characteristics and any challenging behaviour. Despite this there were tentative associations for a number of variables, albeit supported by low numbers of studies.

The assessment of a patient to determine the most appropriate care setting should consider the risk of all challenging behaviours, therefore within this section, we consider whether any patient characteristics feature in multiple outcome categories, and are therefore worthy of greater consideration in patient assessments.

3.6.1 Demographic variables associated with challenging behaviours

Age

Age, level of education and gender were the most commonly assessed demographic variables. Age was assessed as a predictor of challenging behaviours in 28 instances, across 20 studies.[34, 37, 40-42, 44, 45, 47-49, 53, 55, 56, 61, 63-65, 68, 71, 72, 74] Where an association between age and challenging behaviours was found, younger age was associated with greater risk, and this was observed in eight of 28 analyses (Table 10). Age appears not to be relevant as a variable when trying to explain the occurrence of difficulties with emotional and behavioural regulation, with more than 80% of analyses showing no association. However, it may be more relevant with regard to aggression, with a third of analyses demonstrating an association.

Education

Level of education was an independent variable in 26 analyses across 18 studies.[34, 36, 37, 40-42, 47-49, 53, 55-57, 61, 63-65, 71, 72] Overall, 31% of these analyses found an association between education and challenging behaviours (Table 10), the direction of effect always being that a lower level (normally quantified in terms of years in education) of education is associated with the likelihood of the challenging behaviour. Level of education was relevant in aggression analyses, being associated with the outcome in half of the analyses, but there is no evidence to support its relevance to sexually inappropriate behaviour or difficulties with emotional and behavioural regulation.

Twenty four analyses across 16 studies assessed the possible association of gender with likelihood of challenging behaviours.[30, 37, 40-42, 44, 45, 47-49, 56, 61, 63, 64, 68, 71, 74] As with age and education, there were only two studies in the sexually inappropriate behaviour pool,[48, 49] with the remaining 22 analyses split evenly between aggression and difficulties with emotional and behavioural regulation. All of the analyses (n=4) that found an association between gender and challenging behaviours observed that risk was greater in males, and all were associated with aggression,[30, 45, 48, 68] although in the 2007 study by Alderman gender was associated with self-injury only and not aggression against others or objects. Male gender may have some relevance to aggression but none to difficulties with emotional and behavioural regulation, and the evidence for sexually inappropriate behaviour is lacking.

Overall, the age, gender and level of an education of a patient appear to be relevant considerations in determining the risk of aggression, but there is little evidence to suggest they have a bearing on likelihood of sexually inappropriate behaviour or difficulties with emotional and behavioural regulation.

3.6.2 Injury and diagnostic variables associated with challenging behaviours

There were three independent variables that were analysed on more than 10 occasions – aetiology, location or type of brain damage, and measures of injury severity (Table 10). Aetiology was evaluated in 13 analyses across nine studies.[30, 41, 44, 47-49, 56, 60, 61, 68] There were only three analyses evaluating whether aetiology was associated with sexually inappropriate behaviour and none with difficulties with emotional and behavioural regulation. Although based on a small sample, 38% of statistically significant associations suggest there is evidence to suggest aetiology may be a consideration, however there were no consistent observations within these analyses.

Details about the location or type of brain damage were independent variables in 47 separate analyses across 15 studies.[33, 41, 42, 46-49, 61, 62, 64, 65, 67, 69, 71-73, 75] Seventeen of the analyses were reported in the study by Mazzini et al, which is one of the lowest quality studies.[65] Removing the study by Mazzini et al from consideration would increase the proportion of injury location or type variables associated with challenging behaviours to 23%.[65] While this value is low, it suggests that some variables are worthy of consideration. In particular, for aggression, 38% of analyses identified statistically significant associations, however, reflecting on section 3.4.1.2.3 (detailed description of diagnostic characteristics associated with aggression) these were inconsistent and thus require further investigation.

Measures of injury severity were included in 61 analyses across 21 studies.[34-37, 40-42, 47-49, 53, 55, 56, 58, 61, 63-68, 71-75] Severity was virtually unrelated to aggression as an outcome in the 26 analyses to examine this relationship, however it was relevant in 21% of outcomes related to emotional and behavioural regulation and, based on a sample of only six analyses, 17% of those looking at sexually inappropriate behaviour.

Overall, there is some evidence to suggest that the aetiology of ABI, location or type of brain damage, and injury severity may be possible factors affecting the likelihood of challenging behaviours. However, findings are highly heterogeneous and no firm conclusions can be drawn from the studies included in this review.

3.6.3 Symptom characteristics associated with challenging behaviours

Symptoms of ABI were highly varied and were therefore grouped into those associated with cognitive function (e.g. intelligence, memory, communication, processing speed etc.), physical function (e.g. physical functioning, physical comorbidities, post-traumatic epilepsy, care and support needs etc.) and executive function (e.g. dysexecutive syndrome, inhibition, perseverative errors etc.). Cognitive function was entered into 58 analyses across 18 studies.[33, 37, 44, 45, 47-49, 57, 63, 64, 71, 35, 36, 41, 42, 62, 68] There was a clear divide between outcomes, with 100% of 19 analyses showing no relationship between cognitive function and sexually inappropriate behaviour, but for aggression and emotional and behavioural regulation, 41% and 42% of analyses respectively were statistically significant. Therefore while seemingly not relevant to the risk of sexually inappropriate behaviour, tests of cognitive function appear to be a relevant consideration.

Measures of physical function were entered into analyses as independent variables on 34 occasions across 16 studies.[30, 33, 36, 41-45, 48, 56, 57, 61, 65, 71, 72, 74] More than half (56%) of the analyses found a statistically significant association between patient physical function and the occurrence of challenging behaviours. Most of this evidence came from those analysis considering aggression as the outcome, with nearly two third of analyses identifying a link between poor physical function/status and aggression. Small numbers of analyses for sexually inappropriate behaviour and difficulties with emotional and behavioural regulation render conclusions highly tentative, but in all cases it appears clear that measures of physical status warrant consideration.

In 30 analyses of the association between measures of executive function and challenging behaviour, 73% were statistically significant. Twenty five of these analyses were performed with regard to aggression and sexually inappropriate behaviour, with 70% and 80% found to be statistically significant, respectively. As such there is evidence that executive function plays a role in the risk of challenging behaviours.

3.6.4 Other variables associated with challenging behaviours

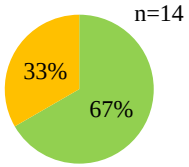
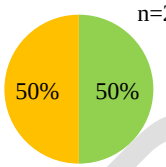
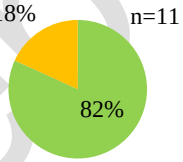
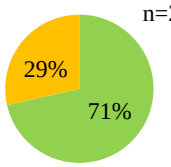
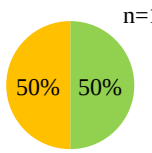
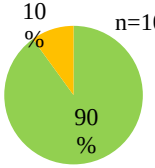
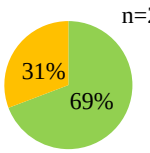
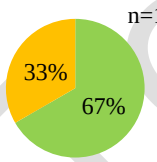
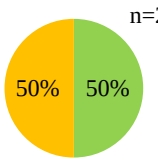
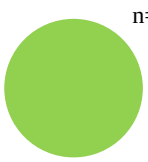
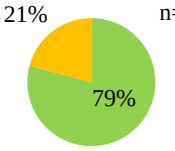
Other independent variables were grouped into three categories: mental health, substance abuse and social outcomes (Table 10). Mental health was the largest category, including measures of constructs including depression, anxiety, adjustment and encompassing terms such as 'psychiatric disorder' used within studies. Although substance abuse is considered a mental health disorder, we took a pragmatic approach to separate this variable from the mental health category, as this is also a functional behaviour that can be considered separate, and is often recorded differently to mental health outcomes.

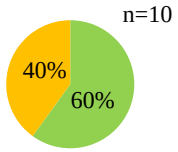
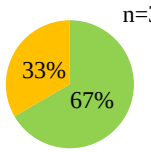
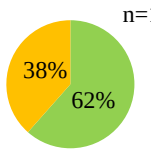
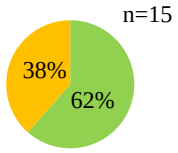
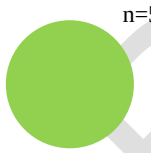
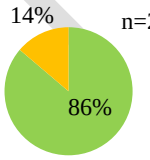
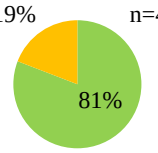
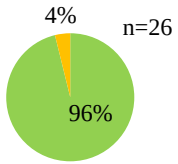
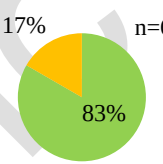
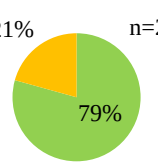
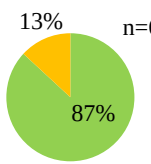
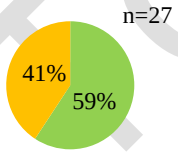
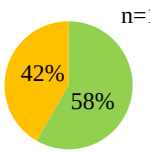
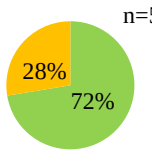
Mental health outcomes were considered 38 times in 18 studies.[33, 34, 36, 41, 42, 44, 45, 47-49, 53, 55-57, 61, 62, 68, 71, 73] The majority of these were considered with respect to aggression, with more than half of these 27 analyses finding a statistically significant association. In the nine analyses looking at sexually inappropriate behaviour, only two were statistically significant, and both of those evaluating difficulties with emotional and behavioural regulation found associations. Mental health here is a broad category; however it is clear that there are associations between mental health outcomes and risk of challenging behaviour. There is further detail of these associations above in section 3.4.

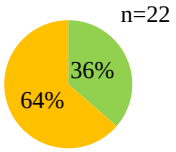
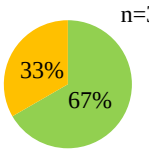
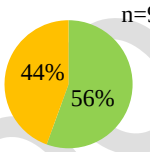
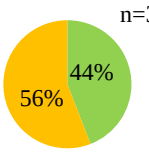
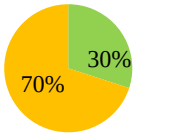
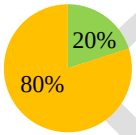
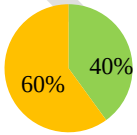
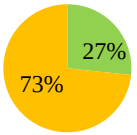
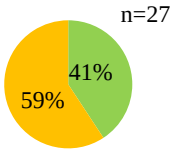
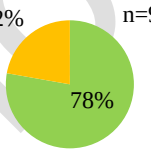
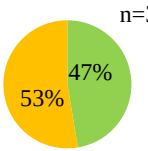
Three quarters of the analyses of the association between substance abuse and challenging behaviours found no relationship, although there were only 12 analyses overall. This suggests there is insufficient evidence to consider history of, or current substance abuse as a predictor of challenging behaviours.

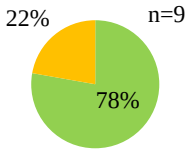
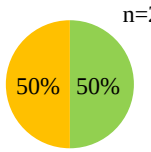
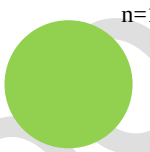
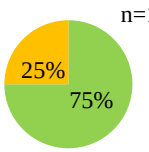
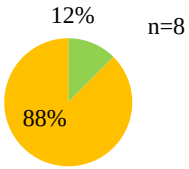
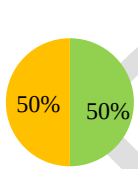
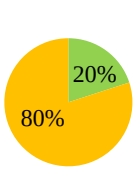
Social outcomes were only assessed ten times, however eight of these analyses found that poorer social status was linked with increased risk of challenging behaviour, in particular this was the case with aggression. These initial findings suggest an association but more research is needed.

Table 10. Breakdown of the proportion of analyses finding associations between patient characteristics and challenging behaviours. Variables evaluated in ten or more analyses are included. Pie charts show the proportion of statistically significant (orange) and non-significant (green) analyses found for each independent variable, within each category of challenging behaviour, as well as for all challenging behaviours combined. The number of analyses included is shown (n=*x*).

	Person characteristic	Aggression	Sexually Inappropriate Behaviour	Other difficulties with emotional or behavioural regulation	All challenging behaviours
DEMOGRAPHIC	**Age** (analyses finding an association between younger age and challenging behaviours)				
	Education (analyses finding an association between less education and challenging behaviours)				
	Gender (analyses finding an association between male gender and challenging behaviours)				

	Person characteristic	Aggression	Sexually Inappropriate Behaviour	Other difficulties with emotional or behavioural regulation	All challenging behaviours
DIOAGNOSTIC	**Aetiology** (analyses finding an association between aetiology of injury and challenging behaviours)			[no analyses]	
	Location or type (analyses finding an association between location or type of brain damage and challenging behaviours)				
	Severity (analyses finding an association between greater injury severity and challenging behaviours)				
SYMPTOMS	**Cognitive function** (analyses finding an association between poorer cognitive function and challenging behaviours)				

Person characteristic		Aggression	Sexually Inappropriate Behaviour	Other difficulties with emotional or behavioural regulation	All challenging behaviours
OTHER VARIABLES	**Physical function** (analyses finding an association between poorer physical function and challenging behaviours)				
	Executive function (analyses finding an association between poorer executive function and challenging behaviours)				
	'Mental health'* (analyses finding an association between poorer mental health and challenging behaviours)				

Person characteristic	Aggression	Sexually Inappropriate Behaviour	Other difficulties with emotional or behavioural regulation	All challenging behaviours
Substance abuse (analyses finding an association between history of or current substance abuse and challenging behaviours)				
Social outcomes (analyses finding an association between poorer social outcomes and challenging behaviours)			[no analyses]	

4 Discussion

4.1 Main findings

We conducted a systematic review of evidence about the use of assessment criteria to inform the need for specialist care of adults with ABI within a secure setting. Despite a detailed search strategy and inclusion criteria, which considered the wide range of potential physical, cognitive and mental health needs of this patient group, and used a variety of supplementary search techniques, we did not identify any evidence either set in, or explicitly about the potential referral of ABI patients to, a secure treatment setting.

We did identify 47 relevant studies which aimed to identify associations between patient characteristics and challenging behaviours which may influence the decision about treatment of persons with an ABI. Depending on the needs of the individual patient, this treatment or care may be best provided within a range of possible settings, including secure services, locked rehabilitation wards or intensive support within the community. We separated studies into three groups according to outcomes of interest: aggression, sexually inappropriate behaviour and other difficulties of emotional or behavioural regulation. Within each group of studies we considered independent variables in four groups – demographic variables, ABI characteristics, symptoms arising from or relating to an ABI and 'other' variables.

There were 18 studies considering patient characteristics associated with aggression, seven looking at sexually inappropriate behaviour and 20 exploring difficulties with emotional and behavioural regulation, including agitation, disinhibition, emotional lability, maladaptive behaviour and other outcomes. While the evidence pertaining to each outcome came from studies that were predominantly of at least moderate quality, it was always based on associative analyses from observational cohort or case control studies. The findings of individual studies examining similar outcomes were highly heterogeneous, with conflicting findings or few sets of data to inform investigation of individual independent variables. A handful of patient characteristics emerged across the three outcome categories as being frequently studied with some evidence of statistically significant associations with challenging behaviours.

In the next stage of synthesis we considered whether any specific patient characteristics were associated with the range of challenging behaviours, and thus potentially worthy of consideration during patient assessment. Younger age and fewer years in education were the

most frequently analysed demographic variables, but only appeared to feature as a factor influencing the occurrence of aggression. In terms of injury and diagnostic variables; ABI aetiology, the location or type of brain damage and severity of injury were frequently evaluated but no observations of consistent associations were made across outcomes. The symptoms arising from ABI were those most commonly found to be statistically significantly associated with challenging behaviours. Specifically, cognitive function was relevant in aggression and difficulties with emotional and behavioural regulation but not in sexually inappropriate behaviour and physical functioning was particularly relevant to aggression. Analyses including measures of executive function provided the most consistent evidence of an association with challenging behaviours, with nearly three quarters of analyses finding a statistically significant association. Finally, of the outcomes that did not fit into the above categories, mental health measures, which were highly varied, were associated with challenging behaviour in 20 of the 39 analyses. There was little evidence about substance abuse or social functioning, although social functioning may be associated with aggression.

We also identified eight studies evaluating the psychometric properties of tools used in the assessment of such challenging behaviours, but there were no tools that were evaluated in more than one study, so evidence about their psychometric properties is sparse and potentially unreliable. These studies were identified in addition to a recent, high-quality systematic review that reviewed the psychometric properties of several measures of aggression. It is reported that whilst some measures of aggression demonstrated sufficient psychometric properties and were supported by moderate to high quality evidence, the quantity of evidence this was based upon, and the range of aspects of validity assessed in particular, was limited.

In summary, the main findings of this review are that there is no evidence base to directly inform decisions about whether patients with ABI who display challenging behaviours require support from a secure setting or not. There is a body of evidence, largely based on observational and case control studies in ABI patients in various other settings and points in their recovery pathway, which may be useful in informing decisions about support requirements for individuals with an ABI. This evidence suggests that certain patient characteristics may be associated with particular challenging behaviours or difficulties which may require support within a secure setting. However, the limitations of the evidence and the synthesis performed in this review mean that only tentative associations can be suggested.

4.2 Limitations of the evidence

Quantity of evidence

Crucially, there is no evidence about the utility of assessment to inform the best care pathway when patients with ABI display challenging behaviours. Ideally there would be research comparing a specific package of assessments (intervention) with existing approaches (control) and evaluating the success of each approach by considering treatment outcomes over time. There are a number of practical and ethical challenges in undertaking such research, and as such it is perhaps not surprising that this type of research does not currently exist. In lieu of this approach, we hoped to find evaluations of treatment pathways, however these were not available for secure settings with this patient group. If future decisions about referral are to be evidence-based then this evidence must first be produced.

Quality of evidence

We synthesised the evidence that was indirectly related to the research questions in order to understand what is known about factors that may influence the need for treatment in specialist services – that is, patient characteristics that may be associated with challenging behaviour. All 46 primary studies were observational cohort or case-control studies, with sample sizes ranging from 14 to 1339, but the mean sample size was 155 and there were only four studies with more than 300 participants.[30, 40, 48 51] This is important when considering that the majority of studies used regression or correlational analyses to identify often small effects, and the fact that only four studies provided a sample size justification.[31, 55, 64, 72] This is compounded in studies exploring associations between multiple dependent and/or independent variables. More than half of the studies relied on convenience sampling and therefore faced a natural restriction on the sample size, but of those recruiting more widely or using database sampling, there a justification of the sample size and description of the power obtained is warranted.

Critical appraisal of the included studies suggested that most of the evidence derived from moderate to high quality studies, albeit within the limitations of their design. However in addition to the dearth of information about sample size justification, the description of the validity and reliability of the independent and dependent variables used was often poor. Study designs were also frequently poorly described and required a degree of interpretation by the review team. This contributed to difficulty in ascertaining whether the exposure or independent variables occurred prior to measurement of outcomes. The evidence from the

eight studies evaluating different assessment or diagnostic tools was disparate. Although a number of analyses within the batch of eight psychometric studies were performed to a very good standard, all of the included measurement tools were only evaluated within single studies, and on a small selection of psychometric properties. A further consequence of this is that the outcomes of interest in the other 38 primary studies were measured with a number of these tools. As highlighted in quality appraisal, this was one of the most common flaws – for both dependent and independent variables – and further reduces the confidence in findings.

Sample characteristics

Studies were identified from a range of countries, with only 12 set in the UK. Given the UK's distinctive health and social care system, the applicability of findings from non-UK studies might be reduced. However, given our focus on patient characteristics, this is unlikely to be a major limitation of the present review.

It is notable that a number of studies explicitly excluded patients with particular characteristics from their sample. These include 18 studies excluding those with a psychiatric disorder or substance abuse and 18 excluding those with significant neurocognitive or comprehension deficits. As evidenced by several other studies in this review, psychiatric disorders and substance abuse may be important considerations influencing the need for specialist secure services, while the exclusion of those with more severe neurocognitive deficits in some studies means that such patients are underrepresented in this review.

Heterogeneity

Heterogeneity exists across many aspects of the included studies, including geographical and institutional settings, patient characteristics, study design, analytical approach, use of assessment tools and outcome measures. For this reason, we took an approach to synthesis that combined a description of findings from individual studies within outcome groups, followed by efforts to identify independent variables that showed statistically significant associations in the included studies and may be worth future investigation (e.g. in larger, higher quality studies).

4.3 Strengths and limitations of this review

We used an extensive search strategy tailored to the topic area, combining database searches with a range of supplementary techniques. These included affiliation searches, which are not typically seen in systematic reviews. Our approach also benefitted from stakeholder input,

which helped define search terms, refine inclusion criteria and review the study settings. It was often unclear whether studies were conducted in a secure setting which met the criteria for secure services as defined by the physical, procedural and relational security measures indicated in service specifications for adult secure services, therefore clarification of this point by topic experts was essential.

We believe it is a strength of this review that, although we did not identify studies able to directly answer our research questions, we provide a systematic review of the next best evidence – that which can be used to indirectly inform the decision about likely future support needs and therefore decisions about appropriate treatment settings. Given the lack of evidence synthesis in this topic area, we believe these findings make a valuable contribution to the knowledge base, despite the limitations of the evidence.

We were unfortunately unable to involve patients or members of the public in this review. This was due to both logistical reasons associated with the review timeline, and the perceived difficulty associated with recruiting the vulnerable people that would have been required to share their experience of acquired brain injury, challenging behaviour and treatment referral decisions, ideally with regard to secure settings. This is a challenge that will face others working in this field but efforts should be made to overcome it.

Our approach to synthesis may be considered a limitation, as we relied on a descriptive and broad narrative approach. However as discussed above, this approach was deemed the most appropriate given the evidence available. More restrictive inclusion criteria may have reduced the heterogeneity in the sample, but we valued a systematic review of the diverse but relevant evidence currently available in relation to our research questions.

The second stage of our synthesis required the grouping of heterogeneous outcomes and was unable to explore the sometimes conflicting findings therein. However, it was beyond the scope of this review to attempt to go into such detailed explanations. We were interested in highlighting variables worthy of consideration in patient assessments, rather than investigating the underlying mechanisms beneath potentially causative relationships. This meant that only studies which examined factors which may be linked to a challenging behaviour, or difficulty, that could require support from a secure service were included. Where the link to a challenging behaviour was not explicit, studies were not eligible for inclusion. One implication of this was that studies measuring or evaluating patient characteristics associated with aspects of dysexecutive syndrome, such as perseveration, were

not always included. To fully understand links between patient characteristics and dysexecutive syndrome, we recommend a separate, more focused review, on this topic. Furthermore it should be noted that as a result of this approach to the analysis of key variables (section 3.6), the influence of the quality of individual studies was not able to be taken into account.

The inclusion of international evidence in this review was considered a strength because it allowed us to capture evidence relevant to the UK context. However, it must be noted that the health systems in other countries may not be directly comparable to the UK, and this should be considered when interpreting international studies.

5 Conclusions

5.1 Implications for further research

Due to the dearth of literature we are unable to directly answer our research questions. Therefore, our main recommendation is that high quality primary research is urgently needed in this area to inform decisions about the need for referral to secure services for people with ABI who display challenging behaviour. As a starting point, any published evaluations of existing referral pathways or decisions about care would provide valuable insight into the success of these processes, while important considerations could be identified by mixed methods studies. The work of Melzer and colleagues provides valuable qualitative and survey evidence about decision-making during referrals and access to medium secure settings in the UK, although this work was not focused on the specific needs of people with ABI.[10, 78, 79]

The evidence identified in this systematic review may aid the development of future assessment protocols for those patients with ABI who display challenging behaviours, which could be evaluated in primary research. Although there are significant challenges associated with conducting research of this nature, efforts to do so will be highly valued. Further value may be attributed to research which endeavours to include individuals with more severe neuro-cognitive difficulties, substance or alcohol misuse or mental health difficulties, given the higher prevalence of such difficulties within the ABI population. This would improve the relevance of the research and help to ensure future care pathways and design of secure services meet the support needs of this population.

The research we have identified examining the links between different patient characteristics and occurrence of challenging behaviours is as yet inconclusive. Where possible, much larger samples are required in correlational (regression) studies, with better description of study design and patient outcome measures. The variables most frequently found to be associated with challenging behaviours in this systematic review should be studied further. Section 3.6 of this report highlights patient characteristics which were most frequently found to be associated with challenging behaviour in people with ABI, in particular younger age and fewer years in education, cognitive and physical function, measures of executive function and mental health measures. These patient characteristics may warrant greater focused attention in further primary research about people with ABI who are referred for evaluation for treatment in secure settings. However, we recognise that designing and conducting research

within secure settings may be challenging and require consideration of service factors unique to each setting.

Studies evaluating the psychometric properties of assessment tools evaluating challenging behaviour would benefit from further research. More studies are required to increase the evidence base supporting use of individual assessment tools, with a greater range of psychometric constructs being evaluated. Furthermore, tools assessing challenging behaviours other than aggression have largely been unevaluated, or only considered by single studies. To facilitate further research regarding the relationship between patient characteristics and challenging behaviour, as indicated above, we suggest that research focusing on developing and/or evaluating the psychometric properties of existing measures of challenging behaviour should be a research priority.

5.2 Implications for clinical practice

Given the absence of primary research relating to the research questions of our review, there is no evidence to support decisions about care pathway for patients living with an ABI whose behaviour is challenging and whom may benefit from referral to a secure service setting.

Whilst there is some moderate quality evidence to support the consideration of various patient characteristics in the assessment informing a patient's rehabilitation needs, the findings are heterogeneous and often conflicting. This precludes the identification of a definitive list of patient demographic, diagnostic and symptom characteristics which are associated with behaviours or difficulties that could help identify patients living with an ABI who may require support from secure services.

Development of future care pathways for individuals living with an ABI for whom support within a secure treatment setting may be appropriate should be considered after the research recommendations detailed above have been addressed.

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Contribution of authors

Liz Shaw (https://orcid.org/0000-0002-6092-5019) was involved in all stages of the review, including direction, planning searches, screening, data extraction, critical appraisal, synthesis and write-up. She led clinical expert involvement and the first stage of synthesis and was a key author of the final manuscript.

Michael Nunns (https://orcid.org/0000-0001-5500-0911) was involved in all stages of the review, including direction, planning searches, screening, data extraction, critical appraisal, synthesis and write-up. He led the second stage of synthesis and was a key author of the final manuscript.

Simon Briscoe (https://orcid.org/0000-0002-6982-4521) was involved in direction, designing and conducting database and supplementary searches, screening and write-up. He also managed the reference library.

Amelia Mosley (https://orchid.org/0000-0003-1650-2868) was heavily involved in the conception and direction of the review, and contributed to development of the protocol. She contributed to screening, interpretation of findings, and critically edited the final report.

Daniel Dalton (https://orchid.org/0000-0003-2339-8704) was heavily involved in the conception and direction of the review, and contributed to development of the protocol and screening.

Rob Anderson (https://orcid.org/0000-0002-3523-8559) guided the direction of the review, advised on all stages of conducting the review, critically read and edited all sections of the report.

Jo Thompson Coon (https://orcid.org/0000-0002-5161-0234) guided the direction of the review, advised on all stages of conducting the review, and critically read and edited all sections of the report. She is the guarantor of the report.

Data-sharing statement: All data requests should be submitted to the corresponding author for consideration. Access to available anonymised data may be granted following review.

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Appendix 1. Literature search strategies

A1.1 Bibliographic databases

Database: CINAHL

Host: EBSCO

Data Parameters: n/a

Date Searched: 27.6.2019

Searcher: SB

Hits: 1153

Strategy:

1. TI (((brain or forebrain) N2 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*))) OR AB (((brain or forebrain) N2 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*)))
2. TI concussion OR AB concussion
3. (MH "Brain Injuries+")
4. TI ((cerebr* or crani* or intercrani* or intracrani* or capitis) N2 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*)) OR AB ((cerebr* or crani* or intercrani* or intracrani* or capitis) N2 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*))
5. (MH "Cerebral Edema+")
6. TI (head N2 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*)) OR AB (head N2 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*))
7. (MH "Head Injuries")
8. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7

9. TI (bleed* N2 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)) OR AB (bleed* N2 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)) OR AB (bleed* N2 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)) OR AB (bleed* N2 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis))
10. TI "blow to the head" OR AB "blow to the head"
11. TI ((brain N2 (cancer* or carcinoma* or neoplasm* or tumo?r*))) OR AB ((brain N2 (cancer* or carcinoma* or neoplasm* or tumo?r*)))
12. (MH "Brain Neoplasms")
13. TI ("cortical pseudolaminar necrosis" or "laminar necrosis") OR AB ("cortical pseudolaminar necrosis" or "laminar necrosis")
14. TI ((coup or contrecoup) N2 injur*) OR AB ((coup or contrecoup) N2 injur*)
15. TI "diffuse axonal injur*" OR AB "diffuse axonal injur*"
16. TI "eggshell fracture*" OR AB "eggshell fracture*"
17. TI ((encephalopathy or encephalomalacia)) OR AB ((encephalopathy or encephalomalacia))
18. TI "extracranial CNS injur*" OR AB "extracranial CNS injur*"
19. TI "hypoxic isch?emic injury" OR AB "hypoxic isch?emic injury"
20. TI ((intracerebral or intracranial) N0 (bleeding or h?emorrhage or injur*)) OR AB ((intracerebral or intracranial) N0 (bleeding or h?emorrhage or injur*))
21. (intraparenchymal N0 (bleed* or haemorrhage* or hemorrhage* or tear*)) OR (intraparenchymal N0 (bleed* or haemorrhage* or hemorrhage* or tear*))
22. TI "intraventricular h?ematoma" OR AB "intraventricular h?ematoma"
23. TI "leptomeningeal cyst*" OR AB "leptomeningeal cyst*"
24. TI ("neurologic injur*" or neuropathology) OR AB ("neurologic injur*" or neuropathology)
25. TI "second impact syndrome" OR AB "second impact syndrome"
26. TI skull n/0 fracture OR AB skull n/0 fracture

27. TI (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischaemia") OR AB (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischaemia")
28. (MH "Stroke+")
29. (MH "Cerebral Ischemia+")
30. TI "subarachnoid h?ematoma" OR AB "subarachnoid h?ematoma"
31. TI (subdural N0 (h?ematoma or hygroma)) OR AB (subdural N0 (h?ematoma or hygroma))
32. S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31
33. S8 OR S32
34. TI (secure N2 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*)) OR AB (secure N2 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*))
35. TI (forensic N2 (care or healthcare or hospital* or "mental health" or "occupational therap*" or psyc* or service* or unit* or ward*)) OR AB (forensic N2 (care or healthcare or hospital* or "mental health" or "occupational therap*" or psyc* or service* or unit* or ward*))
36. (MH "Forensic Psychiatry")
37. (MH "Forensic Psychology")
38. TI (locked N2 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*)) OR AB (locked N2 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*))
39. TI ("in reach" N2 (hospital or service*)) OR AB ("in reach" N2 (hospital or service*))
40. TI (psychiatric N2 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)) OR AB (psychiatric N2 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*))

41. TI (("neuro rehab*" or neurorehab* or neuropsyc* or neurobehav*) N2 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)) OR AB (("neuro rehab*" or neurorehab* or neuropsyc* or neurobehav*) N2 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*))
42. (MH "Hospitals, Psychiatric")
43. (MH "Psychiatric Units")
44. TI ("mental health" N2 (admission* or care or department* or hospital* or rehab* or service* or setting* or unit* or ward*)) OR AB ("mental health" N2 (admission* or care or department* or hospital* or rehab* or service* or setting* or unit* or ward*))
45. (MH "Mental Health Services")
46. S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45
47. S33 AND S46
48. TI ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) N1 (assessment or criter* or decision* or questionnaire* or test* or tool*)) OR AB ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) N1 (assessment or criter* or decision* or questionnaire* or test* or tool*))
49. TI (assessment N1 (criter* or decision* or questionnaire* or referral* or symptom* or tool*)) OR AB (assessment N1 (criter* or decision* or questionnaire* or referral* or symptom* or tool*))
50. TI (sensitiv* or accura* or "predictive value" or prediction* or psychometric*) OR AB (sensitiv* or accura* or "predictive value" or prediction* or psychometric*)
51. TI (validat* N1 (scale* or index*)) OR AB (validat* N1 (scale* or index*))
52. (MH "Sensitivity and Specificity")
53. (MH "Diagnosis")
54. (MH "Severity of Illness Indices")
55. S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54

56. TI ("challeng* behav*" or aggressive* or aggression or violent* or violence) OR AB ("challeng* behav*" or aggressive* or aggression or violent* or violence)

57. (MH "Violence/PC/DI")

58. (MH "Social Behavior Disorders/DI/PC")

59. (MH "Aggression/DI/PC")

60. TI (illegal* or legal* or crime or criminal* or offender*) OR AB (illegal* or legal* or crime or criminal* or offender*)

61. (MH "Crime/PC")

62. TI (memory N1 (disorder* or loss or impair*)) OR AB (memory N1 (disorder* or loss or impair*))

63. (MH "Memory Disorders/DI/PC")

64. S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63

65. S33 AND S55 AND S64

66. S47 OR S65

Notes: Date limited 2000 to date of search and limited to English language studies.

Database: HMIC

Host: Ovid

Data Parameters: 1979 to May 2019

Date Searched: 26.6.2019

Searcher: SB

Hits: 252

Strategy:

1. ((brain or forebrain) adj3 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*)).tw.

2. concussion*.tw.

3. ((cerebr* or crani* or intercrani* or intracrani* or capitis) adj3 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*)).tw.
4. (head adj3 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*)).tw.
5. or/1-4
6. (bleed* adj3 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)).tw.
7. "blow to the head".tw.
8. (brain adj3 (cancer* or carcinoma* or neoplasm* or tumo?r*)).tw.
9. ("cortical pseudolaminar necrosis" or "laminar necrosis").tw.
10. ((coup or contrecoup) adj3 injur*).tw.
11. "diffuse axonal injur*".tw.
12. "eggshell fracture*".tw.
13. (encephalopathy or encephalomalacia).tw.
14. "extracranial CNS injur*".tw.
15. "hypoxic isch?emic injury".tw.
16. ((intracerebral or intracranial) adj1 (bleeding or h?emorrhage or injur*)).tw.
17. (intraparenchymal adj1 (bleed* or haemorrhage* or hemorrhage* or tear*)).tw.
18. "intraventricular h?ematoma".tw.
19. "leptomeningeal cyst*".tw.
20. ("neurologic injur*" or neuropathology).tw.
21. "second impact syndrome".tw.
22. (skull adj1 fracture).tw.
23. (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischemia").tw.
24. "subarachnoid h?ematoma".tw.
25. (subdural adj1 (h?ematoma or hygroma)).tw.

26. or/6-25

27. 5 or 26

28. (secure adj3 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*)).tw.

29. (forensic adj3 (care or healthcare or hospital* or service* or unit* or ward* or psyc* or "mental health" or "occupational therapy")).tw.

30. (locked adj2 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*)).tw.

31. ("in reach" adj3 (hospital* or service*)).tw.

32. (psychiatric adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

33. ((“neuro rehab*” or neurorehab or neuropsyc* or neurobehav*) adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

34. ("mental health" adj3 (admission* or care or department* or hospital* or service* or setting* or unit* or ward*)).tw.

35. or/28-34

36. 27 and 35

37. ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) adj2 (assessment or criter* or decision* or questionnaire* or test* or tool*)).tw.

38. (assessment adj2 (criter* or decision* or questionnaire* or referral* or symptom* or tool*)).tw.

39. (sensitiv* or accura* or "predictive value" or prediction*).tw.

40. (validat* adj2 (scale* or index*)).tw.

41. psychometric*.tw.

42. or/37-41

43. 27 and 42

44. ("challeng* behav*" or aggressive* or aggression or violent* or violence).tw.

45. (illegal* or legal* or crime or criminal* or offender*).tw.

46. (memory adj2 (disorder* or loss or impair*)).tw.

47. or/44-46

48. 27 and 47

49. 36 or 43 or 48

50. 50. limit 49 to yr="2000 -Current"

Database: MEDLINE

Host: Ovid

Data Parameters: 1946 to June Week 3 2019

Date Searched: 26.6.2019

Searcher: SB

Hits: 2562

Strategy:

1. ((brain or forebrain) adj3 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*)).tw.
2. concussion*.tw.
3. ((cerebr* or crani* or intercrani* or intracrani* or capitis) adj3 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*)).tw.
4. exp Craniocerebral Trauma/
5. (head adj3 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*)).tw.
6. or/1-5
7. (bleed* adj3 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)).tw.
8. "blow to the head".tw.
9. (brain adj3 (cancer* or carcinoma* or neoplasm* or tumo?r*)).tw.

10. exp Brain Neoplasms/
11. ("cortical pseudolaminar necrosis" or "laminar necrosis").tw.
12. ((coup or contrecoup) adj3 injur*).tw.
13. "diffuse axonal injur*".tw.
14. "eggshell fracture*".tw.
15. (encephalopathy or encephalomalacia).tw.
16. "extracranial CNS injur*".tw.
17. "hypoxic isch?emic injury".tw.
18. ((intracerebral or intracranial) adj1 (bleeding or h?emorrhage or injur*)).tw.
19. (intraparenchymal adj1 (bleed* or haemorrhage* or hemorrhage* or tear*)).tw.
20. "intraventricular h?ematoma".tw.
21. "leptomeningeal cyst*".tw.
22. ("neurologic injur*" or neuropathology).tw.
23. neuropathology/
24. "second impact syndrome".tw.
25. (skull adj1 fracture).tw.
26. (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischaemia").tw.
27. exp Stroke/
28. exp Brain Ischemia/
29. "subarachnoid h?ematoma".tw.
30. (subdural adj1 (h?ematoma or hygroma)).tw.
31. or/7-30
32. 6 or 31
33. (secure adj3 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*)).tw.

34. (forensic adj3 (care or healthcare or hospital* or "mental health" or "occupational therap*" or psyc* or service* or unit* or ward*)).tw.
35. Forensic Psychiatry/
36. forensic psychology/
37. (locked adj3 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*)).tw.
38. ("in reach" adj3 (hospital or service*)).tw.
39. (psychiatric adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.
40. (("neuro rehab*" or neurorehab* or neuropsyc* or neurobehav*) adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.
41. Hospitals, Psychiatric/
42. Psychiatric Department, Hospital/
43. ("mental health" adj3 (admission* or care or department* or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.
44. Mental Health Services/
45. or/33-44
46. 32 and 45
47. ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) adj2 (assessment or criter* or decision* or questionnaire* or test* or tool*)).tw.
48. (assessment adj2 (criter* or decision* or questionnaire* or referral* or symptom* or tool*)).tw.
49. (sensitiv* or accura* or "predictive value" or prediction*).tw.
50. (validat* adj2 (scale* or index*)).tw.
51. "Sensitivity and Specificity"/
52. Diagnosis/

53. "Severity of Illness Index"/

54. psychometric*.tw.

55. or/47-54

56. ("challeng* behav*" or aggressive* or aggression or violent* or violence).tw.

57. Violence/di, pc [Diagnosis, Prevention & Control]

58. Social Behavior Disorders/di, pc [Diagnosis, Prevention & Control]

59. (illegal* or legal* or crime or criminal* or offender*).tw.

60. Crime/pc, px [Prevention & Control, Psychology]

61. (memory adj2 (disorder* or loss or impair*)).tw.

62. Memory Disorders/di [Diagnosis]

63. or/56-62

64. 32 and 55 and 63

65. 46 or 64

66. limit 65 to (english language and yr="2000 -Current")

Database: MEDLINE In-Process & Other Non-Indexed Citations

Host: Ovid

Data Parameters: 1946 to June 25, 2019

Date Searched: 26.6.2019

Searcher: SB

Hits: 356

Strategy:

1. ((brain or forebrain) adj3 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*)).tw.
2. concussion*.tw.

3. ((cerebr* or crani* or intercrani* or intracrani* or capitis) adj3 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*)).tw.
4. (head adj3 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*)).tw.
5. or/1-4
6. (bleed* adj3 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)).tw.
7. "blow to the head".tw.
8. (brain adj3 (cancer* or carcinoma* or neoplasm* or tumo?r*)).tw.
9. ("cortical pseudolaminar necrosis" or "laminar necrosis").tw.
10. ((coup or contrecoup) adj3 injur*).tw.
11. "diffuse axonal injur*".tw.
12. "eggshell fracture*".tw.
13. (encephalopathy or encephalomalacia).tw.
14. "extracranial CNS injur*".tw.
15. "hypoxic isch?emic injury".tw.
16. ((intracerebral or intracranial) adj1 (bleeding or h?emorrhage or injur*)).tw.
17. (intraparenchymal adj1 (bleed* or haemorrhage* or hemorrhage* or tear*)).tw.
18. "intraventricular h?ematoma".tw.
19. "leptomeningeal cyst*".tw.
20. ("neurologic injur*" or neuropathology).tw.
21. "second impact syndrome".tw.
22. (skull adj1 fracture).tw.
23. (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischemia").tw.
24. "subarachnoid h?ematoma".tw.
25. (subdural adj1 (h?ematoma or hygroma)).tw.

26. or/6-25

27. 5 or 26

28. (secure adj3 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*)).tw.

29. (forensic adj3 (care or healthcare or hospital* or service* or unit* or ward* or psyc* or "mental health" or "occupational therapy")).tw.

30. (locked adj2 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*)).tw.

31. ("in reach" adj3 (hospital* or service*)).tw.

32. (psychiatric adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

33. ((“neuro rehab*” or neurorehab or neuropsyc* or neurobehav*) adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

34. ("mental health" adj3 (admission* or care or department* or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

35. or/28-34

36. 27 and 35

37. ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) adj2 (assessment or criter* or decision* or questionnaire* or test* or tool*)).tw.

38. (assessment adj2 (criter* or decision* or questionnaire* or referral* or symptom* or tool*)).tw.

39. (sensitiv* or accura* or "predictive value" or prediction*).tw.

40. (validat* adj2 (scale* or index*)).tw.

41. psychometric*.tw.

42. or/37-41

43. ("challeng* behav*" or aggressive* or aggression or violent* or violence).tw.

44. (illegal* or legal* or crime or criminal* or offender*).tw.

45. (memory adj2 (disorder* or loss or impair*)).tw.

46. or/43-45

47. 27 and 42 and 46

48. 36 or 47

49. limit 48 to yr="2000 -Current"

Database: PsycINFO

Host: Ovid

Data Parameters: 1806 to June Week 3 2019

Date Searched: 26.6.2019

Searcher: SB

Hits: 1649

Strategy:

1. ((brain or forebrain) adj3 (aneurysm* or damage or edema or h?emorrhage* or infarction* or injur* or oedema or swell* or trauma* or wound*)).tw.
2. concussion*.tw.
3. exp BRAIN CONCUSSION/
4. exp traumatic brain injury/
5. brain injuries/
6. brain damage/
7. ((cerebr* or crani* or intercrani* or intracrani* or capitis) adj3 (atrophy or contusion* or damage or edema or h?emorrhage* or infarction* or injur* or laceraton* or oedema or swell* or trauma*)).tw.
8. cerebral atrophy/
9. (head adj3 (bleed* or damage or fractur* or injur* or swell* or trauma* or wound*)).tw.
10. exp head injuries/

11. or/1-10
12. (bleed* adj3 (brain or cerebr* or crani* or intercrani* or intracrani* or capitis)).tw.
13. "blow to the head".tw.
14. (brain adj3 (cancer* or carcinoma* or neoplasm* or tumo?r*)).tw.
15. exp Brain Neoplasms/
16. ("cortical pseudolaminar necrosis" or "laminar necrosis").tw.
17. ((coup or contrecoup) adj3 injur*).tw.
18. "diffuse axonal injur*".tw.
19. "eggshell fracture*".tw.
20. (encephalopathy or encephalomalacia).tw.
21. "extracranial CNS injur*".tw.
22. "hypoxic isch?emic injury".tw.
23. ((intracerebral or intracranial) adj1 (bleeding or h?emorrhage or injur*)).tw.
24. (intraparenchymal adj1 (bleed* or haemorrhage* or hemorrhage* or tear*)).tw.
25. "intraventricular h?ematoma".tw.
26. "leptomeningeal cyst*".tw.
27. ("neurologic injur*" or neuropathology).tw.
28. neuropathology/
29. "second impact syndrome".tw.
30. (skull adj1 fracture).tw.
31. (stroke or "cerebro vascular accident*" or "cerebrovascular accident*" or "cerebral ischemia").tw.
32. cerebral ischemia/
33. cerebrovascular accidents/
34. "subarachnoid h?ematoma".tw.
35. (subdural adj1 (h?ematoma or hygroma)).tw.

36. or/12-35

37. 11 or 36

38. (secure adj3 (care or healthcare or hospital* or "mental health" or service* or unit* or ward*)).tw.

39. (forensic adj3 (care or healthcare or hospital* or service* or unit* or ward* or psyc* or "mental health" or "occupational therapy")).tw.

40. Forensic Psychiatry/

41. forensic psychology/

42. (locked adj2 (care or healthcare or hospital* or "mental health" or rehab* or service* or unit* or ward*)).tw.

43. ("in reach" adj3 (hospital* or service*)).tw.

44. (psychiatric adj3 (admission* or care or department* or healthcare or hospital* or rehab* or service* or setting* or unit* or ward*)).tw.

45. ((“neuro rehab*” or neurorehab or neuropsyc* or neurobehav*) adj3 (admission* or care or department* or hospital* or service* or setting* or unit* or ward*)).tw.

46. psychiatric units/

47. ("mental health" adj3 (admission* or care or department* or hospital* or service* or setting* or unit* or ward*)).tw.

48. Mental Health Services/

49. or/38-48

50. 37 and 49

51. ((diagnos* or "disease severity" or psyc* or referral* or risk* or screening) adj2 (assessment or criter* or decision* or questionnaire* or test* or tool*)).tw.

52. (assessment adj2 (criter* or decision* or questionnaire* or referral* or symptom* or tool*)).tw.

53. (sensitiv* or accura* or "predictive value" or prediction*).tw.

54. (validat* adj2 (scale* or index*)).tw.

55. test sensitivity/

56. diagnosis/

57. Psychodiagnosis/

58. "severity (disorders)"/

59. psychometric*.tw.

60. or/51-59

61. ("challeng* behav*" or aggressive* or aggression or violent* or violence).tw.

62. violence/

63. behavior disorders/

64. antisocial behavior/

65. (illegal* or legal* or crime or criminal* or offender*).tw.

66. crime prevention/

67. crime/

68. (memory adj2 (disorder* or loss or impair*)).tw.

69. memory disorders/

70. or/61-69

71. 37 and 60 and 70

72. 50 or 71

73. limit 72 to (english language and yr="2000 -Current")

Database: Social Policy and Practice

Host: Ovid

Data Parameters: 201904

Date Searched: 26.6.2019

Searcher: SB

Hits: 219

Strategy: see HMIC search strategy

Database: ASSIA

Host: ProQuest

Data Parameters: n/a

Date Searched: 27.6.2019

Searcher: SB

Hits: 366 (search 1); 135 (search 2)

Strategy:

Search 1

((ti,ab((brain OR forebrain OR head) near/2 (aneurysm* OR damage OR edema OR h?emorrhage* OR infarction* OR injur* OR oedema or swell* OR trauma* or wound*))) OR MAINSUBJECT.EXACT("Brain injuries") OR MAINSUBJECT.EXACT("Head injuries")) AND (ti,ab(secure OR forensic OR locked OR psyc* or neuro* OR “mental health”) OR MAINSUBJECT.EXACT("Secure units") OR MAINSUBJECT.EXACT("Forensic units") OR MAINSUBJECT.EXACT("Mental health services"))

Search 2

((ti,ab((brain OR forebrain OR head) near/2 (aneurysm* OR damage OR edema OR h?emorrhage* OR infarction* OR injur* OR oedema or swell* OR trauma* OR wound*))) OR MAINSUBJECT.EXACT("Brain injuries") OR MAINSUBJECT.EXACT("Head injuries")) AND ((ti,ab(sensitiv* OR accura* OR "predictive value" OR prediction* OR diagnos* OR "disease severity" OR psyc* OR referral* OR risk* OR screening)) OR MAINSUBJECT.EXACT("Diagnosis")) AND (ti,ab("challeng* behav*" OR aggressive* OR aggression OR violent* OR violence OR illegal* OR legal* OR crime OR criminal* OR offender*) OR MAINSUBJECT.EXACT("Challenging behaviour") OR MAINSUBJECT.EXACT("Aggression") OR MAINSUBJECT.EXACT("Criminal behaviour") OR (memory NEAR/1 (disorder* OR loss OR impair*)) OR MAINSUBJECT.EXACT("Memory disorders"))

Notes: Date limited 2000 to date of search and English language studies.

A1.1.1 Bibliographic database search results

Table 11. Bibliographic database search results

Database	Hits
CINAHL	1153
HMIC	252
MEDLINE	2562
MEDLINE In-Process	356
PsycINFO	1649
Social Policy and Practice	219
ASSIA	501
Total records	6692
Duplicate records	1716
Unique records	4976

A1.2 Clinical Trials Registries

Registry: ClinicalTrials.gov

Data Parameters: n/a

Date Searched: 27/8/2019

Searcher: SB

Hits: 81

Strategy:

Condition or disease: "brain injury" OR "brain injuries" OR "head injury" OR "head injuries" OR "head wound" OR "head wounds"

Other terms: secure OR forensic OR psychiatric

Registry: ICTRP Search Portal

Data Parameters: Recruitment status: ALL; Searched for trials with results only.

Date Searched: 28/8/2019

Searcher: SB

Hits: 94

Strategy: "brain injury" OR "brain injuries" OR "head injury" OR "head injuries" OR "head wound" OR "head wounds" (Title field)

A1.3 Web searches

Website: Brain Injury Rehabilitation Trust (BIRT)

URL: https://www.thedtgroup.org/research/research-publications

Date Searched: 14/8/2019

Searcher: SB

Hits: Not detailed (website does not report the number of results per page)

Strategy: Navigated to webpage listing research publications (see URL above) and inspected for relevant studies.

Website: Centre for Mental Health

URL: https://www.centreformentalhealth.org.uk/publications

Date Searched: 14/8/2019

Searcher: SB

Hits: 1

Strategy:

Title field: injury

Title field: injuries

Title field: trauma

Title field: traumatic

Website: Headway

URL: https://www.headway.org.uk/about-brain-injury/individuals/information-library/

Date Searched: 14/8/2019

Searcher: SB

Hits: Not detailed (website does not report the number of results per page)

Strategy: Navigated to Information Library (see URL above) and inspected for relevant studies.

Website: MIND

URL: https://www.mind.org.uk/

Date Searched: 14/8/2019

Searcher: SB

Hits: 84

Strategy: head OR brain injury

Website: The Royal College of Psychiatrists

URL: https://www.rcpsych.ac.uk/improving-care/ccqi/resources/publications-archive?searchTerms=publications

Date Searched: 14/8/2019

Searcher: SB

Hits: Not detailed (website does not report the number of results per page)

Strategy: Navigated to Publications archive (see URL above) and inspected for relevant studies.

Website: The United Kingdom Acquired Brain Injury Forum

URL: https://www.ukabif.org.uk/

Date Searched: 14/8/2019

Searcher: SB

Hits: n/a (browsing strategy used)

Strategy: Browsed website for relevant studies.