National Institute for Health and Care Excellence

FINAL

Rehabilitation after traumatic injury

Supplement 1: Methods

NICE guideline NG211

Development of the guideline and methods

January 2022

FINAL

Developed by the National Guideline Alliance, which is a part of the Royal College of Obstetricians and Gynaecologists

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN: 978-1-4731-4398-2

Contents

Development of the guideline

Remit

The National Institute for Health and Care Excellence (NICE) commissioned the National Guideline Alliance (NGA) to develop a guideline for rehabilitation after traumatic injury.

For further details of what the guideline does and does not cover see: https://www.nice.org.uk/guidance/ng211/history

Methods

Introduction

This section summarises methods used to identify and review the evidence, to consider cost effectiveness, and to develop guideline recommendations. This guideline was developed in accordance with methods described in Developing NICE guidelines: the manual.

Declarations of interest were recorded and managed in accordance with NICE's 2018 policy on declaring and managing interests for NICE advisory committees.

Developing the review questions and outcomes

The review questions considered in this guideline were based on the key areas identified in the guideline scope .They were drafted by the NGA technical team, and refined and validated by the guideline committee.

The review questions were based on the following frameworks:

- intervention reviews – using population, intervention, comparison and outcome (PICO)
- qualitative reviews – using population, phenomenon of interest and context

These frameworks guided the development of review protocols, the literature searching process, and critical appraisal and synthesis of evidence. They also facilitated development of recommendations by the committee.

Literature searches, critical appraisal and evidence reviews were completed for all review questions.

The review questions and evidence reviews corresponding to each question (or group of questions) are summarised in Table 1.

Table 1: Summary of review questions and index to evidence reviews

Evidence review	Review question	Type of review
[A.1/A.2] Identification and assessment of rehabilitation needs after traumatic injury	[A.1a] What should be included in initial rehabilitation needs identification and assessment for adults after traumatic injury?	Intervention
[A.1/A.2] Identification and assessment of rehabilitation needs after traumatic injury	[A.1b] What should be included in initial rehabilitation needs identification and assessment for children and young people after traumatic injury?	Intervention
[A.1/A.2] Identification and	[A.2a] What are the views and preferences of adults who have used rehabilitation services	Qualitative

Evidence review	Review question	Type of review
assessment of rehabilitation needs after traumatic injury	after traumatic injury about assessment of their rehabilitation needs	
[A.1/A.2] Identification and assessment of rehabilitation needs after traumatic injury	[A.2b] What are the views and preferences of children and young people who have used rehabilitation services after traumatic injury about assessment of their rehabilitation needs	Qualitative
[B.1] Physical interventions for people with complex rehabilitation needs after traumatic injury	[B.1a] What physical rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?	Intervention
[B.1] Physical interventions for people with complex rehabilitation needs after traumatic injury	[B.1b] What physical rehabilitation interventions are effective and acceptable for children and young people with complex rehabilitation needs after traumatic injury?	Intervention
[B.2] Cognitive interventions for people with complex rehabilitation needs after traumatic injury	[B.2a] What cognitive rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?	Intervention
[B.2] Cognitive interventions for people with complex rehabilitation needs after traumatic injury	[B.2b] What cognitive rehabilitation interventions are effective and acceptable for children and young people with complex rehabilitation needs after traumatic injury?	Intervention
[B.3] Psychological and psychosocial interventions for people with complex rehabilitation needs after traumatic injury	[B.3a] What psychological and psychosocial rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?	Intervention
[B.3] Psychological and psychosocial interventions for people with	[B.3b] What psychological and psychosocial rehabilitation interventions are effective and acceptable for children and young people with complex rehabilitation needs after traumatic injury?	Intervention

Evidence review	Review question	Type of review
complex rehabilitation needs after traumatic injury		
[B.4] Rehabilitation interventions relating to participation in society for people with complex rehabilitation needs after traumatic injury	[B.4a] What rehabilitation interventions relating to participation in society are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?	Intervention
[B.4] Rehabilitation interventions relating to participation in society for people with complex rehabilitation needs after traumatic injury	[B.4b] What rehabilitation interventions relating to participation in society are effective and acceptable for children and young people with complex rehabilitation needs after traumatic injury?	Intervention
[C.1] Specific programmes and packages in amputation for people with complex rehabilitation needs after traumatic injury	[C.1a] For adults with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?	Intervention
[C.1] Specific programmes and packages in amputation for people with complex rehabilitation needs after traumatic injury	[C.1b] For children and young people with complex rehabilitation needs after traumatic injury that results in limb reconstruction, limb loss or amputation, what specific rehabilitation programmes and packages, including prosthetics, are effective and acceptable?	Intervention
[C.2] Specific programmes and packages in nerve injury for people with complex rehabilitation needs after traumatic injury	[C.2a] For adults with complex rehabilitation needs after traumatic injury that involves nerve injury, what specific rehabilitation programmes and packages are effective and acceptable?	Intervention
[C.2] Specific programmes and	[C.2b] For children and young people with complex rehabilitation needs after traumatic	Intervention

Evidence review	Review question	Type of review
packages in nerve injury for people with complex rehabilitation needs after traumatic injury	injury that involves nerve injury, what specific rehabilitation programmes and packages are effective and acceptable?	
[C.3] Specific programmes and packages in spinal cord injury for people with complex rehabilitation needs after traumatic injury	[C.3a] For adults with complex rehabilitation needs after traumatic injury that involves spinal cord injury, what specific rehabilitation programmes and packages are effective and acceptable?	Intervention
[C.3] Specific programmes and packages in spinal cord injury for people with complex rehabilitation needs after traumatic injury	[C.3b] For children and young people with complex rehabilitation needs after traumatic injury that involves spinal cord injury, what specific rehabilitation programmes and packages are effective and acceptable?	Intervention
[C.4] Specific programmes and packages in chest injury for people with complex rehabilitation needs after traumatic injury	[C.4a] For adults with complex rehabilitation needs after traumatic injury that involves chest injury, what specific rehabilitation programmes and packages are effective and acceptable?	Intervention
[C.4] Specific programmes and packages in chest injury for people with complex rehabilitation needs after traumatic injury	[C.4b] For children and young people with complex rehabilitation needs after traumatic injury that involves chest injury, what specific rehabilitation programmes and packages are effective and acceptable?	Intervention
[D.1] Service coordination: Inpatient settings for people with complex rehabilitation needs after traumatic injury	[D.1a] What are the best methods to coordinate rehabilitation services for adults with complex rehabilitation needs after traumatic injury whilst they are an inpatient, including when transferring between inpatient settings?	Mixed methods (intervention and qualitative)
[D.1] Service coordination: Inpatient settings for people with	[D.1b] What are the best methods to coordinate rehabilitation services for children and young people with complex rehabilitation needs after traumatic injury whilst they are an	Mixed methods (intervention and qualitative)

Evidence review	Review question	Type of review
complex rehabilitation needs after traumatic injury	inpatient, including when transferring between inpatient settings?	
[D.2] Service coordination: Inpatient to outpatient settings for people with complex rehabilitation needs after traumatic injury	[D.2a] What are the best methods to deliver and coordinate rehabilitation services and social services for adults with complex rehabilitation needs after traumatic injury when they transfer from inpatient to outpatient rehabilitation services?	Mixed methods (intervention and qualitative)
[D.2] Service coordination: Inpatient to outpatient settings for people with complex rehabilitation needs after traumatic injury	[D.2b] What are the best methods to deliver and coordinate rehabilitation services and social services for children and young people with complex rehabilitation needs after traumatic injury when they transfer from inpatient to outpatient rehabilitation services?	Mixed methods (intervention and qualitative)
[D.3] Service coordination: Barriers and facilitators to accessing rehabilitation services following discharge to the community for people with complex rehabilitation needs after traumatic injury	[D.3a] What are the barriers and facilitators to accessing rehabilitation services, including follow-up, following discharge to the community for adults with complex rehabilitation needs after traumatic injury?	Qualitative
[D.3] Service coordination: Barriers and facilitators to accessing rehabilitation services following discharge to the community for people with complex rehabilitation needs after traumatic injury	[D.3b] What are the barriers and facilitators to accessing rehabilitation services, including follow-up, following discharge to the community for children and young people with complex rehabilitation needs after traumatic injury?	Qualitative
[D.4] Service coordination:	[D.4a] What are the support needs and preferences of adults who have complex	Qualitative

Evidence review	Review question	Type of review
Support needs and preferences following discharge to out-patient or community rehabilitation services for people with complex rehabilitation needs after traumatic injury	rehabilitation needs after traumatic injury when they transfer from inpatient to outpatient or community rehabilitation services?	
[D.4] Service coordination: Support needs and preferences following discharge to out-patient or community rehabilitation services for people with complex rehabilitation needs after traumatic injury	[D.4b] What are the support needs and preferences of children and young people who have complex rehabilitation needs after traumatic injury when they transfer from inpatient to outpatient or community rehabilitation services?	Qualitative

[1]*Original health economic analysis conducted*

The COMET database was searched for core outcome sets relevant to this guideline. No core outcome sets were identified and therefore the outcomes were chosen based on committee discussions.

Additional information related to development of the guideline is contained in:

- Supplement 1 (Methods; this document)
- Supplement 2 (NGA staff list).

Searching for evidence

Scoping search

During the scoping phase, searches were conducted for previous guidelines, economic evaluations, health technology assessments and systematic reviews. Searches of websites of organisations and internet search engines were also undertaken for relevant policies and related documents.

Systematic literature search

Systematic literature searches were undertaken to identify published evidence relevant to each review question.

Databases were searched using subject headings, free-text terms and, where appropriate, study type filters. Where possible, searches were limited to retrieve studies published in English. All the searches were conducted between January 2019 and March 2020 in the following databases: Medline, Medline-in-Process, Cochrane Central Register of Controlled Trials (CCTR), Cochrane Database of Systematic Reviews (CDSR), and Embase. For review questions related to cognitive rehabilitation or psychological and psychosocial interventions, PsycInfo was also searched. For review questions where qualitative evidence was of interest, PsycInfo, Social Policy and Practice, and Social Care Online were also searched.

Searches were run once for all reviews during development. Searches for the following questions were updated in November 2020, 14 weeks in advance of the final committee meeting. These questions were prioritised for update searches because they were the oldest searches and covered the areas where new evidence was most likely to impact the recommendations. All of the searches that were updated were limited by study type filter to randomized controlled trials only.

- C.1a & C.1b
- C.2a & C.2b
- C.3a & C.3b
- C.4a & C.4b
- B.1a & B.1b

Details of the search strategies, including the study-design filters used and databases searched, are provided in Appendix B of each evidence review.

Economic systematic literature search

Systematic literature searches were also undertaken to identify published economic evidence. Databases were searched using subject headings, free-text terms and, where appropriate, an economic evaluations search filter.

Searches using the search strategies derived from the review questions, combined with a search filter for economic evaluations, were conducted between January 2019 and March 2020 in Medline, Medline in Process, CCTR and Embase. Where possible, searches were limited to studies published in English.

For review questions where qualitative evidence was of interest targeted searches were conducted if the committee highlighted areas relevant to health economics when discussing the qualitative evidence. This resulted in a targeted search for rehabilitation prescription being conducted for questions A.2a & A.2b.

As with the general literature searches, the economic literature searches were run once for all reviews during development. Searches for the following questions were updated in November, 14 weeks in advance of the final committee meeting.

- C.1a & C.1b
- C.2a & C.2b
- C.3a & C.3b
- C.4a & C.4b
- B.1a & B.1b

Details of the health economics search strategies, including the study-design filters used and databases searched, are provided in Appendix B of each evidence review.

Quality assurance

Search strategies were quality assured by cross-checking reference lists of relevant studies, analysing search strategies from published systematic reviews and asking members of the committee to highlight key studies. The principal search strategies for each search were also quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist (McGowan 2016).

Expert witness

When there is little or no evidence identified for an important topic from systematic reviews, the committee can also use expert testimony (either from an individual or from an organisation) to make recommendations. The expert witness was decided after a group discussion by the guideline committee, after considering candidates who had the relevant expertise. A call for evidence was not made as the committee were not aware of any ongoing or recently completed trials that would affect their recommendations.

When developing the review protocols, the committee emphasised the importance of intensity of rehabilitation and highlighted this as a potential guideline area for economic analysis. We found no evidence for intensity of rehabilitation that met our inclusion criteria for any of the review questions that included intensity of rehabilitation as a comparison. The committee were aware of the extensive use of intensive rehabilitation in military populations, and the associated benefits that have been reported in the literature. However, these benefits tended to be reported in small non-randomised studies that did not meet the inclusion criteria agreed in the relevant guideline reviews. Therefore, the committee agreed to invite a military expert to provide evidence on:

- Definition and components of intensive rehabilitation
- Trauma population (and sub-groups) where intensive rehabilitation is most effective
- Timing and duration of intensive rehabilitation
- Benefits and harms of intensive rehabilitation
- Health economics of intensive rehabilitation, including resource implications and potential capacity of NHS delivery

The testimony was provided orally alongside presentation slides for clarity. This will not be presented due to the Ministry of Defence privacy policy but relevant points for recommendations have been included in the summary of evidence section of evidence review B.1. Following the presentation of the evidence, the committee discussed and considered it before agreeing recommendations. A copy of the expert testimony form was included as an appendix in evidence review B.1.

Reviewing evidence

Systematic review process

The evidence was reviewed in accordance with the following approach.

- Potentially relevant articles were identified from the search results for each review question by screening titles and abstracts. Full-text copies of the articles were then obtained.
- Full-text articles were reviewed against pre-specified inclusion and exclusion criteria in the review protocol (see Appendix A of each evidence review).
- Key information was extracted from each article on study methods and results, in accordance with factors specified in the review protocol. The information was presented in a summary table in the corresponding evidence review and in a more detailed evidence table (see Appendix E of each evidence review).
- Included studies were critically appraised using an appropriate checklist as specified in Developing NICE guidelines: the manual. Further detail on appraisal of the evidence is provided below.
- Summaries of evidence by outcome were presented in the corresponding evidence review and discussed by the committee.

Review questions selected as high priorities for economic analysis (and those selected as medium priorities and where economic analysis could influence recommendations) and complex review questions were subject to dual screening and study selection. With the exception of 4 (straightforward) review questions, dual screening was undertaken for all the review questions through a random sample of at least 5% of articles. Any discrepancies were resolved by discussion between the first and second reviewers or by reference to a third (senior) reviewer. For the remaining review questions, internal (NGA) quality assurance processes included consideration of the outcomes of screening, study selection and data extraction and the committee reviewed the results of study selection and data extraction. The review protocol for each question specifies whether dual screening and study selection was undertaken for that particular question.

Drafts of all evidence reviews were checked by a senior reviewer.

Type of studies and inclusion/exclusion criteria

Inclusion and exclusion of studies was based on criteria specified in the corresponding review protocol.

Systematic reviews with meta-analyses were considered to be the highest quality evidence that could be selected for inclusion.

For intervention reviews, randomised controlled trials (RCTs) were prioritised for inclusion because they are considered to be the most robust type of study design that could produce an unbiased estimate of intervention effects. Where there was limited evidence from RCTs, non-randomised studies (NRS) were considered for inclusion.

For qualitative reviews, studies using focus groups, structured interviews or semi-structured interviews were considered for inclusion. Where qualitative evidence was sought, data from surveys or other types of questionnaire were considered for inclusion only if they provided data from open-ended questions, but not if they reported only quantitative data.

The committee was consulted about any uncertainty regarding inclusion or exclusion of studies. A list of excluded studies for each review question, including reasons for exclusion is presented in Appendix D of the corresponding evidence review.

Narrative reviews, posters, letters, editorials, comment articles, unpublished studies and studies published in languages other than English were excluded. Conference abstracts were not considered for inclusion because conference abstracts typically do not have sufficient information to allow for full critical appraisal.

Methods of combining evidence

When planning reviews (through preparation of protocols), the following approaches for data synthesis were discussed and agreed with the committee.

Data synthesis for intervention reviews

Pairwise meta-analysis

Meta-analysis to pool results from RCTs was conducted where possible using Cochrane Review Manager (RevMan5) software. However, we were only able to perform 1 meta-analysis due to between-study differences in interventions, comparators or outcomes. Where non-randomised evidence was used, this was not meta-analysed.

For dichotomous outcomes, such as pain category, the Mantel–Haenszel method with a fixed effect model was used to calculate risk ratios (RRs).

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation; SD) are required for meta-analysis. Data for continuous outcomes, such as activities of daily living, were meta-analysed using an inverse-variance method for pooling weighted mean differences (WMDs). Where SDs were not reported for each intervention group, the standard error (SE) of the mean difference was calculated from other reported statistics (p values or 95% confidence intervals; CIs) and then meta-analysis was conducted as described above.

If a study reported only the summary statistic and 95% CI the generic-inverse variance method was used to enter data into RevMan5. If the control event rate was reported this was used to generate the absolute risk difference in GRADEpro. If

multivariable analysis was used to derive the summary statistic but no adjusted control event rate was reported, no absolute risk difference was calculated.

When evidence was based on studies that reported descriptive data or medians with or without interquartile ranges or p values, this information was included in the corresponding GRADE tables (see below) without calculating relative or absolute effects. Consequently, imprecision of the effect estimate could not be assessed as per standard methods for the quality assessment of this type of evidence. Imprecision was instead assessed using sample size (see below).

For some reviews, evidence was either stratified from the outset or separated into subgroups when heterogeneity was encountered. The stratifications and potential subgroups were pre-defined at the protocol stage (see the protocols for each review for further detail). Where evidence was stratified or subgrouped the committee considered on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee considered, based on their experience, whether it was reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others

When meta-analysis was undertaken, the results were presented visually using forest plots generated using RevMan5 (see Appendix F of relevant evidence reviews).

When case series were included, descriptive data from the studies were included and no further analysis was performed.

Data synthesis for qualitative reviews

Where possible, a meta-synthesis was conducted to combine evidence from qualitative studies. Whenever studies identified a qualitative theme relevant to the protocol, this was extracted and the main characteristics were summarised. When all themes had been extracted from studies, common concepts were categorised and tabulated. This included information on how many studies had contributed to each theme identified by the NGA technical team.

Themes from individual studies were integrated into a wider context and, when possible, overarching categories of themes with sub-themes were identified. Themes were derived from data presented in individual studies. When themes were extracted from 1 primary study only, theme names used in the guideline mirrored those in the source study. However, when themes were based on evidence from multiple studies, the theme names were assigned by the NGA technical team. The names of overarching categories of themes were also assigned by the NGA technical team.

Emerging themes were placed into a thematic map representing the relationship between themes and overarching categories. The purpose of such a map is to show relationships between overarching categories and associated themes.

Synthesis of quantitative and qualitative data

For the mixed methods reviews, a parallel synthesis of the data was undertaken, with quantitative and qualitative data analysed and synthesised separately. These results

were primarily integrated through the committee's interpretation of them, but this process was complemented by a summary overview table constructed by the NGA technical team, which presented the findings underpinned by both qualitative and quantitative evidence. Specifically, the table listed the sub-themes identified in the qualitative evidence that were also addressed by the identified quantitative evidence along with the results of the corresponding quantitative evidence, but the contents of the table was restricted to the results of the quantitative evidence and the qualitative themes this evidence spoke to. Therefore, it did not include all the themes identified in the qualitative evidence nor all the quantitative outcomes. Aided by this table, the committee completed the synthesis of these mixed data through their discussions of the evidence. Their interpretation of the relationship between the quantitative and qualitative data is described in the committee's discussion of the evidence section of all the mixed methods reviews.

Appraising the quality of evidence

Intervention studies

Pairwise meta-analysis

GRADE methodology for intervention reviews

For intervention reviews, the evidence for outcomes from included RCTs and comparative non-randomised studies was evaluated and presented using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology developed by the international GRADE working group.

When GRADE was applied, software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking account of individual study quality factors and any meta-analysis results. Results were presented in GRADE profiles (GRADE tables). In addition to this detailed summary, we also included a complementary narrative summary of the result, which did not take the form of evidence statements, but rather focused on summarising the results in a manner that emphasised accessibility and quality of the results. This summary therefore did not tend to contain numerical information (e.g., actual effect sizes and CIs or study size), but rather just whether there was a clinically important effect and the quality of it (see also below).

The selection of outcomes for each review question was agreed during development of the associated review protocol in discussion with the committee. The evidence for each outcome was examined separately for the quality elements summarised in Table 2. Criteria considered in the rating of these elements are discussed below. Each element was graded using the quality ratings summarised in Table 3. Footnotes to GRADE tables were used to record reasons for grading a particular quality element as having a 'serious' or 'very serious' quality issue. The ratings for each component were combined to obtain an overall assessment of quality for each outcome as described in Table 4.

The initial quality rating was based on the study design, and both RCTs and NRS assessed by ROBINS-I (the only types of intervention studies included in the guideline) start as 'high' quality evidence. The rating was then modified according to

the assessment of each quality element (Table 2). Each quality element considered to have a 'serious' or 'very serious' quality issue was downgraded by 1 or 2 levels respectively (for example, evidence starting as 'high' quality was downgraded to 'moderate' or 'low' quality).

Table 2: Summary of quality elements in GRADE for intervention reviews

Quality element	Description
Risk of bias ('Study limitations')	This refers to limitations in study design or implementation that reduce the internal validity of the evidence
Inconsistency	This refers to unexplained heterogeneity in the results
Indirectness	This refers to differences in study populations, interventions, comparators or outcomes between the available evidence and inclusion criteria specified in the review protocol
Imprecision	This occurs when a study has few participants or few events of interest, resulting in wide confidence intervals that cross minimally important thresholds
Publication bias	This refers to systematic under- or over-estimation of the underlying benefit or harm resulting from selective publication of study results

Table 3: GRADE quality ratings (by quality element)

Quality issues	Description
None or not serious	No serious issues with the evidence for the quality element under consideration
Serious	Issues with the evidence sufficient to downgrade by 1 level for the quality element under consideration
Very serious	Issues with the evidence sufficient to downgrade by 2 levels for the quality element under consideration

Table 4: Overall quality of the evidence in GRADE (by outcome)

Overall quality grading	Description
High	Further research is very unlikely to change the level of confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on the level of confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on the level of confidence in the estimate of effect and is likely to change the estimate
Very low	The estimate of effect is very uncertain

Assessing risk of bias in intervention reviews

Bias is a systematic error, or consistent deviation from the truth in results obtained. When a risk of bias is present the true effect can be either under- or over-estimated.

Risk of bias in RCTs was assessed using the revised Cochrane risk of bias tool (RoB 2; see Appendix H in Developing NICE guidelines: the manual).

The Cochrane risk of bias tool assesses the following possible sources of bias:

- risk of bias arising from the randomization process
- risk of bias due to deviations from the intended interventions
- risk of bias due to missing outcome data
- risk of bias due to measurement of the outcome
- risk of bias in selection of the reported result

A study with a poor methodological design does not automatically imply high risk of bias; the bias is considered individually for each outcome and it is assessed whether the chosen design and methodology will impact on the estimation of the intervention effect.

More details about the Cochrane risk of bias tool can be found in Section 8 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011).

For systematic reviews of RCTs the AMSTAR checklist was used and for systematic reviews of other study types the ROBIS checklist was used (see Appendix H in Developing NICE guidelines: the manual).

For non-randomised studies the ROBINS-I checklist was used (see Appendix H in Developing NICE guidelines: the manual).

Assessing inconsistency in intervention reviews

Inconsistency refers to unexplained heterogeneity in results of meta-analysis. When estimates of treatment effect vary widely across studies (that is, there is heterogeneity or variability in results), this suggests true differences in underlying effects. Inconsistency is, thus, only truly applicable when statistical meta-analysis is conducted (that is, results from different studies are pooled). When outcomes were derived from a single study the rating 'no serious inconsistency' was used when assessing this domain, as per GRADE methodology (Santesso 2016).

Inconsistency was assessed visually by inspecting forest plots and observing whether there was considerable heterogeneity in the results of the meta-analysis (for example if the point estimates of the individual studies consistently showed benefits or harms). This was supported by calculating the I-squared statistic for the meta-analysis with an I-squared value of more than 50% indicating considerable heterogeneity, and more than 80% indicating very serious heterogeneity. When considerable or very serious heterogeneity was observed, possible reasons were explored and subgroup analyses were performed as pre-specified in the review protocol where possible. In the case of unexplained heterogeneity, sensitivity analyses were planned based on the quality of studies, eliminating studies at high risk of bias (in relation to randomisation, allocation concealment and blinding, and/or missing outcome data).

When considerable heterogeneity was present, we planned to re-run the meta-analysis using the Der-Simonian and Laird method with a random effects model and use this for the final analysis. However, none of the meta-analyses were subject to

considerable or very considerable heterogeneity so no such analyses were conducted.

When no plausible explanation for the heterogeneity could be found, the quality of the evidence was downgraded in GRADE for inconsistency.

Assessing indirectness in intervention reviews

Directness refers to the extent to which populations, interventions, comparisons and outcomes reported in the evidence are similar to those defined in the inclusion criteria for the review and was assessed by comparing the PICO elements in the studies to the PICO defined in the review protocol. Indirectness is important when such differences are expected to contribute to a difference in effect size, or may affect the balance of benefits and harms considered for an intervention.

Assessing imprecision and importance in intervention reviews

Imprecision in GRADE methodology refers to uncertainty around the effect estimate and whether or not there is an important difference between interventions (that is, whether the evidence clearly supports a particular recommendation or appears to be consistent with several candidate recommendations). Therefore, imprecision differs from other aspects of evidence quality because it is not concerned with whether the point estimate is accurate or correct (has internal or external validity). Instead, it is concerned with uncertainty about what the point estimate actually represents. This uncertainty is reflected in the width of the CI.

The 95% CI is defined as the range of values within which the population value will fall on 95% of repeated samples, were the procedure to be repeated. The larger the study, the smaller the 95% CI will be and the more certain the effect estimate.

Imprecision was assessed in the guideline evidence reviews by considering whether the width of the 95% CI of the effect estimate was relevant to decision making, considering each outcome independently. This is illustrated in Figure 1, which considers a positive outcome for the comparison of two treatments. Three decision-making zones can be differentiated, bounded by the thresholds for minimal importance (minimally important differences; MIDs) for benefit and harm.

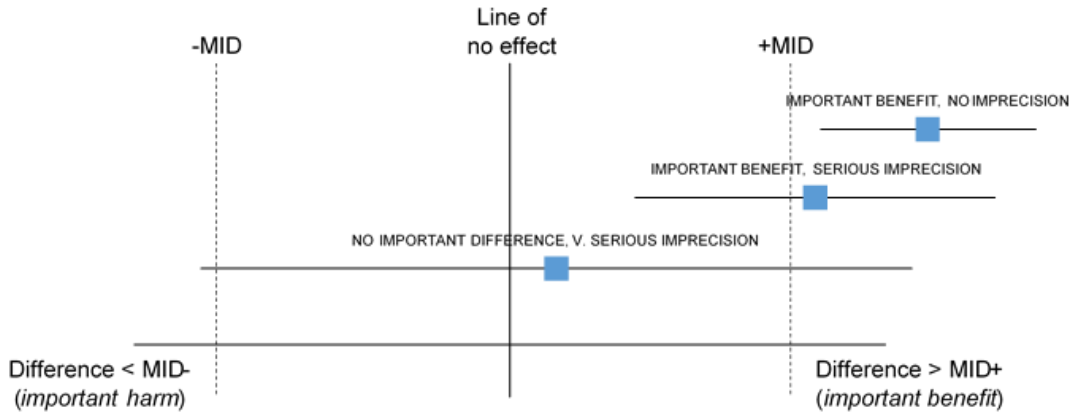
When the CI of the effect estimate is wholly contained in 1 of the 3 zones there is no uncertainty about the size and direction of effect, therefore, the effect estimate is considered precise; that is, there is no imprecision.

When the CI crosses 2 zones, it is uncertain in which zone the true value of the effect estimate lies and therefore there is uncertainty over which decision to make. The CI is consistent with 2 possible decisions, therefore, the effect estimate is considered to be imprecise in the GRADE analysis and the evidence is downgraded by 1 level (‘serious imprecision’).

When the CI crosses all 3 zones, the effect estimate is considered to be very imprecise because the CI is consistent with 3 possible decisions and there is therefore a considerable lack of confidence in the results. The evidence is therefore downgraded by 2 levels in the GRADE analysis (‘very serious imprecision’).

Implicitly, assessing whether a CI is in, or partially in, an important zone, requires the guideline committee to estimate an MID or to say whether they would make different decisions for the 2 confidence limits.

Figure 1: Assessment of imprecision and importance in intervention reviews using GRADE



MID: minimally important difference

Defining minimally important differences for intervention reviews

The committee was asked whether there were any recognised or acceptable MIDs in the published literature and community relevant to the review questions under consideration. The committee was not aware of any MIDs that could be used for the guideline.

In the absence of published or accepted MIDs, the committee agreed to use the MIDs suggested in GRADE to assess imprecision. For dichotomous outcomes minimally important thresholds for a RR of 0.8 and 1.25 respectively were therefore used as MIDs in the guideline. If dichotomous outcome data were reported as odds ratios (ORs) these were converted to RRs, if possible, and imprecision was assessed based on the RR.

If studies only reported descriptive data, medians with or without interquartile ranges, ORs that could not be converted to RRs, or p-values, imprecision was assessed based on sample size using 200 and 400 as cut-offs for very serious and serious imprecision respectively. The committee used these numbers based on commonly used optimal information size thresholds also suggested in GRADE. In these cases, the committee considered the potential clinical importance of a result through discussion and, where applicable, this was reported in the relevant 'committee discussion of the evidence' section.

The same thresholds were used as MIDs in the guideline for all dichotomous outcomes considered in intervention evidence reviews. For continuous outcomes, GRADE suggests that MIDs are equal to half the median SD of the control groups at baseline (or at follow-up if the SD is not available a baseline) and this approach was therefore taken for continuous outcomes.

Assessing publication bias in intervention reviews

Where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias. Where fewer than 10 studies were included for an outcome, the committee subjectively assessed the likelihood of publication bias based on factors such as the proportion of trials funded by industry and the propensity for publication bias in the topic area.

Qualitative reviews

GRADE-CERQual methodology for qualitative reviews

For qualitative reviews an adapted GRADE Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) approach (Lewin 2015) was used. In this approach the quality of evidence is considered for each theme in the evidence. The themes may have been identified in the primary studies or they may have been identified by considering the reports of a number of studies. Quality elements assessed using GRADE-CERQual are listed and defined in Table 5. Each element was graded using the levels of concern summarised in Table 6.

The ratings for each component were combined to obtain an overall assessment of confidence in each review finding or 'theme' as described in Table 7. 'Confidence' in this context refers to the extent to which the review finding is a reasonable representation of the phenomenon of interest set out in the protocol. Similar to other types of evidence all review findings start off with 'high confidence' and are rated down by one or more levels if there are concerns about any of the individual CERQual components. In line with advice from the CERQual developers, the overall assessment does not involve numerical scoring for each component but in order to ensure consistency across and between guidelines, the NGA established some guiding principles for overall ratings. For example, a review finding would not be downgraded (and therefore would be assessed with 'high' confidence) if all 4 components had 'no or very minor' concerns or 3 'no or very minor' and 1 'minor'. At the other extreme, a review finding would be downgraded 3 times (to 'very low') if at least 2 components had serious concerns or at least 3 had moderate concerns. A basic principle was that if any components had serious concerns then overall confidence in the review finding would be downgraded at least once (potentially more depending on the other ratings). Transparency about overall judgements is provided in the CERQual tables, including a brief reference to components for which there were concerns in the 'overall confidence' cell.

Table 5: GRADE quality elements for qualitative reviews

Quality element	Description
Methodological limitations	Limitations in study design and implementation may bias interpretation of qualitative themes identified. High risk of bias for the majority of the evidence reduces confidence in review findings. Qualitative studies are not usually randomised and therefore would not be downgraded for study design from the outset (they start as high quality)

Quality element	Description
Relevance of evidence	This refers to the extent to which the evidence supporting the review findings is applicable to the context specified in the review question
Coherence of findings	This refers to the extent to which review findings are well grounded in data from the contributing primary studies and provide a credible explanation for patterns identified in the evidence
Adequacy of data (theme saturation or sufficiency)	This corresponds to a similar concept in primary qualitative research, that is, whether a theoretical point of theme saturation was achieved, at which point no further citations or observations would provide more insight or suggest a different interpretation of the particular theme. Individual studies that may have contributed to a theme or sub-theme may have been conducted in a manner that by design would have not reached theoretical saturation at an individual study level

Table 6: CERQual levels of concern (by quality element)

Level of concern	Definition
None or very minor concerns	Unlikely to reduce confidence in the review finding
Minor concerns	May reduce confidence in the review finding
Moderate concerns	Will probably reduce confidence in the review finding
Serious concerns	Very likely to reduce confidence in the review finding

Table 7: Overall confidence in the evidence in CERQual (by review finding)

Overall confidence level	Definition
High	It is highly likely that the review finding is a reasonable representation of the phenomenon of interest
Moderate	It is likely that the review finding is a reasonable representation of the phenomenon of interest
Low	It is possible that the review finding is a reasonable representation of the phenomenon of interest
Very low	It is unclear whether the review finding is a reasonable representation of the phenomenon of interest

Assessing methodological limitations in qualitative reviews

Methodological limitations in qualitative studies were assessed using the Critical Appraisal Skills Programme (CASP) checklist for qualitative studies (see appendix H in Developing NICE guidelines: the manual). Overall methodological limitations were derived by assessing the methodological limitations across the 6 domains summarised in Table 8.

Table 8: Methodological limitations in qualitative studies

Aim and appropriateness of qualitative evidence	This domain assesses whether the aims and relevance of the study were described clearly and whether qualitative research methods were appropriate for investigating the research question
Rigour in study design or validity of theoretical approach	This domain assesses whether the study approach was documented clearly and whether it was based on a theoretical framework (such as ethnography or grounded theory). This does not necessarily mean that the framework has to be stated explicitly, but a detailed description ensuring transparency and reproducibility should be provided
Sample selection	This domain assesses the background, the procedure and reasons for the method of selecting participants. The assessment should include consideration of any relationship between the researcher and the participants, and how this might have influenced the findings
Data collection	This domain assesses the documentation of the method of data collection (in-depth interviews, semi-structured interviews, focus groups or observations). It also assesses who conducted any interviews, how long they lasted and where they took place
Data analysis	This domain assesses whether sufficient detail was documented for the analytical process and whether it was in accordance with the theoretical approach. For example, if a thematic analysis was used, the assessment would focus on the description of the approach used to generate themes. Consideration of data saturation would also form part of this assessment (it could be reported directly or it might be inferred from the citations documented that more themes could be found)
Results	This domain assesses any reasoning accompanying reporting of results (for example, whether a theoretical proposal or framework is provided)

Assessing relevance of evidence in qualitative reviews

Relevance (applicability) of findings in qualitative research is the equivalent of indirectness for quantitative outcomes, and refers to how closely the aims and context of studies contributing to a theme reflect the objectives outlined in the guideline review protocol.

Assessing coherence of findings in qualitative reviews

For qualitative research, a similar concept to inconsistency is coherence, which refers to the way findings within themes are described and whether they make sense. This concept was used in the quality assessment across studies for individual themes. This does not mean that contradictory evidence was automatically downgraded, but that it was highlighted and presented, and that reasoning was provided. Provided the themes, or components of themes, from individual studies fit into a theoretical framework, they do not necessarily have to reflect the same perspective. It should, however, be possible to explain these by differences in context (for example, the views of healthcare professionals might not be the same as those of family members, but they could contribute to the same overarching themes).

Assessing adequacy of data in qualitative reviews

Adequacy of data (theme saturation or sufficiency) corresponds to a similar concept in primary qualitative research in which consideration is made of whether a theoretical point of theme saturation was achieved, meaning that no further citations or observations would provide more insight or suggest a different interpretation of the theme concerned. As noted above, it is not equivalent to the number of studies contributing to a theme, but rather to the depth of evidence and whether sufficient quotations or observations were provided to underpin the findings.

Additional summaries of the evidence

In addition to the detailed summaries of the results in GRADE and GRADE-CERQual tables, we also included a complementary narrative summary of each set of result, which did not take the form of evidence statements, but rather focused on summarising the results in a manner that emphasised accessibility and quality of the results. This summary therefore did not tend to contain numerical information (e.g., actual effect sizes and confidence intervals or study sizes), but rather just whether there was a clinically important effect (for quantitative reviews), which themes had emerged (for qualitative reviews) and the quality of this evidence.

Reviewing economic evidence

Inclusion and exclusion of economic studies

Titles and abstracts of articles identified through the economic literature searches were independently assessed for inclusion using the predefined eligibility criteria listed in Table 9.

Table 9: Inclusion and exclusion criteria for systematic reviews of economic evaluations

Inclusion criteria
Intervention or comparators in accordance with the guideline scope
Study population in accordance with the guideline scope

Inclusion criteria
Only studies from Organisation for Economic Co-operation and Development countries were included, as the aim of the review was to identify economic information transferable to the UK context
Full economic evaluations (cost-utility, cost effectiveness, cost-benefit or cost-consequence analyses) assessing both costs and outcomes associated with interventions of interest; cost/cost-offset analyses were also considered for inclusion
Only studies published from 2010 onwards were included in the review
Exclusion criteria
Abstracts containing insufficient methodological details
Cost-of-illness type studies

Once the screening of titles and abstracts was completed, full-text copies of potentially relevant articles were requested for detailed assessment. Inclusion and exclusion criteria were applied to articles obtained as full-text copies.

Details of economic evidence study selection, lists of excluded studies, economic evidence tables, the results of quality assessment of economic evidence (see below) and health economic evidence profiles are presented in respective evidence chapters.

Appraising the quality of economic evidence

The quality of economic evidence was assessed using the economic evaluations checklist specified in Developing NICE guidelines: the manual.

Economic modelling

The aims of the economic input to the guideline were to inform the guideline committee of potential economic issues to ensure that recommendations represented a cost effective use of healthcare resources. Economic evaluations aim to integrate data on healthcare benefits (ideally in terms of quality-adjusted life-years; QALYs) with the costs of different options. In addition, the economic input aimed to identify areas of high resource impact; these are recommendations which (while cost effective) might have a large impact on commissioners so need special attention.

The guideline committee prioritised the following review questions for economic modelling where it was thought that economic considerations would be particularly important in formulating recommendations.

- [B.1a] What physical rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?
- [B.1b] What physical rehabilitation interventions are effective and acceptable for children and young people with complex rehabilitation needs after traumatic injury?
- [B.2a] What cognitive rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?
- [B.3a] What psychological and psychosocial rehabilitation interventions are effective and acceptable for adults with complex rehabilitation needs after traumatic injury?

- [D.2a] What are the best methods to deliver and coordinate rehabilitation services and social care services for adults with complex rehabilitation needs after traumatic injury when they transfer from inpatient to outpatient rehabilitation services?

The effectiveness review for cognitive rehabilitation interventions [B.2] was empty and useful modelling was not possible. The effectiveness reviews for (1) psychological and psychosocial rehabilitation interventions [B.3], (2) physical rehabilitation interventions in adults and children [B.1], and (3) the best methods to deliver and coordinate rehabilitation services and social care services [D.2], identified a number of single heterogeneous and very low or low quality studies. The recommendations were based on the committee expert opinion and represented standard practice across the NHS. The committee did not identify any area in these reviews that would benefit from original economic modelling.

The committee identified an additional economic priority that spanned a number of reviews and aimed to assess the potential cost-effectiveness of concentrated rehabilitation package that would include physical, cognitive, psychological and psychosocial rehabilitation interventions. The methods and results of the de novo economic analysis are reported in Appendix J of the relevant evidence report (Physical rehabilitation [B.1]).

When new economic analysis was not prioritised, the committee made a qualitative judgement regarding cost-effectiveness by considering expected differences in resource and cost use between options, alongside clinical effectiveness evidence identified from the clinical evidence review.

Cost effectiveness criteria

As specified in Developing NICE guidelines: the manual an intervention was considered to be cost effective if any of the following criteria applied (provided that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more effective compared with all the other relevant alternative strategies)
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy
- the intervention provided important benefits at an acceptable additional cost when compared with the next best strategy.

The committee's considerations of cost effectiveness are discussed explicitly under the heading 'The committee's discussion of the evidence' and 'Cost effectiveness and resource use' in the relevant evidence reviews

Developing recommendations

Guideline recommendations

Recommendations were drafted on the basis of the committee's interpretation of the available evidence, taking account of the balance of benefits, harms and costs

between different courses of action along with the quality of the evidence, the clinical importance of the findings and the associated uncertainty surrounding the effect sizes of quantitative results. When effectiveness and economic evidence was of poor quality, conflicting or absent, the committee drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential benefits and harms, the economic costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, person's preferences and equality issues.

Due to a lack of evidence in many of the guideline areas, many of the recommendations were made based on the expertise and experience of the committee. Nevertheless, the committee was able to agree that most of the recommendations should be strong because they are either standard practice already or there were compelling reasons for why they should be strong, including evidence. These reasons were always captured in the 'committee discussion of the evidence' sections of the relevant evidence reviews. Where the recommendations were weak (that is, 'Consider' recommendations), the underlying reasons for this have also been explicitly justified in the 'committee discussion of the evidence' sections of the relevant evidence reviews.

In addition, due to the nature of rehabilitation treatments and therapies being so individualised and tailored to the person and the nature of their injuries, it was often the case, based on committee expertise, that the effectiveness of the intervention was difficult to generalise across the broad population leading to many recommendations using the term 'consider' to emphasise not only the uncertainty within the evidence but also that practitioners should actively 'consider' the individual suitability of a number of interventions when putting together a package of rehabilitation care and treatment.

Evidence reviews were undertaken separately for the adult and child/young person populations and reported separately to the committee. The questions were identical for both populations. In looking at both evidence reviews for each question the committee agreed recommendations that largely applied to both adults and children and young people and their justification for making these recommendations was largely the same for both.

The committee agreed that in all but a few areas it was appropriate to extrapolate evidence from the adult population and apply it to the child and young person population because rehabilitation interventions were often the same in principle regardless of age and were always tailored to meet the needs of the individual and made age appropriate anyway as part of that tailoring, which is implicit in the recommendations. The outcomes that were important for the committee were also largely the same for adults, children and young people. There was very little evidence for children and young people across the reviews. In a small number of cases the committee agreed recommendations that applied to adults only or to children and young people only or to other more specific sub populations within the whole population such as older adults, vulnerable adults, or younger children and where this is the case it has been specified clearly in the recommendation itself.

The main considerations specific to each recommendation are outlined under the heading 'The committee's discussion of the evidence' within each evidence review.

For further details refer to Developing NICE Guidelines: the manual.

Research recommendations

When areas were identified for which evidence was lacking, the committee considered making recommendations for future research. While all areas without evidence or with only poor evidence were considered for potential research recommendations, the committee agreed to only make 5 research recommendations in total because they wanted to focus only on research recommendations that could be prioritised and promoted for funding by national funding bodies. These 5 research recommendations covered the research questions that the committee agreed were of the highest priority for future research in the area of rehabilitation after traumatic injury. For further details refer to Developing NICE Guidelines: the manual and the Research Recommendations Process and Methods guide.

Validation process

This guideline was subject to a 6-week public consultation and feedback process. All comments received from registered stakeholders were responded to in writing and posted on the NICE website at publication. For further details refer to Developing NICE guidelines: the manual.

Updating the guideline

Following publication, NICE will undertake a surveillance review to determine whether the evidence base has progressed sufficiently to consider altering the guideline recommendations and warrant an update. For further details refer to Developing NICE guidelines: the manual.

Funding

The NGA was commissioned by NICE to develop this guideline.

References

Hayden 2013

Jill A. Hayden, Danielle A. van der Windt, Jennifer L. Cartwright, Pierre Côté, Claire Bombardier. Assessing Bias in Studies of Prognostic Factors. Ann Intern Med. 2013;158:280–286. doi: 10.7326/0003-4819-158-4-201302190-00009

Higgins 2011

Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.1 (updated September 2020). Cochrane, 2020. Available from www.training.cochrane.org/handbook (accessed 20 May 2021)

Lewin 2015

Lewin S, Glenton C, Munthe-Kaas H et al. (2015) Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). PLoS Med 12(10), e1001895

McGowan 2016

McGowan J, Sampson M, Salzwedel DM et al. (2016) PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. Journal of Clinical Epidemiology 75: 40–6

NICE 2014

National Institute for Health and Care Excellence (NICE) (2014) Developing NICE guidelines: the manual (updated 2018). Available from https://www.nice.org.uk/process/pmg20/chapter/introduction (accessed 20 May 2021)

NICE 2018

National Institute for Health and Care Excellence (NICE) (2018) NICE Policy on conflicts of interest (updated 2021). Available from https://www.nice.org.uk/about/who-we-are/policies-and-procedures (accessed 20 May 2021)

Santesso 2016

Santesso N, Carrasco-Labra A, Langendam M et al. (2016) Improving GRADE evidence tables part 3: detailed guidance for explanatory footnotes supports creating and understanding GRADE certainty in the evidence judgments. Journal of clinical epidemiology 74, 28-39