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Mapping Outcomes for Recovery of Consciousness in Studies from 1986 to 2020: A scoping review protocol

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Complete List of Authors:	Weaver, Jennifer; Colorado State University College of Health and Human Sciences, Department of Occupational Therapy; The George Washington University School of Medicine and Health Sciences Cogan, Alison; Veterans Affairs Greater Los Angeles Healthcare System Bhandari, Parie; The George Washington University School of Medicine and Health Sciences Awan, Bint-e; The George Washington University School of Medicine and Health Sciences Jacobs, Erica; The George Washington University School of Medicine and Health Sciences Pape, Ariana; The George Washington University School of Medicine and Health Sciences Nguyen, Chantal; The George Washington University School of Medicine and Health Sciences Guernon, Ann; Lewis University - College of Nursing and Health Professions; Hines Veterans Affairs Hospital Harrod, Tom; The George Washington University School of Medicine and Health Sciences Team, Recovery of Consciousness; The George Washington University School of Medicine and Health Sciences Pape, Theresa; Hines Veterans Affairs Hospital Mallinson, Trudy; The George Washington University School of Medicine and Health Sciences
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SCHOLARONE™
Manuscripts

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3 1 **Mapping Outcomes for Recovery of Consciousness in Studies from 1986 to 2020: A scoping**
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5
6 2 **review protocol**

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8 3 Jennifer Weaver, PhD^{1,2}; Alison Cogan, PhD³; Parie Bhandari, BA²; Bint-e Awan, BA²; Erica
9
10 4 Jacobs, BS²; Ariana Pape, MD²; Chantal Nguyen, MD²; Ann Guernon, PhD^{4,5}; Tom Harrod,
11
12 5 MLS, MS²; The Recon Team; Theresa Bender Pape, DrPH⁵; Trudy Mallinson, PhD²
13
14
15 6

16
17 7 ¹College of Health and Human Sciences, Colorado State University; ²School of Medicine and
18
19 8 Health Sciences, The George Washington University, Washington, DC; ³Veterans Affairs
20
21 9 Greater Los Angeles Healthcare System, Los Angeles, CA, ⁴College of Nursing and Health
22
23 10 Sciences, Lewis University, Romeoville, IL; ⁵Hines Veterans Affairs Hospital, Hines, IL
24
25
26 11

27
28 12 **Corresponding Author:** Jennifer Weaver, PhD

29
30
31 13 Assistant Professor, Department of Occupational Therapy, College of Health and Human
32
33 14 Sciences, Colorado State University, 1573 Campus Delivery, Fort Collins, CO 80523. Email:
34
35 15 jen.weaver@colostate.edu
36
37

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39
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43
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45
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47
48 21 Lindsey, PhD, CCC-SLP; Angela Hartman, OTD; Kristen Maisano, OTD; Erika Cooley; Jessica
49
50 22 Rudin Portnoff OTR/L, CBIS; Bailey Widener, MSOT, MPH, CBIS, OTR/L; Sarah
51
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2
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4
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2
3 25 **Abstract**
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5 26 **Introduction:** Historically, heterogeneous outcome assessments have been used to measure
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8 27 recovery of consciousness in patients with disorders of consciousness (DoC) following traumatic
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10 28 brain injury (TBI), making it difficult to compare across studies. To date, however, there is no
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12 29 comprehensive review of clinical outcome assessments that are used in intervention studies of
13
14 30 adults with DoC. The objective of this scoping review is to develop a comprehensive inventory
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16 31 of clinical outcome assessments for recovery of consciousness that have been used in clinical
17
18 32 studies of adults with DoC following TBI.
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20

21 33 **Methods and Analysis:** The methodological framework for this review is: 1) identify the
22
23 34 research questions, 2) identify relevant studies, 3) select studies, 4) chart the data, 5) collate,
24
25 35 summarize and report results and 6) consult stakeholders to drive knowledge translation. We will
26
27 36 identify relevant studies by searching the following electronic bibliographic databases: PubMed,
28
29 37 Scopus, EMBASE, PsycINFO, and The Cochrane Library (including Cochrane Database of
30
31 38 Systematic Reviews, Cochrane Central Register of Controlled Trials, and Cochrane
32
33 39 Methodology Register). Criteria for article inclusion are published in the English-language, peer-
34
35 40 reviewed studies of interventions aimed at facilitating recovery of consciousness among adults (\geq
36
37 41 18 years) with DoC following a severe TBI, published from January 1986 to December 2020.
38
39 42 Articles meeting inclusion criteria at this stage will undergo a full text review. We will chart the
40
41 43 data by applying the World Health Organization International Classification of Functioning,
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43 44 Disability and Health Framework to identify the content areas of clinical outcome assessments.
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45 45 To support knowledge translation efforts, we will involve clinicians and researchers experienced
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47 46 in TBI care throughout the project from conceptualization of the study through dissemination of
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49 47 results.
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3 48 **Dissemination:** Results will be presented at national conferences and published in peer reviewed
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5 49 journals.

6
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8 50 **Keywords:** Traumatic Brain Injury; Disorders of Consciousness; Common Data Elements,
9
10 51 Clinical Outcome Assessments

11 12 13 14 15 53 **Strengths and limitations of this study**

- 16
17 54 • The proposed scoping review will result in a comprehensive catalogue of outcome
18
19 55 assessments utilized in traumatic brain injury research aimed at facilitating recovery of
20
21 56 consciousness among adults with DoC. These outcome assessments will be grouped
22
23 57 according to the WHO ICF domains and sub-domains in order to identify key trends and
24
25 58 gaps in concepts of interest.
- 26
27 59 • To the authors' knowledge, this will be the first study to identify whether the introduction
28
29 60 of NINDS CDEs influenced outcome assessment reporting among studies that received
30
31 61 federal funding in the United States.
- 32
33 62 • Our search is limited to articles published since 1986, therefore we may miss outcome
34
35 63 assessments for DoC that were used prior to this date.
- 36
37 64 • It is possible that our search strategy will miss relevant studies; we will mitigate this risk
38
39 65 by searching multiple databases and manually searching review articles and meta-
40
41 66 analyses.
- 42
43 67 • Studies reporting US federal funding published after the introduction of NINDS CDEs
44
45 68 may have been conducted prior to 2010 and therefore the authors may not have been
46
47 69 strongly encouraged to use NINDS CDEs.
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INTRODUCTION

72 **Rationale**

73 To date, there has been limited success in clinical trials for treatment of patients with severe
74 traumatic brain injury (TBI) that result in disorders of consciousness (DoC).¹⁻³ Representing a
75 continuum of impaired consciousness, DoC is based on a person's ability to demonstrate arousal
76 and/or awareness. The DoC continuum includes comatose, vegetative state/unresponsive
77 wakefulness syndrome, minimally conscious state, and emergence from the minimally conscious
78 state.⁴ Recovery of consciousness for people with DoC following a severe TBI is uncertain and
79 difficult to predict.⁵⁻⁷ Accurate measurement of recovery of consciousness for people in DoC is
80 essential for diagnosis and prognosis as well as determining the efficacy and effectiveness of
81 interventions.^{5,8-10} To date, there has been no review of the range of clinical outcome assessments
82 used in measuring recovery of consciousness.

83 Historically, measuring recovery of consciousness in clinical trials has involved a range
84 of clinical outcome assessments measuring different concepts of interest (e.g., response to pain,
85 awareness), making it difficult to compare results across studies.¹¹⁻¹⁴ The National Institute of
86 Neurological Disorders and Stroke (NINDS), part of the US National Institutes of Health (NIH),
87 established a set of Common Data Elements (CDEs) for TBI in 2010 with the goal of promoting
88 comparability of study findings. Traumatic brain injury researchers applying for United States
89 (US) federal funding sources including NIH, Department of Defense, Department of Veteran's
90 Affairs are strongly encouraged to use NINDS CDEs for outcome measurement to improve
91 comparability across trials. Further, a data repository for TBI research was created as a result of
92 collaboration between NIH and the Federal Interagency Traumatic Brain Injury Research

93 Informatics System;¹⁵ federally funded researchers may be required to submit their data to this
 94 repository in the future. This requirement provides additional incentive to use NINDS CDEs.¹⁵⁻¹⁷

95 CDEs are categorized as core, basic, or supplemental. The ‘core’ designation indicates
 96 data elements pertinent for all TBI studies. Basic CDEs are specific to studies of populations
 97 within TBI, such as ‘concussion/mild TBI’, ‘acute hospitalized’, ‘moderate/severe TBI:
 98 rehabilitation’, and ‘epidemiology’. Basic CDEs for ‘moderate/severe TBI: rehabilitation’
 99 include, but are not limited to, pupil reactivity, death date and time, hospital discharge
 100 destination, and alteration of consciousness duration.¹⁸ Supplemental CDEs are optional and may
 101 be appropriate depending on the research question and scope.¹⁶ Only two supplemental CDEs are
 102 related to recovery of consciousness in adults: the Galveston Orientation Amnesia Test and JFK
 103 Coma Recovery Scale-Revised (CRS-R) (Table 1).¹⁸

104 Table 1. Examples of Common Data Elements

Type of CDE	Definition	Example of CDE
General Core	Recommended for all NIH-funded studies: General	C00031: Race Expanded Category
Disease-specific Core	Recommended for all NIH-funded studies: Disease specific (TBI)	C01001: Glasgow Coma Scale (GCS) - motor response scale
Basic*	Recommended for all TBI NIH-funded studies: Specific to sub-diseases (e.g., Epidemiology and Moderate/Severe: Rehabilitation)	C07155: Disability Rating Scale Total Score
Supplemental	Recommended for NIH-funded studies: Specific to study design or type of research	C07145: JFK Coma Recovery Scale-Revised – Total Score

105 *Basic CDEs are comparable to Supplemental-Highly Recommended CDEs for other diagnostic
 106 categories.

107 Two studies have described the implementation of CDEs in TBI research.^{13,19} Yue et al
 108 (2013) described the implementation of CDEs for a multicenter prospective study and note
 109 recommendations for future data collection procedures as well as the success in transferring the
 110 data to FITBIR. Stead et al (2013) used CDEs to describe TBI patients in emergency

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3 111 departments and were able to compare results to several other published studies. Although the
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5 112 goal of the NINDS CDE project is to improve consistency and comparability across clinical
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7 113 studies of patients with DoC following severe TBI by encouraging more consistent use of
8
9 114 clinical outcome assessments, there is currently no evidence to indicate whether this outcome has
10
11 115 been achieved.

14 116 **Objective**

16
17 117 The primary objective of this scoping review is to develop a comprehensive inventory of
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19 118 clinical outcome assessments in clinical trials aimed at recovery of consciousness for patients
20
21 119 with DoC after TBI. Secondary objectives are to examine the trends in primary outcomes over
22
23 120 time and whether reporting of NINDS CDEs increased after their introduction in 2010 in studies
24
25 121 that received US federal funding.

28 122 **METHODS AND ANALYSIS**

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30
31 123 A scoping review is an appropriate method to achieve the stated objectives because we
32
33 124 want to identify characteristics of clinical outcome assessments used to evaluate the recovery of
34
35 125 consciousness following a severe TBI.²⁰ The scoping review will be conducted based on the
36
37 126 Arksey and O'Malley²¹ methodological framework that has been refined by Levac et al²². The
38
39 127 methodological framework for this review will include: 1) identify the research questions, 2)
40
41 128 identify relevant studies, 3) select studies, 4) chart the data, 5) collate, summarize and report
42
43 129 results, and 6) stakeholder engagement to drive knowledge translation.^{21,22}

46 130 **1. Identify the Research Questions**

48 131 ***Primary question***

- 50
51 132 • What clinical outcome assessments have been used in published studies about recovery of
52
53 133 consciousness for adults with severe TBI in states of disordered consciousness?

55 134 ***Secondary questions***

- 1
2
3 135 • How have the outcomes assessments used to measure DoC in adults with severe TBI
4
5
6 136 changed over time?
7
8 137 • Did frequency of reporting clinical outcome assessments classified as NINDS CDEs
9
10 138 change after their introduction in 2010 among federally funded studies in the US?

12 139 2. Identify Relevant Studies

14 140 The search strategy was developed in collaboration with a research librarian. Our search terms
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16
17 141 are broad to identify all eligible studies. These search terms encompass three primary categories:
18
19 142 severe TBI, recovery of consciousness, and outcomes.

21 143 *Search terms*

22
23
24 144 An in-depth outline of the full search strategy is reported in Table 2.

25
26 145 Table 2. Examples of the search strategy that will generate the articles to review for the research
27 146 question.

28 Database	29 Search Terms	30 Customization
31 Cochrane	32 (“traumatic brain injury”) OR (coma) OR (“persistent vegetative state”) OR (“minimally conscious state”) OR (“consciousness disorder”) OR (“disorder* of consciousness”) AND ((recovery) OR (“activities of daily living”) OR (awareness) OR (wakefulness)) AND (“critical care outcome”) OR (“treatment outcome”) OR (“outcome assessment”) OR (evaluation) OR (assessment))	33 1987-2020, all publication types
34 Embase	35 ((exp traumatic brain injury/ OR traumatic brain injur*.ti,ab.) OR (exp coma/ OR coma*.ti,ab.) OR (exp persistent vegetative state/ OR persistent vegetative state*.ti,ab.) OR (exp minimally conscious state/ OR minimally conscious state*.ti,ab.) OR (exp consciousness disorder/ OR consciousness disorder*.ti,ab. OR disorder* of consciousness.ti,ab.)) AND ((exp convalescence/ OR convalescence.ti,ab. OR recover*.ti,ab.) OR (exp daily life activity/ OR daily life activit*.ti,ab. OR activit* of daily living.ti,ab.) OR (exp awareness/ OR awareness.ti,ab.) OR (exp wakefulness/ OR wakefulness.ti,ab.)) AND ((exp critical care outcome/ OR critical care outcome*.ti,ab.) OR (exp treatment outcome/ OR treatment outcome*.ti,ab.) OR (exp evaluation*.ti,ab.) OR (exp outcome assessment/ OR assessment*.ti,ab.))	36 English, 1986-2020
37 PsycInfo	38 (SU (“traumatic brain injur”) OR TI (“traumatic brain injur”) OR AB (“traumatic brain injur”) OR SU (coma*) OR TI (coma*) OR AB (coma*) OR SU (“persistent vegetative state”) OR TI (“persistent	39 1/1987-12/31/2020, English only

	<p>vegetative state*”) OR AB (“persistent vegetative state*”) OR SU (“minimally conscious state*”) OR TI (“minimally conscious state*”) OR AB (“minimally conscious state*”) OR SU (“consciousness disorder*”) OR TI (“consciousness disorder*”) OR AB (“consciousness disorder*”) OR SU (“disorder* of consciousness”) OR TI (“disorder* of consciousness”) OR AB (“disorder* of consciousness”) AND (SU (recover*) OR TI (recover*) OR AB (recover*) OR SU (“activit* of daily living”) OR TI (“activit* of daily living”) OR AB (“activit* of daily living”) OR SU (awareness) OR TI (awareness) OR AB (awareness) OR SU (wakefulness) OR TI (wakefulness) OR AB (wakefulness)) AND (SU (“critical care outcome*”) OR TI (“critical care outcome*”) OR AB (“critical care outcome*”) OR SU (“treatment outcome*”) OR TI (“treatment outcome*”) OR AB (“treatment outcome*”) OR SU (“outcome assessment*”) OR TI (“outcome assessment*”) OR AB (“outcome assessment*”) OR SU (evaluation*) OR TI (evaluation*) OR AB (evaluation*) OR SU (assessment*) OR TI (assessment*) OR AB (assessment*))</p>	
PubMed	<p>(Severe Traumatic Brain Injury [tiab] OR Brain Injuries, Traumatic [mesh] OR traumatic brain injury [tiab] OR coma, post-head injury [mesh] OR persistent vegetative state [mesh] OR minimally conscious state [tiab] OR consciousness disorders [mesh] OR disorders of consciousness [tiab]) AND (recovery [tiab] OR recovery of function [mesh] OR activities of daily living [mesh] OR awareness [mesh] OR awareness [tiab] OR wakefulness [mesh] OR wakefulness [tiab]) AND (Critical care outcomes [mesh] OR treatment outcome [mesh] OR "outcome assessment (health care)" [mesh] OR disability evaluation [mesh] OR evaluation [tiab] OR patient outcome assessment [mesh] OR assessment [tiab])</p>	<p>Humans, English, 1/1/1986- 12/31/2020</p>
Scopus	<p>(TITLE-ABS-KEY (“traumatic brain injur*”) OR TITLE-ABS-KEY (coma*) OR TITLE-ABS-KEY (“persistent vegetative state*”) OR TITLE-ABS-KEY (“minimally conscious state*”) OR TITLE-ABS-KEY (“consciousness disorder*”) OR TITLE-ABS-KEY (“disorder* of consciousness”)) AND (TITLE-ABS-KEY (recover*) OR TITLE-ABS-KEY (“activit* of daily living”) OR TITLE-ABS-KEY (awareness) OR TITLE-ABS-KEY (wakefulness)) AND (TITLE-ABS-KEY (“critical care outcome*”) OR TITLE-ABS-KEY (“treatment outcome*”) OR TITLE-ABS-KEY (“outcome assessment*”) OR TITLE-ABS-KEY (evaluation*) OR TITLE-ABS-KEY (assessment*))</p>	<p>English</p>

147 *Search dates will include January 1, 1986 to December 31, 2020

148 **Information sources**

1
2
3 149 We will search the following electronic bibliographic databases: PubMed, Scopus, EMBASE,
4
5 150 PsycINFO, and The Cochrane Library (including Cochrane Database of Systematic Reviews,
6
7 151 Cochrane Central Register of Controlled Trials, and Cochrane Methodology Register).
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10 152 ***Synthesis of eligibility criteria***
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12 153 This review will include all published, peer-reviewed studies using an intervention/treatment to
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14 154 facilitate recovery of consciousness for adults (≥ 18 years) with DoC following severe TBI
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17 155 (Table 3).
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176 Table 3. Inclusion and exclusion criteria for the scoping review.

Category	Inclusion Criteria	Exclusion Criteria
Language	English	
Publication Date Range	January 1986 to December 2020	Before 1986
Participant Age	Participant age: ≥ 18 years of age At least one participant in the study was ≥ 18 years of age	All participants were under 18 years of age
Participant Diagnosis	Participant diagnosis: Disordered Consciousness (DoC) following severe TBI DoC was established utilizing a known assessment for evaluating states of consciousness such as the Coma Recovery Scale-Revised (CRS-R) or Glasgow Coma Scale ≤ 8 At least one participant in the study was diagnosed with DoC from a TBI	Participants had brain pathologies such as Alzheimer's Disease or non-traumatic brain injury, and/or were conscious, alert, and oriented Participants had a Diagnostics and Statistical Manual of Mental Disorders (5 th edition) diagnosis of psychiatric disorders
Intervention	Intervention aimed at facilitating recovery of consciousness	Purpose of intervention was not described as facilitating recovery of consciousness
Study Design	All designs of primary, peer-reviewed studies including randomized control trials, observational studies, cohort studies, case control studies, case series, and case reports	Qualitative studies; meta analyses, systematic reviews, and scoping reviews

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178 *Language:* English179 *Publication date:* January 1986 to December 2020

180 *Study Design:* This review will consider all designs of peer-reviewed studies including
 181 randomized control trials, observational studies, cohort studies, case control studies, case series,
 182 and case reports. Meta-analyses and review articles will be excluded.

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3 183 *Setting:* This review will include intervention studies delivered in any setting to adults with DoC
4
5 184 following a severe TBI. There is no restriction on country of origin.

6
7 185 *Participants:* For a study to be included in this review, at least one participant in the study must
8
9 186 have DoC following a severe TBI. A severe TBI resulting in DoC is defined as: a) Glasgow
10
11 187 Coma Scale (GCS) score of 3-8¹² or b) an assessment known for evaluating states of
12
13 188 consciousness, such as the CRS-R.^{5,8} Studies will be excluded if all participants were under 18
14
15 189 years of age, had a Diagnostic and Statistical Manual of Mental Disorders (5th edition) diagnosis
16
17 190 of a psychiatric disorder, had brain pathologies such as Alzheimer's Disease or non-traumatic
18
19 191 brain injury, or were conscious, alert, and oriented. All non-human studies will be excluded.

20
21 192 *Interventions:* Examples of interventions to be included are medication, nutrition, rehabilitation
22
23 193 therapy, non-invasive brain stimulation, and surgery. Studies will be excluded if the purpose of
24
25 194 the intervention/treatment provided was not described as facilitating recovery of consciousness.

31 **3. Select Studies**

32
33 196 Following the search, each identified article will be uploaded to Endnote, a reference
34
35 197 management system. Duplicate articles will be removed. Titles and abstracts will be screened by
36
37 198 two independent reviewers to assess whether articles meet inclusion criteria (Table 4). If studies
38
39 199 are meta-analyses or reviews that are relevant to the research question, we will search the
40
41 200 reference list. Articles that are included by the screening process will undergo a full text review.
42
43 201 Two independent reviewers will read the full text articles to make a final determination of
44
45 202 inclusion. Articles that do not meet inclusion criteria at this stage will be excluded from the final
46
47 203 sample, with rationale documented. Discrepancies about inclusion of articles will be resolved
48
49 204 through further discussion and/or input by a third reviewer.

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206 Table 4. Title and abstract review form

Questions	
1. Is the article written in English?	<input type="checkbox"/> Yes <input type="checkbox"/> No
2. Is the article published after 1985?	<input type="checkbox"/> Yes <input type="checkbox"/> No
3. Is the article about human subjects?	<input type="checkbox"/> Yes <input type="checkbox"/> No
a. Are the human subject's adults (≥ 18 years)	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
b. Do the adults have a traumatic brain injury?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
c. Are the adults unconscious?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
4. Is the article about an intervention?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
a. Is the purpose of the intervention to facilitate recovery of consciousness?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
b. Is it a meta-analysis, scoping review, or systematic review?	<input type="checkbox"/> Yes → Exclude & search the reference list. <input type="checkbox"/> No

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208 **4. Chart the Data**

209 Data will be extracted from included articles by independent reviewers using a uniform data
210 extraction tool developed for the study. A sample data extraction table is shown in Table 5.

211 Reviewers will use the Scottish Intercollegiate Guideline Network (SIGN) rating form to

212 evaluate study quality.²³ For each included article, data extraction will include details about the

1
2
3 213 year of publication, funding source, study aims, study design, number of participants (including
4
5 214 number lost to follow up), recruitment, study completion rate, demographics (age, injury
6
7 215 severity, days post-injury) of participants, clinical setting, specific intervention (including control
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9 216 conditions, if applicable), primary and secondary outcomes, timing, and location of outcomes.
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218 Table 5. Data extraction form for full text review.

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Study Information	
Study Title	
Year	
Funding Source	
Inclusion/Exclusion Criteria	
Is the paper relevant to our research question, "What are the content areas of outcomes related to recovery of consciousness that have been used in clinical trials and/or intervention studies for adults with severe traumatic brain injury in states of disordered consciousness?" (i.e. there are outcome measures for people in disorders of consciousness following an intervention)	
<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Adults (≥ 18 years) with primary diagnosis of severe traumatic brain injury; • Identified brain injury is noted to be severe by Glasgow Coma Scale of 8 or less; • At least one of the study participants are in states of disorders of consciousness following a traumatic brain injury; • Addressed outcome related to recovery of consciousness; • Written in English 	

1 2 3 4 5 6 7 8 9 10 11	Exclusion Criteria: • People with documented history of psychiatric illness (DSM criteria), and/or organic brain syndrome such as Alzheimer's Disease. • All study participants are fully conscious; • All study participants are <18 years of age; • Study participants include non-traumatic brain injury <i>only</i>	
12	Study Details	
13	Study design	
14	Sample/number of participants: Include sample size and diagnoses (i.e. DoC following TBI, stroke, anoxia)	
15	Sample/demographics: age, injury severity, days post injury (if reported)	
16	Sample: The study's inclusion criteria	
17	Sample: The study's exclusion criteria	
18	Data Collection Procedures	
19	Intervention characteristics (intervention(s), control condition(s), duration and protocol information)	
20	Primary outcome measure	
21	Context of use for primary outcome measure	
22	Endpoint measure	
23	Secondary outcome measures	
24	Were outcome measures transformed? (Yes/No)	
25	Timing of outcome measures	
26	Results	
27	Observed sample	
28	Number of excluded participants	

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Number of participants lost to follow up	
Primary Outcome (mean, proportion, other effect size index)	
Statistical analyses (description of groups, comparison of groups)	
Key Findings	
<i>**Complete SIGN Quality Rating Based on Study Design</i>	

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221 5. Collate, Summarize and Report Information

222 *Data analysis*

223 We will transfer information from the data extraction forms into STATA to complete descriptive
224 analyses.

225 **Conceptual Framework and Key Concepts**

226 *World Health Organization International Classification of Functioning, Disability and*

227 *Health*: Clinical outcome assessments will be categorized based on the World Health

228 Organization (WHO) International Classification of Functioning, Disability and Health (ICF)

229 framework using relevant concept of interest. This framework has two major components:

230 *Functioning and Disability* which includes the domains of Body Function, Body Structure, and

231 Activities and Participation that impact an individual's daily life; and *Contextual Factors* which

232 includes the domains of Personal Factors and Environmental Factors. Environmental Factors

233 consider the "physical, social and attitudinal environment in which people live and conduct their

234 lives."²⁴ Personal Factors include age, gender, and education; we will not apply this domain in

235 classifying outcome assessments since these generally represent covariates rather than

236 outcomes/endpoints.

237 Clinical outcome assessments will first be categorized into one of the four relevant WHO ICF

238 domains (body structures, body functions, activities and participation, environmental factors)

239 based on the concept of interest they are intended to measure. These categorizations will be

240 mutually exclusive in that each outcome assessment will only be assigned to one domain. ICF

241 domains can be further classified into subdomains.²⁴ We will also assign each outcome

242 assessment to a relevant sub-domain. Should an outcome assessment not fit into a WHO ICF

243 domain, we will create an 'Other' domain. Once all outcome assessments are categorized to a

1
2
3 244 domain, we will thematically analyze the outcome assessments in the ‘Other’ domain to
4
5 245 determine if a new domain is needed. For example, previous literature argues for the inclusion of
6
7
8 246 quality of life as a domain.²⁵
9

10 247 **Common Data Elements:** We will also categorize outcome assessments as to whether they are a
11
12 248 NINDS CDE for moderate/severe TBI. We will test the significance of the introduction for
13
14
15 249 CDEs on outcome reporting before and after 2010 using a chi-square test.
16

17 250 **Presentation of results**

18
19 251 Results will be presented via detailed quantitative and narrative summaries. First, we will present
20
21 252 the PRISMA-Scr flow diagram demonstrating the inclusion of studies.^{26,27} We will also create an
22
23
24 253 outcome map table that categorizes outcome assessments by WHO ICF domain and sub-domain.
25
26 254 We will create two figures to display (1) the frequency of WHO ICF sub-domains in order to
27
28 255 show the gaps in the concepts of interest that outcome assessments address by domain, and (2)
29
30
31 256 the number and percent of studies that received US federal funding by year to show the
32
33 257 proportion that used a CDE as a primary outcome. In addition, we will present a 2x2 table of
34
35 258 CDE status and whether the publication was pre/post the introduction of CDEs.
36

37 259 **Stakeholder Engagement**

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40 260 Clinicians and researchers with extensive experience treating and studying recovery of
41
42 261 consciousness following a TBI have been involved in the development of this scoping review
43
44
45 262 protocol. We have formed the Recovery of Consciousness (RECON) study team to continuously
46
47 263 engage these stakeholders throughout the scoping review process, inclusive of study selection
48
49 264 through dissemination of results.
50

51 265 **Patient and Public Involvement**

52
53
54 266 No patient involvement.
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3 267 **ETHICS AND DISSEMINATION**
4

5 268 No ethical approval is required for this study as it is not determined to be human subjects
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7
8 269 research. Results will be presented at a national rehabilitation conference and submitted to a
9
10 270 peer-reviewed journal for publication.

11
12 271 ***Reporting of protocol and study records***
13

14 272 We registered this scoping review with PROSPERO (CRD42017058383). This study protocol
15
16
17 273 and future reports will follow PRISMA-ScR guidelines for the publication of scoping reviews.²⁶
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4

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page or Line number
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Lines 1-2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Line 272
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Title page
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Line 274
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Lines 276-277
Sponsor	5b	Provide name for the review funder and/or sponsor	Lines 276-277
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Lines 2-115
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Lines 116-121
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Lines 152-194
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Lines 148-151
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits,	Lines 143-147

		such that it could be repeated	
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Lines 196-197
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Lines 197-204
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Lines 208-221
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Lines 208-221
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Lines 208-221
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Lines 208-221
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Lines 251-258 (Scoping review quantitative and narrative summaries planned)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Lines 196-197

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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BMJ Open

Mapping Outcomes for Recovery of Consciousness in Studies from 1986 to 2020: A scoping review protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-056538.R1
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Date Submitted by the Author:	18-Mar-2022
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Primary Subject Heading:	Research methods
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	REHABILITATION MEDICINE, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Neurological injury < NEUROLOGY

SCHOLARONE™
Manuscripts

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3 1 **Mapping Outcomes for Recovery of Consciousness in Studies from 1986 to 2020: A scoping**
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6 2 **review protocol**

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8 3 Jennifer Weaver, PhD^{1,2}; Alison Cogan, PhD³; Parie Bhandari, BA²; Bint-e Awan, BA²; Erica
9
10 4 Jacobs, BS²; Ariana Pape, MD²; Chantal Nguyen, MD²; Ann Guernon, PhD^{4,5}; Tom Harrod,
11
12 5 MLS, MS²; The Recon Team; Theresa Bender Pape, DrPH⁵; Trudy Mallinson, PhD²
13
14
15 6

16
17 7 ¹College of Health and Human Sciences, Colorado State University; ²School of Medicine and
18
19 8 Health Sciences, The George Washington University, Washington, DC; ³Veterans Affairs
20
21 9 Greater Los Angeles Healthcare System, Los Angeles, CA, ⁴College of Nursing and Health
22
23 10 Sciences, Lewis University, Romeoville, IL; ⁵Hines Veterans Affairs Hospital, Hines, IL
24
25
26 11

27
28 12 **Corresponding Author:** Jennifer Weaver, PhD

29
30
31 13 Assistant Professor, Department of Occupational Therapy, College of Health and Human
32
33 14 Sciences, Colorado State University, 1573 Campus Delivery, Fort Collins, CO 80523. Email:
34
35 15 jen.weaver@colostate.edu
36
37

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43
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45
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47
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49
50 22 Rudin Portnoff OTR/L, CBIS; Bailey Widener, MSOT, MPH, CBIS, OTR/L; Sarah
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3 23 Hollingsworth, PT, DPT; Coty Wardwell, PT, DPT; Julianne Angel, OTR/L, CSRS, CBIS;
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3 25 **Abstract**
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5 26 **Introduction:** Historically, heterogeneous outcome assessments have been used to measure
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8 27 recovery of consciousness in patients with disorders of consciousness (DoC) following traumatic
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10 28 brain injury (TBI), making it difficult to compare across studies. To date, however, there is no
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12 29 comprehensive review of clinical outcome assessments that are used in intervention studies of
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14 30 adults with DoC. The objective of this scoping review is to develop a comprehensive inventory
15
16 31 of clinical outcome assessments for recovery of consciousness that have been used in clinical
17
18 32 studies of adults with DoC following TBI.
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21 33 **Methods and Analysis:** The methodological framework for this review is: 1) identify the
22
23 34 research questions, 2) identify relevant studies, 3) select studies, 4) chart the data, 5) collate,
24
25 35 summarize and report results and 6) consult stakeholders to drive knowledge translation. We will
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27 36 identify relevant studies by searching the following electronic bibliographic databases: PubMed,
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29 37 Scopus, EMBASE, PsycINFO, and The Cochrane Library (including Cochrane Database of
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31 38 Systematic Reviews, Cochrane Central Register of Controlled Trials, and Cochrane
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33 39 Methodology Register). Criteria for article inclusion are published in the English-language, peer-
34
35 40 reviewed studies of interventions aimed at facilitating recovery of consciousness among adults (\geq
36
37 41 18 years) with DoC following a severe TBI, published from January 1986 to December 2020.
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39 42 Articles meeting inclusion criteria at this stage will undergo a full text review. We will chart the
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41 43 data by applying the World Health Organization International Classification of Functioning,
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43 44 Disability and Health Framework to identify the content areas of clinical outcome assessments.
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45 45 To support knowledge translation efforts, we will involve clinicians and researchers experienced
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47 46 in TBI care throughout the project from conceptualization of the study through dissemination of
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49 47 results.
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3 48 **Ethics and Dissemination:** Results will be presented at national conferences and published in
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6 49 peer reviewed journals.

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8 50 **Keywords:** Traumatic Brain Injury; Disorders of Consciousness; Common Data Elements,
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10 51 Clinical Outcome Assessments

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15 53 **Strengths and limitations of this study**

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17 54 • The proposed scoping review will result in a comprehensive catalogue of outcome
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19 55 assessments utilized in traumatic brain injury research aimed at facilitating recovery of
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21 56 consciousness among adults with DoC.
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24 57 • The outcome assessments will be grouped according to the WHO ICF domains and sub-
25
26 58 domains to identify key trends and gaps in concepts of interest.
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29 59 • To the authors' knowledge, this will be the first study to identify whether the introduction
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31 60 of NINDS CDEs influenced outcome assessment reporting among studies that received
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33 61 federal funding in the United States.
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36 62 • Studies reporting US federal funding published after the introduction of NINDS CDEs
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38 63 may have been conducted prior to 2010 and therefore the authors may not have been
39
40 64 strongly encouraged to use NINDS CDEs.
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43 65 • It is possible that our search strategy will miss relevant studies; we will mitigate this risk
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45 66 by searching multiple databases and manually searching review articles and meta-
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47 67 analyses.
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INTRODUCTION

71 **Rationale**

72 To date, there has been limited success in clinical trials for treatment of patients with severe
73 traumatic brain injury (TBI) that result in disorders of consciousness (DoC).¹⁻³ Representing a
74 continuum of impaired consciousness, DoC is based on a person's ability to demonstrate arousal
75 and/or awareness. The DoC continuum includes comatose, vegetative state/unresponsive
76 wakefulness syndrome, minimally conscious state, and emergence from the minimally conscious
77 state.⁴ Recovery of consciousness for people with DoC following a severe TBI is uncertain and
78 difficult to predict.⁵⁻⁷ Accurate measurement of recovery of consciousness for people in DoC is
79 essential for diagnosis and prognosis as well as determining the efficacy and effectiveness of
80 interventions.^{5,8-10} To date, there has been no review of the range of clinical outcome assessments
81 used in measuring recovery of consciousness.

82 Historically, measuring recovery of consciousness in clinical trials has involved a range
83 of clinical outcome assessments measuring different concepts of interest (e.g., response to pain,
84 awareness), making it difficult to compare results across studies.¹¹⁻¹⁴ The National Institute of
85 Neurological Disorders and Stroke (NINDS), part of the US National Institutes of Health (NIH),
86 established a set of Common Data Elements (CDEs) for TBI in 2010 with the goal of promoting
87 comparability of study findings. Traumatic brain injury researchers applying for United States
88 (US) federal funding sources including NIH, Department of Defense, Department of Veteran's
89 Affairs are strongly encouraged to use NINDS CDEs for outcome measurement to improve
90 comparability across trials. Further, a data repository for TBI research was created as a result of
91 collaboration between NIH and the Federal Interagency Traumatic Brain Injury Research
92 (FITBIR) Informatics System;¹⁵ federally funded researchers may be required to submit their

93 data to this repository in the future. This requirement provides additional incentive to use NINDS
94 CDEs.¹⁵⁻¹⁷

95 CDEs are categorized as core, basic, or supplemental. The ‘core’ designation indicates
96 data elements pertinent for all TBI studies. Basic CDEs are specific to studies of populations
97 within TBI, such as ‘concussion/mild TBI’, ‘acute hospitalized’, ‘moderate/severe TBI:
98 rehabilitation’, and ‘epidemiology’. Basic CDEs for ‘moderate/severe TBI: rehabilitation’
99 include, but are not limited to, pupil reactivity, death date and time, hospital discharge
100 destination, and alteration of consciousness duration.¹⁸ Supplemental CDEs are optional and may
101 be appropriate depending on the research question and scope.¹⁶ Only two supplemental CDEs are
102 related to recovery of consciousness in adults: the Galveston Orientation Amnesia Test and JFK
103 Coma Recovery Scale-Revised (CRS-R) (Table 1).¹⁸

104 Table 1. Examples of Common Data Elements

Type of CDE	Definition	Example of CDE
General Core	Recommended for all NIH-funded studies: General	C00031: Race Expanded Category
Disease-specific Core	Recommended for all NIH-funded studies: Disease specific (TBI)	C01001: Glasgow Coma Scale (GCS) - motor response scale
Basic*	Recommended for all TBI NIH-funded studies: Specific to sub-diseases (e.g., Epidemiology and Moderate/Severe: Rehabilitation)	C07155: Disability Rating Scale Total Score
Supplemental	Recommended for NIH-funded studies: Specific to study design or type of research	C07145: JFK Coma Recovery Scale-Revised – Total Score

105 *Basic CDEs are comparable to Supplemental-Highly Recommended CDEs for other diagnostic
106 categories.

107 Two studies have described the implementation of CDEs in TBI research.^{13,19} Yue et al
108 (2013) described the implementation of CDEs for a multicenter prospective study and note
109 recommendations for future data collection procedures as well as the success in transferring the
110 data to FITBIR. Stead et al (2013) used CDEs to describe TBI patients in emergency

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3 111 departments and were able to compare results to several other published studies. Although the
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5 112 goal of the NINDS CDE project is to improve consistency and comparability across clinical
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7 113 studies of patients with DoC following severe TBI by encouraging more consistent use of
8
9 114 clinical outcome assessments, there is currently no evidence to indicate whether this outcome has
10
11 115 been achieved.

14 116 **Objective**

16
17 117 The primary objective of this scoping review is to develop a comprehensive inventory of
18
19 118 clinical outcome assessments in clinical trials aimed at recovery of consciousness for patients
20
21 119 with DoC after TBI. Secondary objectives are to examine the trends in primary outcomes over
22
23 120 time and whether reporting of NINDS CDEs increased after their introduction in 2010 in studies
24
25 121 that received US federal funding.

28 122 **METHODS AND ANALYSIS**

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31 123 A scoping review is an appropriate method to achieve the stated objectives because we
32
33 124 want to identify characteristics of clinical outcome assessments used to evaluate the recovery of
34
35 125 consciousness following a severe TBI.²⁰ The scoping review will be conducted based on the
36
37 126 Arksey and O'Malley²¹ methodological framework that has been refined by Levac et al²². The
38
39 127 methodological framework for this review will include: 1) identify the research questions, 2)
40
41 128 identify relevant studies, 3) select studies, 4) chart the data, 5) collate, summarize and report
42
43 129 results, and 6) stakeholder engagement to drive knowledge translation.^{21,22}

46 130 **1. Identify the Research Questions**

48 131 ***Primary question***

- 50
51 132 • What clinical outcome assessments have been used in published studies about recovery of
52
53 133 consciousness for adults with severe TBI in states of disordered consciousness?

55 134 ***Secondary questions***

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3 135 • How have the outcomes assessments used to measure DoC in adults with severe TBI
4
5
6 136 changed over time?
7
8 137 • Did frequency of reporting clinical outcome assessments classified as NINDS CDEs
9
10 138 change after their introduction in 2010 among federally funded studies in the US?

12 139 2. Identify Relevant Studies

14 140 The search strategy was developed in collaboration with a research librarian. Our search terms
15
16
17 141 are broad to identify all eligible studies. These search terms encompass three primary categories:
18
19 142 severe TBI, recovery of consciousness, and outcomes.

21 143 *Search terms*

22
23
24 144 An in-depth outline of the full search strategy is reported in Table 2.

25
26 145 Table 2. Examples of the search strategy that will generate the articles to review for the research
27 146 question.

28 Database	29 Search Terms	30 Customization
31 Cochrane	32 (“traumatic brain injury”) OR (coma) OR (“persistent vegetative state”) OR (“minimally conscious state”) OR (“consciousness disorder”) OR (“disorder* of consciousness”) AND ((recovery) OR (“activities of daily living”) OR (awareness) OR (wakefulness)) AND (“critical care outcome”) OR (“treatment outcome”) OR (“outcome assessment”) OR (evaluation) OR (assessment))	33 1987-2020, all publication types
34 Embase	35 ((exp traumatic brain injury/ OR traumatic brain injur*.ti,ab.) OR (exp coma/ OR coma*.ti,ab.) OR (exp persistent vegetative state/ OR persistent vegetative state*.ti,ab.) OR (exp minimally conscious state/ OR minimally conscious state*.ti,ab.) OR (exp consciousness disorder/ OR consciousness disorder*.ti,ab. OR disorder* of consciousness.ti,ab.)) AND ((exp convalescence/ OR convalescence.ti,ab. OR recover*.ti,ab.) OR (exp daily life activity/ OR daily life activit*.ti,ab. OR activit* of daily living.ti,ab.) OR (exp awareness/ OR awareness.ti,ab.) OR (exp wakefulness/ OR wakefulness.ti,ab.)) AND ((exp critical care outcome/ OR critical care outcome*.ti,ab.) OR (exp treatment outcome/ OR treatment outcome*.ti,ab.) OR (exp evaluation*.ti,ab.) OR (exp outcome assessment/ OR assessment*.ti,ab.))	36 English, 1986-2020
37 PsycInfo	38 (SU (“traumatic brain injur*”) OR TI (“traumatic brain injur*”) OR AB (“traumatic brain injur*”) OR SU (coma*) OR TI (coma*) OR AB (coma*) OR SU (“persistent vegetative state*”) OR TI (“persistent	39 1/1987-12/31/2020, English only

	<p>vegetative state*”) OR AB (“persistent vegetative state*”) OR SU (“minimally conscious state*”) OR TI (“minimally conscious state*”) OR AB (“minimally conscious state*”) OR SU (“consciousness disorder*”) OR TI (“consciousness disorder*”) OR AB (“consciousness disorder*”) OR SU (“disorder* of consciousness”) OR TI (“disorder* of consciousness”) OR AB (“disorder* of consciousness”) AND (SU (recover*) OR TI (recover*) OR AB (recover*) OR SU (“activit* of daily living”) OR TI (“activit* of daily living”) OR AB (“activit* of daily living”) OR SU (awareness) OR TI (awareness) OR AB (awareness) OR SU (wakefulness) OR TI (wakefulness) OR AB (wakefulness)) AND (SU (“critical care outcome*”) OR TI (“critical care outcome*”) OR AB (“critical care outcome*”) OR SU (“treatment outcome*”) OR TI (“treatment outcome*”) OR AB (“treatment outcome*”) OR SU (“outcome assessment*”) OR TI (“outcome assessment*”) OR AB (“outcome assessment*”) OR SU (evaluation*) OR TI (evaluation*) OR AB (evaluation*) OR SU (assessment*) OR TI (assessment*) OR AB (assessment*))</p>	
PubMed	<p>(Severe Traumatic Brain Injury [tiab] OR Brain Injuries, Traumatic [mesh] OR traumatic brain injury [tiab] OR coma, post-head injury [mesh] OR persistent vegetative state [mesh] OR minimally conscious state [tiab] OR consciousness disorders [mesh] OR disorders of consciousness [tiab]) AND (recovery [tiab] OR recovery of function [mesh] OR activities of daily living [mesh] OR awareness [mesh] OR awareness [tiab] OR wakefulness [mesh] OR wakefulness [tiab]) AND (Critical care outcomes [mesh] OR treatment outcome [mesh] OR "outcome assessment (health care)" [mesh] OR disability evaluation [mesh] OR evaluation [tiab] OR patient outcome assessment [mesh] OR assessment [tiab])</p>	<p>Humans, English, 1/1/1986- 12/31/2020</p>
Scopus	<p>(TITLE-ABS-KEY (“traumatic brain injur*”) OR TITLE-ABS-KEY (coma*) OR TITLE-ABS-KEY (“persistent vegetative state*”) OR TITLE-ABS-KEY (“minimally conscious state*”) OR TITLE-ABS-KEY (“consciousness disorder*”) OR TITLE-ABS-KEY (“disorder* of consciousness”)) AND (TITLE-ABS-KEY (recover*) OR TITLE-ABS-KEY (“activit* of daily living”) OR TITLE-ABS-KEY (awareness) OR TITLE-ABS-KEY (wakefulness)) AND (TITLE-ABS-KEY (“critical care outcome*”) OR TITLE-ABS-KEY (“treatment outcome*”) OR TITLE-ABS-KEY (“outcome assessment*”) OR TITLE-ABS-KEY (evaluation*) OR TITLE-ABS-KEY (assessment*))</p>	<p>English</p>

147 *Search dates will include January 1, 1986 to December 31, 2020

148 **Information sources**

1
2
3 149 We will search the following electronic bibliographic databases: PubMed, Scopus, EMBASE,
4
5 150 PsycINFO, and The Cochrane Library (including Cochrane Database of Systematic Reviews,
6
7 151 Cochrane Central Register of Controlled Trials, and Cochrane Methodology Register).
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9

10 152 ***Synthesis of eligibility criteria***
11

12 153 This review will include all published, peer-reviewed studies using an intervention/treatment to
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14 154 facilitate recovery of consciousness for adults (≥ 18 years) with DoC following severe TBI
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17 155 (Table 3).
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176 Table 3. Inclusion and exclusion criteria for the scoping review.

Category	Inclusion Criteria	Exclusion Criteria
Language	English	
Publication Date Range	January 1986 to December 2020	Before 1986
Participant Age	Participant age: ≥ 18 years of age At least one participant in the study was ≥ 18 years of age	All participants were under 18 years of age
Participant Diagnosis	Participant diagnosis: Disordered Consciousness (DoC) following severe TBI DoC was established utilizing a known assessment for evaluating states of consciousness such as the Coma Recovery Scale-Revised (CRS-R) or Glasgow Coma Scale ≤ 8 At least one participant in the study was diagnosed with DoC from a TBI	Participants had brain pathologies such as Alzheimer's Disease or non-traumatic brain injury, and/or were conscious, alert, and oriented Participants had a Diagnostics and Statistical Manual of Mental Disorders (5 th edition) diagnosis of psychiatric disorders
Intervention	Intervention aimed at facilitating recovery of consciousness	Purpose of intervention was not described as facilitating recovery of consciousness
Study Design	All designs of primary, peer-reviewed studies including randomized control trials, observational studies, cohort studies, case control studies, case series, and case reports	Qualitative studies; meta-analyses, systematic reviews, and scoping reviews

177

178 *Language:* English179 *Publication date:* January 1986 to December 2020

180 *Study Design:* This review will consider all designs of peer-reviewed studies including
 181 randomized control trials, observational studies, cohort studies, case control studies, case series,
 182 and case reports. Meta-analyses and review articles will be excluded.

183 *Setting:* This review will include intervention studies delivered in any setting to adults with DoC
184 following a severe TBI. There is no restriction on country of origin.

185 *Participants:* For a study to be included in this review, at least one participant in the study must
186 have DoC following a severe TBI. A severe TBI resulting in DoC is defined as: a) Glasgow
187 Coma Scale (GCS) score of 3-8¹² or b) an assessment known for evaluating states of
188 consciousness, such as the CRS-R.^{5,8} Studies will be excluded if all participants were under 18
189 years of age, had a Diagnostic and Statistical Manual of Mental Disorders (5th edition) diagnosis
190 of a psychiatric disorder, had brain pathologies such as Alzheimer's Disease or non-traumatic
191 brain injury, or were conscious, alert, and oriented. All non-human studies will be excluded.

192 *Interventions:* Examples of interventions to be included are medication, nutrition, rehabilitation
193 therapy, non-invasive brain stimulation, and surgery. Studies will be excluded if the purpose of
194 the intervention/treatment provided was not described as facilitating recovery of consciousness.

195 **3. Select Studies**

196 Following the search, each identified article will be uploaded to Endnote, a reference
197 management system. Duplicate articles will be removed. Titles and abstracts will be screened by
198 two independent reviewers to assess whether articles meet inclusion criteria (Table 4). If studies
199 are meta-analyses or reviews that are relevant to the research question, we will search the
200 reference list. Articles that are included by the screening process will undergo a full text review.
201 Two independent reviewers will read the full text articles to make a final determination of
202 inclusion. Articles that do not meet inclusion criteria at this stage will be excluded from the final
203 sample, with rationale documented. Discrepancies about inclusion of articles will be resolved
204 through further discussion and/or input by a third reviewer.

206 Table 4. Title and abstract review form

Questions	
1. Is the article written in English?	<input type="checkbox"/> Yes <input type="checkbox"/> No
2. Is the article published after 1985?	<input type="checkbox"/> Yes <input type="checkbox"/> No
3. Is the article about human subjects?	<input type="checkbox"/> Yes <input type="checkbox"/> No
a. Are the human subject's adults (≥ 18 years)	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
b. Do the adults have a traumatic brain injury?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
c. Are the adults unconscious?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
4. Is the article about an intervention?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
a. Is the purpose of the intervention to facilitate recovery of consciousness?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unsure, requires full text review
b. Is it a meta-analysis, scoping review, or systematic review?	<input type="checkbox"/> Yes → Exclude & search the reference list. <input type="checkbox"/> No

207

208 **4. Chart the Data**

209 Data will be extracted from included articles by independent reviewers using a uniform data
 210 extraction tool developed for the study. A sample data extraction table is shown in Table 5.
 211 Reviewers will use the Scottish Intercollegiate Guideline Network (SIGN) rating form to
 212 evaluate study quality.²³ Consistent with the SIGN protocol, case study designs will not be

1
2
3 213 evaluated for quality; other studies' methodological quality will be rated as high, acceptable,
4
5 214 low, or unacceptable-reject.²³ For each included article, data extraction will include details about
6
7 215 the year of publication, funding source, study aims, study design, number of participants
8
9 216 (including number lost to follow up), recruitment, study completion rate, demographics (age,
10
11 217 injury severity, days post-injury) of participants, clinical setting, specific intervention (including
12
13 218 control conditions, if applicable), primary and secondary outcomes, timing, and location of
14
15 219 outcomes.
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221 Table 5. Data extraction form for full text review.

Study Information	
Study Title	
Year	
Funding Source	
Inclusion/Exclusion Criteria	
Is the paper relevant to our research question, "What are the content areas of outcomes related to recovery of consciousness that have been used in clinical trials and/or intervention studies for adults with severe traumatic brain injury (TBI) in disorders of consciousness (DoC)?" (i.e., there are outcome measures for people in DoC following an intervention)	
<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Adults (≥ 18 years) with primary diagnosis of severe TBI; • Identified brain injury is noted to be severe by Glasgow Coma Scale of 8 or less; • At least one of the study participants are in DoC following a TBI; • Addressed outcome related to recovery of consciousness; • Written in English 	
<p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • People with documented history of psychiatric illness (DSM criteria), and/or organic brain syndrome such as Alzheimer’s Disease. • All study participants are fully conscious; • All study participants are < 18 years of age; • Study participants include non-traumatic brain injury <i>only</i> 	
Study Details	
Study design	
Sample/number of participants: Include sample size and diagnoses (i.e., DoC following TBI, stroke, anoxia)	
Sample/demographics: age, injury severity, days post injury (if reported)	

1	Sample: The study's inclusion criteria	
2		
3	Sample: The study's exclusion criteria	
4		
5	Data Collection Procedures	
6		
7	Intervention characteristics (intervention(s), control condition(s), duration and protocol information)	
8		
9	Primary outcome measure	
10		
11	Context of use for primary outcome measure	
12		
13	Endpoint measure	
14		
15	Secondary outcome measures	
16		
17	Were outcome measures transformed? (Yes/No)	
18		
19	Timing of outcome measures	
20	Results	
21	Observed sample	
22		
23	Number of excluded participants	
24		
25	Number of participants lost to follow up	
26		
27	Primary Outcome (mean, proportion, other effect size index)	
28		
29	Statistical analyses (description of groups, comparison of groups)	
30		
31	Key Findings	
32		
33	**Complete SIGN Quality Rating Based on Study Design	
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223 5. Collate, Summarize and Report Information

224 *Data analysis*

225 We will transfer information from the data extraction forms into STATA to complete descriptive
226 analyses. We will categorize studies based on sample size and report this information. We will
227 also categorize studies into five groups (high, acceptable, low, unacceptable-reject or not rated)
228 based on quality rating using SIGN criteria. We will examine whether sample size or quality
229 rating biases results regarding frequency of clinical outcome assessment as well as utilization of
230 CDEs.

231 **Conceptual Framework and Key Concepts**

232 *World Health Organization International Classification of Functioning, Disability and*

233 *Health*: Clinical outcome assessments will be categorized based on the World Health

234 Organization (WHO) International Classification of Functioning, Disability and Health (ICF)

235 framework using relevant concept of interest. This framework has two major components:

236 *Functioning and Disability* which includes the domains of Body Function, Body Structure, and

237 Activities and Participation that impact an individual's daily life; and *Contextual Factors* which

238 includes the domains of Personal Factors and Environmental Factors. Environmental Factors

239 consider the "physical, social and attitudinal environment in which people live and conduct their

240 lives."²⁴ Personal Factors include age, gender, and education; we will not apply this domain in

241 classifying outcome assessments since these generally represent covariates rather than

242 outcomes/endpoints.

243 Clinical outcome assessments will first be categorized into one of the four relevant WHO ICF

244 domains (body structures, body functions, activities and participation, environmental factors)

245 based on the concept of interest they are intended to measure. These categorizations will be

1
2
3 246 mutually exclusive in that each outcome assessment will only be assigned to one domain. ICF
4
5 247 domains can be further classified into subdomains.²⁴ We will also assign each outcome
6
7 248 assessment to a relevant sub-domain. Should an outcome assessment not fit into a WHO ICF
8
9 249 domain, we will create an ‘Other’ domain. Once all outcome assessments are categorized to a
10
11 250 domain, we will thematically analyze the outcome assessments in the ‘Other’ domain to
12
13 251 determine if a new domain is needed. For example, previous literature argues for the inclusion of
14
15 252 quality of life as a domain.²⁵

16
17 253 **Common Data Elements:** We will categorize outcome assessments as to whether they are a
18
19 254 NINDS CDE for moderate/severe TBI. We will test the significance of the introduction for
20
21 255 CDEs on outcome reporting before and after 2010 using a chi-square test.

22 256 **Presentation of results**

23
24 257 Results will be presented via detailed quantitative and narrative summaries. First, we will present
25
26 258 the PRISMA-Scr flow diagram demonstrating the inclusion of studies,^{26,27} including how many
27
28 259 articles were retrieved from each database. We will also create an outcome map table that
29
30 260 categorizes outcome assessments by WHO ICF domain and sub-domain. We will create two
31
32 261 figures to display (1) the frequency of WHO ICF sub-domains to show the gaps in the concepts
33
34 262 of interest that outcome assessments address by domain, and (2) the number and percent of
35
36 263 studies that received US federal funding by year to show the proportion that used a CDE as a
37
38 264 primary outcome. In addition, we will present a 2x2 table of CDE status and whether the
39
40 265 publication was pre/post the introduction of CDEs.

41 266 **Stakeholder Engagement**

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43 267 Clinicians and researchers with extensive experience treating and studying recovery of
44
45 268 consciousness following a TBI have been involved in the development of this scoping review
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3 269 protocol. We have formed the Recovery of Consciousness (RECON) study team to continuously
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5 270 engage these stakeholders throughout the scoping review process, inclusive of study selection
6
7
8 271 through dissemination of results.
9

10 272 **Patient and Public Involvement**

11
12 273 No patient involvement.
13

14 274 **ETHICS AND DISSEMINATION**

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16
17 275 No ethical approval is required for this study as it is not determined to be human subjects
18
19 276 research. Results will be presented at a national rehabilitation conference and submitted to a
20
21 277 peer-reviewed journal for publication.
22

23 278 ***Reporting of protocol and study records***

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26 279 We registered this scoping review with PROSPERO (CRD42017058383). This study protocol
27
28 280 and future reports will follow PRISMA-ScR guidelines for the publication of scoping reviews.²⁶
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3 281 **Contributorship statement:** All authors meet ICJME authorship criteria. Below we provide
4
5 282 specific details on how each author has met the four ICJME criteria for authorship.

6
7
8 283 Criteria #1: Substantial contributions to the conception or design of the work; or the acquisition,
9
10 284 analysis, or interpretation of data for the work.

11
12 285 Contributions to the conception of the work: Jennifer Weaver, Ann Guernon, Theresa
13
14 286 Bender Pape, and Trudy Mallinson; Contributions to the design of the work: Jennifer Weaver,
15
16 287 Alison Cogan, Tom Harrod, and Trudy Mallinson; Contributions to the acquisition of data: Tom
17
18 288 Harrod and Jennifer Weaver; Contributions to the analytic plan: Jennifer Weaver, Trudy
19
20 289 Mallinson, Alison Cogan, Parie Bhandari, Bint-e Awan, Erica Jacobs, Ariana Pape, Chantal
21
22 290 Nguyen, Ann Guernon, and the Recon Team.

23
24
25
26 291 Criteria #2: Drafting the work (i.e., protocol paper) or revising it critically for important
27
28 292 intellectual content.

29
30
31 293 Drafting of the protocol paper: Jennifer Weaver, Alison Cogan, Parie Bhandari, Bint-e
32
33 294 Awan, Erica Jacobs, Ariana Pape, Chantal Nguyen, and Trudy Mallinson; Critically revising the
34
35 295 protocol paper for important intellectual content: Ann Guernon, Theresa Bender Pape, Tom
36
37 296 Harrod, and the Recon Team

38
39
40 297 Criteria # 3: Final approval of the version to be published; AND Criteria #4: Agreement to be
41
42 298 accountable for all aspects of the work in ensuring that questions related to the accuracy or
43
44 299 integrity or any part of the work are appropriately investigated and resolved.

45
46
47 300 All authors provided final approval of the version to be published and are in agreement to
48
49 301 be accountable for all aspects of the work.

50
51 302 **Competing interests:** Authors have no disclosures.
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For peer review only

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For peer review only

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page or Line number (using clean copy)
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	Lines 1-2
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Line 279
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	Title page
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	Lines 12-15; 281-302
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	Lines 303-304
Sponsor	5b	Provide name for the review funder and/or sponsor	Lines 303-304
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	Lines 72-115
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	Lines 116-121
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	Lines 123-194
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	Lines 139-151
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits,	Lines 143-147

		such that it could be repeated	
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	Lines 196-197
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	Lines 197-204
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	Lines 206-223
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Lines 206-223
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Lines 208-223
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	Lines 208-222 and 223-230
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	Lines 223-230; 243-252; 253-256; 257-265 (Scoping review quantitative and narrative summaries planned)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	Lines 228-230
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	Lines 211-214 and Table 5

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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