

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

## Early screening for post-stroke depression, and the effect on functional outcomes, quality of life and mortality: a protocol for a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-050451
Article Type:	Protocol
Date Submitted by the Author:	19-Feb-2021
Complete List of Authors:	Selvaraj, Sudhakar; University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences Arora, Teresa; Zayed University, College of Natural & Health Sciences Montiel, Tahani; University of Texas Health Science Center at Houston, Cizik School of Nursing Grey, Ian; Lebanese American University, Psychology Alfraih, Hind; Zayed University, College of Natural & Health Sciences Suchting, Robert; University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences Savitz, Sean; University of Texas Health Science Center at Houston, Institute for Stroke and Cerebrovascular Disease Sanner Beauchamp, Jennifer; University of Texas Health Science Center at Houston, Östlundh, Linda; United Arab Emirates University College of Medicine and Health Sciences, National Medical Library
Keywords:	PSYCHIATRY, Depression & mood disorders < PSYCHIATRY, STROKE MEDICINE

SCHOLARONE™  
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1  
2  
3 **Title:** Early screening for post-stroke depression, and the effect on functional  
4 outcomes, quality of life and mortality: a protocol for a systematic review and meta-  
5 analysis  
6  
7  
8  
9

## 10 **Authors**

11  
12  
13  
14  
15 Dr. Sudhakar Selvaraj<sup>1\*</sup> (ORCID: 0000-0002-9494-172X); Dr. Teresa Arora<sup>2\*</sup> (ORCID:  
16 0000-0001-8360-7358); Ms. Tahani Casameni Montiel<sup>3</sup> (ORCID: 0000-0001-9626-  
17 0365); Dr. Ian Grey<sup>4</sup> (ORCID: 0000-0001-9773-2539); Ms. Hind Alfraih<sup>2</sup> (ORCID:  
18 0000-0002-5526-1393); Dr. Rob Suchting<sup>1</sup> (ORCID: 0000-0002-2822-3754); Dr. Sean  
19 Savitz<sup>5,6</sup>; | Dr. Jennifer Beauchamp<sup>3,5</sup>; ; Ms. Linda Östlundh<sup>7</sup> (ORCID: 0000-0001-  
20 5091-604X).  
21  
22  
23  
24  
25  
26  
27  
28  
29

## 30 **Author affiliations**

31  
32  
33 <sup>1</sup>Louis. A. Faillace, MD, Department of Psychiatry and Behavioral Sciences, The  
34 University of Texas Health Science Center at Houston, 1941 East Rd, Houston, TX  
35 77054; <sup>2</sup>Zayed University, Abu Dhabi, United Arab Emirates; <sup>3</sup>The University of Texas  
36 Health Science Center at Houston, Cizik School of Nursing; <sup>4</sup>Lebanese American  
37 University, Beirut, Lebanon; <sup>5</sup>Institute for Stroke and Cerebrovascular Disease,  
38 University of Texas Health Science Center at Houston, Houston, TX, US; <sup>6</sup>Department  
39 of Neurology, McGovern Medical School at the University of Texas Health Science  
40 Center at Houston, Houston, TX, US; <sup>7</sup>The National Medical Library, United Arab  
41 Emirates University, College of Medicine and Health Sciences, Al Ain, Abu Dhabi,  
42 United Arab Emirates.  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54

55  
56  
57  
58 \*Joint first authors with equal contribution.  
59  
60

1  
2  
3  
4  
5 **Corresponding author:**  
6  
7  
8  
9

10 Linda Östlundh

11  
12 The National Medical Library,

13  
14 United Arab Emirates University,

15  
16 College of Medicine and Health Sciences,

17  
18 Al Ain,

19  
20 Abu Dhabi,

21  
22 United Arab Emirates  
23  
24  
25  
26  
27

28 Tel: 00971 501126930  
29  
30  
31  
32

33 Email: lostlundh@uaeu.ac.ae  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Abstract

**Introduction:** Post-stroke depression (PSD) is a severe complication of cerebrovascular stroke affecting about one-third of stroke survivors and associated with functional recovery and Quality of Life (QOL) in stroke survivors. Screening for PSD is recommended; however, there are differences in the literature on the impact of early screening on functional outcome. In this systematic review, we synthesize the currently available literature regarding the associations between timing and setting of PSD screening and mortality, QOL, and functional outcomes in stroke survivors.

**Methods and analysis:** We will systematically search electronic databases including PubMed, Embase, APA PsycInfo, Web of Science, Scopus and CINAHL from inception to March 2021. Four reviewers will screen the title and abstract and full-text level records identified in the search in a blinded fashion to determine the study eligibility. Any selection disagreements between the reviewers will be resolved by the study investigator (SS). Data extraction of eligible studies will be conducted by two reviewers using a pre-defined template. We will complete the quality assessment of included articles independently by two reviewers and discrepancies will be resolved by the principal investigator (SS).

**Ethics and dissemination:** Due to the nature of the study design, ethical approval is not required. The systematic review and meta-analysis findings will be published and disseminated in a peer-reviewed journal. Our results will also be disseminated through posters and presentations at appropriate scientific conferences.

**Registration:** This protocol is reported as per the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) guidelines. The protocol

1  
2  
3 has been submitted for review to the international database, PROSPERO CRD:  
4  
5 (Submitted on 2021-02-08, ID no. 235993)  
6  
7  
8  
9

### 10 **Strengths and limitations of this study**

- 14 • Comprehensive systematic review of the associations between post-stroke  
15 depression and stroke outcomes.
- 18 • Rigorous methods, following the PRISMA guidelines, will be conducted to  
20 minimise the risk of bias.
- 24 • Limitations of this review include the exclusion of papers in languages other  
26 than English.

## Introduction

Post-stroke depression (PSD) is a severe complication of cerebrovascular stroke<sup>1</sup> affecting about one-third of stroke survivors<sup>2 3</sup>. PSD appears to be the most common psychiatric sequelae of stroke, independently associated with increased morbidity, mortality and disability<sup>4-6</sup>. PSD is also considered one of the most significant predictors for functional recovery and Quality of Life (QOL) in stroke survivors<sup>7 8</sup>. Stroke survivors with PSD are more likely to commit suicide than patients without PSD<sup>9 10</sup>. Suicide rates are more than double in stroke survivors compared to the general population<sup>11</sup>. Some stroke survivors who developed depression during the acute stroke and with a previous history of depression reported suicidal thoughts as early as four days after the onset of stroke<sup>12</sup>. Disability or dependence in daily living activities (ADLs) of patients who have suffered a stroke may also increase the risk of PSD<sup>13</sup> and suicidal ideation, bringing to light a vicious cycle between PSD and functional disabilities. Therefore, stroke survivors with functional disabilities should be considered at-risk for PSD and suicidal ideation and targeted screening for PSD and suicidal ideation may be warranted.

PSD is consistently associated with poor functional outcomes<sup>1 13</sup>(e.g., inability to perform ADLs independently) and rehabilitation outcomes (e.g. extended rehabilitation length of stay)<sup>13-15</sup>. It is hypothesized that the worse functional outcomes associated with PSD may be due to limited participation in rehabilitation<sup>13 16</sup>. For example, in a retrospective, case-control study of 560 ischemic stroke survivors, those with PSD had worse mobility, longer rehabilitation length of stay, and more insufficient response to rehabilitation efforts than stroke survivors without PSD<sup>14</sup>.



1  
2  
3 Furthermore, stroke survivors adequately treated for PSD with anti-depressants  
4 showed improved functional outcomes compared to anti-depressant therapy non-  
5 responders<sup>14</sup>. However, uncertainty regarding optimal strategies (e.g., timing, dosing,  
6 duration, and pharmaceuticals) for PSD remains<sup>1 17</sup>. Notably, while an independent  
7 association exists between PSD and poor functional recovery<sup>18</sup>, poor functional  
8 outcomes after stroke are also associated with PSD development.  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20

21 Despite the high prevalence of PSD and associated risks, only a minority of stroke  
22 survivors are adequately screened for PSD, and optimal strategies (e.g., timing,  
23 setting (hospital or community outpatient clinic), and methods [e.g., frequency]) for  
24 screening are unknown<sup>1 19</sup>. The risk of depression Stroke survivors is high  
25 immediately after the acute stroke, especially within the three months after a stroke<sup>20</sup>,  
26 during which the prevalence is estimated to be 33%. Interestingly nearly half of those  
27 who had depression in the first three months of acute recovered at one-year<sup>20</sup>.  
28 Routine screening for PSD in at-risk patients (e.g. those with severe functional  
29 disabilities and a history of depression) in the early stroke recovery period is shown  
30 to reduce the risk of PSD<sup>13</sup>. However, other studies did not find supportive evidence  
31 for PSD screening and stroke outcomes<sup>21 22</sup>. However, randomised controlled trials  
32 show screening and collaborative care for depression treatment can improve  
33 functional outcomes in chronic medical conditions, including stroke<sup>23</sup>. The American  
34 Heart Association/American Stroke Association recommends PSD screening and  
35 further research into the effect of PSD on all outcomes and QOL<sup>1</sup>. However,  
36 appropriate processes should be established before screening occurs to assure  
37 correct PSD diagnosis, adequate treatment, and routine follow-up<sup>1</sup>.  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5 The purpose of our review protocol is to update and synthesize the currently available  
6 literature regarding the associations between timing and setting of PSD screening  
7 and mortality, QOL, as well as functional outcomes in stroke survivors.  
8  
9  
10  
11  
12  
13  
14  
15  
16

17 Following two questions will be addressed in our systematic review and meta-  
18 analysis:  
19

- 20  
21 1. Does early screening for post-stroke depression (hospitalized patients after  
22 stroke) affect the short or long-term outcome (stroke, mortality, quality of life)  
23  
24
- 25 2. Do early (<3 months from an acute stroke) depression associated with worse  
26 post-stroke outcomes?  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36

## 37 **Methods and analysis**

38  
39  
40  
41  
42 This protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-  
43 Analyses Protocol (PRISMA-P) guidelines<sup>24</sup>. The PRISMA-P checklist can be found in  
44 the online supplementary materials file 1. The final review will be developed in  
45 accordance with the Preferred Reporting Items for Systematic Reviews and Meta-  
46 Analyses (PRISMA) statement<sup>25</sup> and will be informed by the Cochrane Handbook for  
47 Systematic Reviews of Interventions<sup>26</sup>.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 The protocol is registered on the online international prospective register of  
4 systematic reviews, PROSPERO (Submitted on 2021-02-08, ID no. 235993)  
5  
6  
7  
8  
9  
10  
11  
12

### 13 **Eligibility criteria**

#### 14 15 16 17 ***Inclusion criteria***

18  
19  
20  
21  
22 Our pre-defined inclusion criteria, throughout the screening process, are as follows:  
23  
24  
25

- 26 1. Uses a validated depression scale for screening after a stroke diagnosis;
- 27 2. Human subjects;
- 28 3. Longitudinal/prospective studies only;
- 29 4. English language only;
- 30 5. Peer-reviewed and published article;
- 31 6. Reports on a short or long-term outcome (quality of life, functional recovery  
32 [motor/disability index], mortality, aphasia, recurrent stroke/morbidity);
- 33 7. Stroke diagnosis;
- 34 8. Reports on the relationship between PSD and at least one outcome measure  
35 (see point 6);
- 36 9. The depression measurement should be obtained at the time of Stroke  
37 diagnosis or within three months of the diagnosis.  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55

#### 56 ***Exclusion criteria***

57  
58  
59  
60

Our pre-defined exclusion criteria, throughout the screening process, are as follows:

1. Studies involving animals;
2. Conference abstracts or papers;
3. Editorials/letter to the editor unless it reports original research data;
4. Patients with any primary psychiatric illness, except for anxiety/depression;
5. Patients with Dementia, Epilepsy, Cancer, or Multiple Sclerosis;
6. Patients with neurological or neurodegenerative conditions, except for stroke/neurovascular;
7. Reviews of any kind;
8. Questionnaire validation studies;
9. Case studies;
10. Randomised controlled trials;
11. Paediatric studies (samples that include patients under the age of 18 years);
12. Studies assessing the effectiveness of medication;
13. Protocol papers;
14. Studies with retrospective design;
15. Less than one-year follow-up;
16. Theses and dissertations.

### **Information sources and search strategy**

A comprehensive search of peer-reviewed literature from six electronic databases will be conducted from their inception to March 2021. The following medical and health sciences databases will be included: PubMed, Embase, APA PsycInfo, Scopus, Web

1  
2  
3 of Science and CINAHL. A medical librarian (LÖ) will use PubMed and PubMed's  
4 MeSH to systematically identify relevant search terms and synonyms for review and  
5 further suggestions by a subject specialist (SS). All keywords will be searched in a  
6 combination of the fields: "title", "abstract," and in "MeSH"/"thesaurus". We will limit the  
7 search to English papers only. No additional filters or geographical limitations will be  
8 used to ensure the best possible literature inclusion. Hand screening of reference lists  
9 of included papers will be conducted. A search log with search technical specifications,  
10 results and notes for all databases included in the search will be appended to the  
11 review. A preliminary search performed in PubMed in February 2021 is available in  
12 the online supplementary materials file 2.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27

## 28 **Data management**

29  
30  
31  
32  
33 The result from the database search will be uploaded to the systematic review  
34 software, Covidence<sup>27</sup>. Automatic de-duplication and screening will be conducted in  
35 the software. The finally selected references will be exported to a reference  
36 management software for the manuscript preparation.  
37  
38  
39  
40  
41  
42  
43  
44

## 45 **Selection of studies**

46  
47  
48  
49 All unique records identified in the database search will be screened for eligibility  
50 against the pre-defined inclusion and exclusion criteria by four independent reviewers.  
51 TA and HA will conduct the initial title and abstract screening and TM and IG will screen  
52 the papers selected for full-text review. After each screening module, eventual  
53 conflicts identified by the software will be resolved by a fifth reviewer (SS). All stages  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 of the screening and selection processes in Covidence follow the PRISMA workflow<sup>25</sup>.  
4  
5 The screening process's blinding will be based on the authors' responsibility in the  
6  
7 software settings before the screening process.  
8  
9  
10  
11  
12

13 The search result, de-duplication, screening and selection process, including reasons  
14  
15 for study exclusion, will be documented in a PRISMA flow diagram. Cabells Predatory  
16  
17 Reports<sup>28</sup> will be used to verify that eventual Open Access papers selected are not  
18  
19 published in potentially predatory journals.  
20  
21  
22

### 23 24 25 **Data extraction**

26  
27  
28  
29  
30 An extraction template will be used to extract relevant data from each of the included  
31  
32 studies. Information about population characteristics, length of follow-up, depression  
33  
34 scale used, time of screening for depression, stroke disability ratings, Rehabilitation  
35  
36 length of stay, mobility status and quality of life scores will be documented. The effect  
37  
38 size/measure of association between post-stroke depression screening and outcome  
39  
40 variables of interest, along with 95% confidence intervals (95% CIs) will also be  
41  
42 extracted. Two reviewers will extract the information independently and any  
43  
44 discrepancies will be resolved by the primary study investigator (SS).  
45  
46  
47  
48  
49  
50

### 51 **Quality assessment of individual studies**

52  
53  
54  
55  
56 Two reviewers will independently assess the quality of evidence and the risk of bias  
57  
58 of all eligible studies using the Newcastle Ottawa Scale. Eventual disagreements  
59  
60

1  
2  
3 between the reviewers will be discussed with the study's lead investigator (SS) until a  
4  
5 consensus is reached.  
6  
7  
8  
9

## 10 11 **Data analysis and synthesis** 12 13

14  
15  
16 The systematic review will identify and report the number of qualifying articles and  
17  
18 provide an overall summary of these. Information surrounding the sample size,  
19  
20 population, outcomes will be compared across the studies. Articles that contain  
21  
22 appropriate statistical information for meta-analysis will be assessed by the team  
23  
24 statistician (RS). The meta-analysis will calculate a pooled prevalence/odds ratio and  
25  
26 95% CI for each outcome variable of interest. To account for potential sources of  
27  
28 heterogeneity, we will use random effects models in all analyses. Both a narrative  
29  
30 and pooled prevalence will be reported. A forest plot will be used to provide a visual  
31  
32 summary of the point estimate and 95% confidence interval for each study and the  
33  
34 overall pooled effect. Visual inspection of funnel plots with trim and fill as well as  
35  
36 Egger's test of asymmetry, will be used to identify sources of bias. Individual study  
37  
38 influence will be evaluated via leave-one-out jackknife sensitivity analysis, whereby  
39  
40 the overall pooled effect is calculated while omitting each study in turn. Analyses will  
41  
42 be conducted using the package metafor<sup>29</sup> in the R Statistical Computing  
43  
44 Environment<sup>30</sup> by the team statistician (RS). We will assess confidence in estimates  
45  
46 by evaluating sources of bias in the main patient outcomes. We will follow the  
47  
48 Grading of Recommendations Assessment, Development, and Evaluation  
49  
50 (GRADE) guidelines<sup>31</sup>.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Review status

A preliminary search was performed in PubMed in February 2021 (see Supplementary file 1). The review is set to start in March 2021.

## Potential amendments

To avoid reporting bias of the review, we do not intend to modify the protocol. However, if necessary, any changes to the timeframe or process of the review will be reported through updates in the online registered PROSPERO protocol.

## Patient and public involvement

No patients or members of the public are involved in this study.

## Ethics and dissemination

Our institutional ethics board policies exempts ethical approval for systematic reviews. The review results will be published in a peer-reviewed journal and disseminated through posters and presentations at scientific conferences.

**Authors' contributions:** The protocol draft was prepared by LÖ, TA & SS. The search will be performed by LÖ and the title and abstract screening will be conducted by TA & HA. The full-text screening will be completed by TCM & IG. Data



1  
2  
3 extraction will be completed by TA and overseen by the team statistician (RS). SS &  
4  
5 JB conceptualized the research questions and the study design.  
6  
7  
8  
9  
10  
11  
12  
13  
14

## 15 **Funding**

16  
17  
18 This research received no specific grant from any funding agency in public,  
19 commercial or not-for-profit sectors. The publication cost for the protocol paper was  
20 covered by the National Medical Library at the United Arab Emirates University.  
21  
22  
23  
24  
25

26 **Competing interest:** None declared.  
27  
28  
29

30 **Word Count:** 3105  
31  
32  
33  
34  
35  
36  
37

## 38 **References**

- 
- 39  
40  
41  
42  
43 1. Towfighi A, Ovbiagele B, El Husseini N, et al. Poststroke Depression: A Scientific  
44 Statement for Healthcare Professionals From the American Heart  
45 Association/American Stroke Association. *Stroke* 2017;48(2):e30-e43. doi:  
46 10.1161/STR.000000000000113  
47  
48  
49  
50  
51  
52 2. Robinson RG, Price TR. Post-stroke depressive disorders: a follow-up study of 103  
53 patients. *Stroke* 1982;13(5):635-41.  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 3. Ayerbe L, Ayis S, Wolfe CD, et al. Natural history, predictors and outcomes of  
4 depression after stroke: systematic review and meta-analysis. *Br J Psychiatry*  
5  
6 2013;202(1):14-21. doi: 10.1192/bjp.bp.111.107664  
7  
8
- 9  
10 4. Hadidi N, Treat-Jacobson DJ, Lindquist R. Poststroke depression and functional  
11 outcome: a critical review of literature. *Heart & lung* 2009;38(2):151-62.  
12  
13
- 14 5. Chemerinski E, Robinson RG, Kosier JT. Improved recovery in activities of daily  
15 living associated with remission of poststroke depression. *Stroke*  
16  
17 2001;32(1):113-17.  
18  
19
- 20 6. Singh RDS, Pandhi A, Alexandrov AV. Post Stroke Depression. *Cerebrovascular*  
21  
22 *Diseases: IntechOpen* 2019.  
23  
24
- 25 7. Carod-Artal FJ, Egido JA. Quality of life after stroke: the importance of a good  
26 recovery. *Cerebrovasc Dis* 2009;27 Suppl 1:204-14. doi: 10.1159/000200461  
27  
28
- 29 8. Carod-Artal J, Egido JA, Gonzalez JL, et al. Quality of life among stroke survivors  
30 evaluated 1 year after stroke: experience of a stroke unit. *Stroke*  
31  
32 2000;31(12):2995-3000. doi: 10.1161/01.str.31.12.2995  
33  
34
- 35 9. Eriksson M, Glader EL, Norrving B, et al. Poststroke suicide attempts and completed  
36 suicides: a socioeconomic and nationwide perspective. *Neurology*  
37  
38 2015;84(17):1732-8. doi: 10.1212/WNL.0000000000001514  
39  
40
- 41 10. Bartoli F, Pompili M, Lillia N, et al. Rates and correlates of suicidal ideation among  
42 stroke survivors: a meta-analysis. *J Neurol Neurosurg Psychiatry*  
43  
44 2017;88(6):498-504. doi: 10.1136/jnnp-2017-315660  
45  
46
- 47 11. Fuller-Thomson E, Tulipano MJ, Song M. The association between depression,  
48 suicidal ideation, and stroke in a population-based sample. *Int J Stroke*  
49  
50 2012;7(3):188-94. doi: 10.1111/j.1747-4949.2011.00702.x  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 12. Santos CO, Caeiro L, Ferro JM, et al. A study of suicidal thoughts in acute stroke  
4 patients. *J Stroke Cerebrovasc Dis* 2012;21(8):749-54. doi:  
5 10.1016/j.jstrokecerebrovasdis.2011.04.001  
6  
7  
8  
9  
10 13. Kutlubaev MA, Hackett ML. Part II: predictors of depression after stroke and impact  
11 of depression on stroke outcome: an updated systematic review of  
12 observational studies. *Int J Stroke* 2014;9(8):1026-36. doi: 10.1111/ijvs.12356  
13  
14  
15  
16  
17 14. Paolucci S, Iosa M, Coiro P, et al. Post-stroke Depression Increases Disability  
18 More Than 15% in Ischemic Stroke Survivors: A Case-Control Study. *Front*  
19 *Neurol* 2019;10:926. doi: 10.3389/fneur.2019.00926  
20  
21  
22  
23  
24 15. van de Weg FB, Kuik DJ, Lankhorst GJ. Post-stroke depression and functional  
25 outcome: a cohort study investigating the influence of depression on functional  
26 recovery from stroke. *Clin Rehabil* 1999;13(3):268-72. doi:  
27 10.1191/026921599672495022  
28  
29  
30  
31  
32  
33 16. Subramanian SK, Chilingaryan G, Sveistrup H, et al. Depressive symptoms  
34 influence use of feedback for motor learning and recovery in chronic stroke.  
35 *Restor Neurol Neurosci* 2015;33(5):727-40. doi: 10.3233/RNN-150508  
36  
37  
38  
39  
40 17. Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain  
41 hemorrhage: a meta-analysis. *Neurology* 2012;79(18):1862-5. doi:  
42 10.1212/WNL.0b013e318271f848  
43  
44  
45  
46  
47 18. Schmid AA, Kroenke K, Hendrie HC, et al. Poststroke depression and treatment  
48 effects on functional outcomes. *Neurology* 2011;76(11):1000-5. doi:  
49 10.1212/WNL.0b013e318210435e  
50  
51  
52  
53  
54 19. Herrmann N, Seitz D, Fischer H, et al. Detection and treatment of post stroke  
55 depression: results from the registry of the Canadian stroke network. *Int J*  
56 *Geriatr Psychiatry* 2011;26(11):1195-200. doi: 10.1002/gps.2663  
57  
58  
59  
60

- 1  
2  
3 20. Ayerbe L, Ayis S, Crichton S, et al. The natural history of depression up to 15 years  
4 after stroke: the South London Stroke Register. *Stroke* 2013;44(4):1105-10.  
5  
6 doi: 10.1161/STROKEAHA.111.679340  
7  
8
- 9  
10 21. Dowrick C, Buchan I. Twelve month outcome of depression in general practice:  
11 does detection or disclosure make a difference? *BMJ* 1995;311(7015):1274-6.  
12  
13 doi: 10.1136/bmj.311.7015.1274  
14  
15
- 16  
17 22. Williams JW, Jr., Mulrow CD, Kroenke K, et al. Case-finding for depression in  
18 primary care: a randomized trial. *Am J Med* 1999;106(1):36-43. doi:  
19  
20 10.1016/s0002-9343(98)00371-4  
21  
22
- 23  
24 23. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with  
25 depression and chronic illnesses. *N Engl J Med* 2010;363(27):2611-20. doi:  
26  
27 10.1056/NEJMoa1003955  
28  
29
- 30  
31 24. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic  
32 review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*  
33  
34 2015;4:1. doi: 10.1186/2046-4053-4-1  
35  
36
- 37  
38 25. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic  
39 reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*  
40  
41 2009;62(10):1006-12. doi: 10.1016/j.jclinepi.2009.06.005  
42  
43
- 44  
45 26. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic  
46 Reviews of Interventions. 2nd ed. Chichester (UK): John Wiley & Sons 2019.  
47  
48
- 49  
50 27. Covidence systematic review software [program]. Melbourne, Australia: Veritas  
51 Health Innovation, 2021.  
52  
53
- 54  
55 28. Report CP. Cabells Predatory Report Beaumont, Texas, USA, 2021.  
56  
57
- 58  
59 29. Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package. *Journal*  
60  
of *Statistical Software* 2010;36(1):1-48. doi: 10.18637/jss.v036.i03

1  
2  
3 30. R: A language and environment for statistical computing. R Foundation for  
4  
5 Statistical Computing [program]. Vienna, Austria.  
6  
7

8  
9 31. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, et al.  
10  
11 GRADE guidelines: 4. Rating the quality of evidence—study limitations  
12  
13 (risk of bias). *J Clin Epidemiol* 2011;64(4):407-15.  
14  
15  
16  
17  
18

---

19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## Supplementary materials file 1: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist

**Title:** Early screening for post-stroke depression, and the effect on functional outcomes, quality of life and mortality: a protocol for a systematic review and meta-analysis

**Authors:** Dr. Sudhakar Selvaraj, Dr. Teresa Arora, Ms. Tahani Casameni Montiel, Dr. Ian Grey, Ms. Hind Alfraih, Dr. Rob Suchting, Sean Savitz, Dr. Jennifer Beauchamp and Ms. Linda Östlundh

Section and topic	Item No	Checklist item	Reported on page
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	<b>1</b>
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	<b>4 and 8</b> (Submitted to PROSPERO on 2021-02-08, ID no. 235993)
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	<b>1</b>
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<b>13-14</b>
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	<b>14</b>
Sponsor	5b	Provide name for the review funder and/or sponsor	N/A
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
<b>INTRODUCTION</b>			

Rationale	6	Describe the rationale for the review in the context of what is already known	<b>5-7</b>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<b>5-7</b>
<b>METHODS</b>			
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	<b>8-9</b>
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	<b>9-10</b>
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<b>10 and supplementary materials file 2</b>
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<b>10</b>
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)	<b>10-11</b>
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	<b>11</b>
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	<b>11</b>
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<b>11</b>
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	<b>11-12</b>
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<b>12</b>
	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 $\tau$ )	<b>12</b>

	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	12

**\* 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.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

12



## Supplementary materials file 2: preliminary search strategy

**Source:** PubMed

**Search date:** 2021-02-08

**Search specifications:** All search terms are searched in the search fields “title”, “abstract” and in MeSH (when available). A filter for English language is applied.

**Result:** 1,311

### Preliminary search strategy:

```
((("Stroke"[Mesh] OR Stroke*[Title/Abstract] OR "Cerebrovascular Accident*" [Title/Abstract] OR CVA[Title/Abstract] OR CVAs[Title/Abstract] OR "Cerebrovascular Apoplexy"[Title/Abstract] OR "Brain Vascular Accident*" [Title/Abstract]) AND (depression*[Title/Abstract] OR depressed[Title/Abstract] OR depressive[Title/Abstract] OR "Depression"[Mesh] OR "post-traumatic stress disorder"[Title/Abstract] OR "PSD"[Title/Abstract] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "Depressive Disorder"[Mesh:NoExp] OR "Depressive Disorder, Major"[Mesh])) AND ("Mass Screening"[Mesh:NoExp] OR screen*[Title/Abstract] OR diagnos*[Title/Abstract] OR "Diagnosis"[Mesh:NoExp] OR "hospital anxiety and depression scale"[Title/Abstract] OR "HADS-D"[Title/Abstract] OR "geriatric depression scale"[Title/Abstract] OR "GDS"[Title/Abstract] OR "Patient Health Questionnaire"[Title/Abstract] OR "PHQ-9"[Title/Abstract] OR "Patient Health Questionnaire"[Mesh] OR "Beck depression inventory"[Title/Abstract] OR "stroke aphasia depression questionnaire"[Title/Abstract] OR "Aphasia depression rating scale"[Title/Abstract] OR "International Classification of Diseases"[Mesh] OR "ICD-10"[Title/Abstract] OR "International Classification of Diseases"[Title/Abstract] OR "ICD-9"[Title/Abstract])) AND (prospective[Title/Abstract] OR "follow-up"[Title/Abstract] OR followup[Title/Abstract] OR longitudinal[Title/Abstract] OR "long-term"[Title/Abstract] OR cohort[Title/Abstract] OR "Cohort Studies"[Mesh:NoExp] OR "Follow-Up Studies"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Prospective Studies"[Mesh]))
```

# BMJ Open

## Early screening for post-stroke depression, and the effect on functional outcomes, quality of life and mortality: a protocol for a systematic review and meta-analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-050451.R1
Article Type:	Protocol
Date Submitted by the Author:	14-Jun-2021
Complete List of Authors:	<p>Selvaraj, Sudhakar; University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences          Arora, Teresa; Zayed University, College of Natural &amp; Health Sciences          Montiel, Tahani; University of Texas Health Science Center at Houston, Cizik School of Nursing          Grey, Ian; Lebanese American University, Psychology          Alfraih, Hind; Zayed University, College of Natural &amp; Health Sciences          Fadipe , Melissa; The University of Texas Health Science Center at Houston Cizik School of Nursing          Suchting, Robert; University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences          Savitz, Sean; University of Texas Health Science Center at Houston, Institute for Stroke and Cerebrovascular Disease          Sanner Beauchamp, Jennifer; University of Texas Health Science Center at Houston,          Östlundh, Linda; United Arab Emirates University College of Medicine and Health Sciences, National Medical Library</p>
<b>Primary Subject Heading</b>:	Mental health
Secondary Subject Heading:	Diagnostics, Cardiovascular medicine
Keywords:	PSYCHIATRY, Depression & mood disorders < PSYCHIATRY, STROKE MEDICINE

SCHOLARONE™  
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

**Title:** Early screening for post-stroke depression, and the effect on functional outcomes, quality of life and mortality: a protocol for a systematic review and meta-analysis

## Authors

Dr. Sudhakar Selvaraj<sup>1\*</sup> (ORCID: 0000-0002-9494-172X); Dr. Teresa Arora<sup>2\*</sup> (ORCID: 0000-0001-8360-7358); Ms. Tahani Casameni Montiel<sup>3</sup> (ORCID: 0000-0001-9626-0365); Dr. Ian Grey<sup>4</sup> (ORCID: 0000-0001-9773-2539); Ms. Hind Alfraih<sup>2</sup> (ORCID: 0000-0002-5526-1393); Ms. Melissa Fadipe<sup>3</sup> (ORCID: 0000-0001-9927-4797); Dr. Robert Suchting<sup>1</sup> (ORCID: 0000-0002-2822-3754); Dr. Sean Savitz<sup>5,6</sup>; Dr. Jennifer Beauchamp<sup>3,5</sup>; Ms. Linda Östlundh<sup>7</sup> (ORCID: 0000-0001-5091-604X).

## Author affiliations

<sup>1</sup>Louis. A. Faillace, MD, Department of Psychiatry and Behavioral Sciences, The University of Texas Health Science Center at Houston, 1941 East Rd, Houston, TX 77054; <sup>2</sup>Zayed University, College of Natural and Health Sciences, Abu Dhabi, United Arab Emirates; <sup>3</sup>The University of Texas Health Science Center at Houston, Cizik School of Nursing; <sup>4</sup>Department of Cognitive Sciences, United Arab Emirates University, Al Ain, Abu Dhabi, United Arab Emirates; <sup>5</sup>Institute for Stroke and Cerebrovascular Disease, University of Texas Health Science Center at Houston, Houston, TX, US; <sup>6</sup>Department of Neurology, McGovern Medical School at the University of Texas Health Science Center at Houston, Houston, TX, US; <sup>7</sup>The National Medical Library, United Arab Emirates University, College of Medicine and Health Sciences, Al Ain, Abu Dhabi, United Arab Emirates.

\*Joint first authors with equal contribution.

1  
2  
3  
4  
5 **Corresponding author:**  
6  
7  
8  
9

10 Linda Östlundh

11  
12 The National Medical Library,

13  
14 United Arab Emirates University,

15  
16 College of Medicine and Health Sciences,

17  
18 Al Ain,

19  
20 Abu Dhabi,

21  
22 United Arab Emirates  
23  
24  
25  
26  
27

28 Tel: 00971 501126930  
29  
30  
31  
32

33 Email: lostlundh@uaeu.ac.ae  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Abstract

**Introduction:** Post-Stroke depression (PSD) is a severe complication of cerebrovascular Stroke affecting about one-third of Stroke survivors. Moreover, PSD is associated with functional recovery and Quality of Life (QOL) in Stroke survivors. Screening for PSD is recommended. There are, however, differences in the literature on the impact of early screening on functional outcomes. In this systematic review, we synthesize the currently available literature regarding the associations between timing and setting of PSD screening and mortality, QOL, and functional outcomes in Stroke survivors.

**Methods and analysis:** We will systematically search electronic databases including PubMed, Embase, APA PsycInfo, Web of Science, Scopus and CINAHL from inception to May 2021. Four reviewers will screen the title and abstract and full-text level records identified in the search in a blinded fashion to determine the study eligibility. Any selection disagreements between the reviewers will be resolved by the study investigator. Data extraction of eligible studies will be conducted by two reviewers using a pre-defined template. We will complete the quality assessment of included articles independently by two reviewers using the Newcastle Ottawa Scale. Eventual discrepancies will be resolved by the principal investigator.

**Ethics and dissemination:** Due to the nature of the study design, ethical approval is not required. The systematic review and meta-analysis findings will be published and disseminated in a peer-reviewed journal. Our results will also be disseminated through posters and presentations at appropriate scientific conferences.

**Registration:** This protocol is reported as per the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) guidelines. The protocol

1  
2  
3 is published online in the International Prospective Register of Systematic Reviews,  
4  
5 PROSPERO (CRD42021235993).  
6  
7  
8  
9

### 10 **Strengths and limitations of this study**

- 13 • Comprehensive systematic review of the associations between Post-Stroke  
14 Depression (PSD) and Stroke outcomes.  
15
- 16 • Rigorous methods, following the PRISMA guidelines, will be conducted to  
17 minimise the risk of bias.  
18
- 19 • Limitations of this review include the exclusion of papers in languages other  
20 than English and unpublished, grey materials.  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Introduction

Post-Stroke Depression (PSD) is characterized by depressed or dysphoric mood, reduced motivation, energy and libido, as well as sleep disorders. It is a severe complication of cerebrovascular Stroke<sup>1</sup> affecting about one-third of Stroke survivors<sup>2</sup>. PSD appears to be the most common psychiatric sequelae of Stroke, and is independently associated with increased morbidity, mortality and disability<sup>4-6</sup>. PSD is also considered one of the most significant predictors for functional recovery and Quality of Life (QOL) in Stroke survivors<sup>7 8</sup>. Stroke survivors with PSD are more likely to commit suicide than patients without PSD<sup>9 10</sup>. Suicide rates are more than double in Stroke survivors compared to the general population<sup>11</sup>. Some Stroke survivors who subsequently developed Depression, and had a previous history of Depression, reported suicidal thoughts as early as four days after the onset of Stroke<sup>12</sup>. Disability or dependence in activities of daily living (ADLs) of patients who have suffered a Stroke may also increase the risk of PSD<sup>13</sup> and suicidal ideation. This highlights an important, yet vicious cycle between PSD and functional disabilities. Therefore, Stroke survivors with functional disabilities should be considered at-risk for PSD and suicidal ideation. Thus, targeted screening for PSD and suicidal ideation is warranted.

PSD has been consistently associated with poorer functional outcomes<sup>1 13</sup> (e.g. inability to perform ADLs independently) and rehabilitation outcomes (e.g. extended duration of inpatient rehabilitation)<sup>13-15</sup>. It has been hypothesized that poorer functional outcomes (mortality, limitation of daily activities, Stroke recurrences, cognitive impairment) associated with PSD may be due to limited rehabilitation participation<sup>13 16</sup>. For example, in a retrospective, case-control study of 560 ischemic



1  
2  
3 Stroke survivors, those with PSD had worse mobility, longer rehabilitation length of  
4 stay, and greater insufficient response to rehabilitation efforts (as measured by lower  
5 Barthel Index (BI) and Rivermead Mobility Index (RMI)) than Stroke survivors without  
6 PSD<sup>14</sup>. Furthermore, Stroke survivors adequately treated for PSD with anti-  
7 depressants showed improved functional outcomes compared to anti-depressant  
8 therapy non-responders<sup>14</sup>. However, uncertainty regarding optimal strategies for  
9 treating PSD remains (e.g., timing, dosing, duration, and pharmaceuticals)<sup>1 17</sup>.  
10 Notably, while an independent association exists between PSD and poor functional  
11 recovery<sup>18</sup>, severe functional disabilities after stroke are also related to PSD<sup>19</sup>.  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

26 The period of time immediately after a Stroke event is critical. For example, studies  
27 have shown that a substantial functional recovery occurs within three months after  
28 the first onset of Stroke<sup>20</sup>, compared to the later chronic phase<sup>21</sup>. Rehabilitation and  
29 training can improve recovery during the period immediately after focal brain damage.  
30 Moreover, these rehabilitation interventions are critical for the functional restoration  
31 of Stroke patients<sup>20 22</sup>. PSD is a key factor that can influence Stroke recovery. Despite  
32 the high prevalence of PSD, and its associated risks, only a minority of Stroke  
33 survivors are adequately screened for PSD. Despite this, optimal strategies (timing,  
34 setting, and methods) for PSD screening are currently unclear<sup>1 23</sup>. The risk of  
35 depression in Stroke survivors is high immediately after the acute Stroke, especially  
36 within the three months after a Stroke<sup>24</sup>, during which the prevalence is estimated to  
37 be 33%. Interestingly, nearly half of those who had Depression in the first three  
38 months of acute Stroke recovered at one-year<sup>24</sup>. Routine screening for PSD in at-risk  
39 patients (e.g. those with severe functional disabilities and a history of Depression) in  
40 the early Stroke recovery period has been shown to reduce the risk of PSD<sup>13</sup>.  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 However, other studies did not find supportive evidence for PSD screening and Stroke  
4 outcomes<sup>25 26</sup>. Nevertheless, randomised controlled clinical trials show that screening  
5 and collaborative care for depression treatment, can improve functional outcomes in  
6 chronic medical conditions, including Stroke<sup>27</sup>. The American Heart  
7 Association/American Stroke Association (AHA/ASA) recommends screening for  
8 PSD in patients after acute Stroke, as well as further research into the effect of PSD  
9 on all outcomes, including QOL<sup>1</sup>. To optimize the care for Stroke patients, appropriate  
10 processes should be established before screening occurs to assure correct PSD  
11 diagnosis, adequate treatment, and routine follow-up<sup>1</sup>.  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

26 A meta-analysis revealed an increased risk of mortality in those with PSD<sup>28</sup>, where  
27 the estimated hazard ratio was 1.59. However, there are differences in published  
28 studies on the relationship between PSD and Stroke recurrences. Sibolt et al. (2013)<sup>29</sup>  
29 found that PSD was associated with increased ischemic Stroke recurrence.  
30 Conversely, Ayerbe et al. (2014)<sup>30</sup> reported that PSD at three months was not  
31 associated with higher risk of total Stroke recurrence over a five-year follow up period.  
32 Another systematic review and meta-analysis found a significant relationship between  
33 PSD and poor functional outcomes<sup>13</sup>. None of the available systematic reviews have  
34 specifically investigated symptoms of Depression at the acute Stroke period on all  
35 Stroke-related outcomes. Collectively, it is not clear whether early Depression  
36 screening at acute stages of Stroke can impact Stroke recurrences, QOL, and/or  
37 mortality.  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55

56 The purpose of our review protocol is to update and synthesize the currently available  
57 literature in order to quantify the degree to which early onset PSD symptoms are  
58  
59  
60

1  
2  
3 associated with mortality, QOL, and functional outcomes in Stroke survivors. The  
4  
5 primary research aims of this systematic review and meta-analysis are as follows:  
6  
7  
8  
9

- 10 1. To investigate if early PSD symptoms in hospitalized patients immediately after  
11 a Stroke is associated with worse Stroke-related disability within three months  
12 after an acute Stroke event.  
13  
14
- 15 2. To investigate if early PSD (at acute hospital admission or within three months)  
16 is associated with long-term (>one-year) Stroke-related health outcomes  
17 (Stroke-related disability, Stroke recurrence, mortality, QOL).  
18  
19  
20  
21  
22  
23  
24  
25

26 We hypothesize that patients with early post-stroke depression at hospital or within 3  
27 months, will have a substantial disability, poorer quality of life and increased mortality.  
28  
29  
30  
31

### 32 **Methods and analysis**

33  
34 This protocol follows the Preferred Reporting Items for Systematic Reviews and Meta-  
35 Analyses Protocol (PRISMA-P) guidelines<sup>31</sup>. The PRISMA-P checklist can be found in  
36 the online Supplementary Material file 1. The final review will be developed in  
37 accordance with the 2020 Preferred Reporting Items for Systematic Reviews and  
38 Meta-Analyses (PRISMA) statement<sup>32</sup> and will be informed by the Cochrane Handbook  
39 for Systematic Reviews of Interventions<sup>33</sup>.  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

50 The protocol is registered on the International Prospective Register of Systematic  
51 Reviews, PROSPERO (CRD42021235993).  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Eligibility criteria

### *Inclusion criteria*

Our pre-defined inclusion criteria, throughout the screening process, are as follows:

1) Uses a validated Depression scale for screening after a Stroke diagnosis; 2) human subjects; 3) longitudinal/prospective studies only; 4) English language only; 5) peer-reviewed, published articles only; 6) reports on a short and/or long-term outcome (quality of life, functional recovery [motor/disability index], mortality, aphasia, recurrent Stroke/morbidity); 7) Stroke diagnosis; 8) reports on the relationship between PSD and at least one outcome measure (see point 6); and 9) the Depression measurement should be obtained at the time of Stroke diagnosis or within three months of the diagnosis. We will check if the clinical diagnosis of stroke was made as per the World Health Organization (WHO) definition of stroke: “*rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin*”. Therefore we will exclude transient ischemic attack (TIA) and stroke symptoms caused by subdural hemorrhage, tumors, poisoning, or trauma<sup>34</sup>. We will include validated depression instruments<sup>35</sup> including Diagnostic and Statistical Manual of Mental Disorders (DSM), International classification of diseases (ICD), and specific scales such as Center for Epidemiologic Studies Depression Scale (CES-D), Patient Health Questionnaire (PHQ-9), Hospital Anxiety and Depression Scale (HADS), and Hamilton Depression Rating Scale (HDRS), Beck depression inventory

1  
2  
3 (BDI), stroke aphasia depression questionnaire, Aphasia depression rating scale,  
4  
5 geriatric depression scale (GDS).  
6  
7  
8  
9

### 10 ***Exclusion criteria***

11  
12  
13

14 Our pre-defined exclusion criteria, throughout the screening process, are as follows:  
15  
16  
17

18  
19 1) Studies involving animals; 2) conference abstracts, posters or papers; 3)  
20 editorials/letter to the editor, unless it reports original research data that meets our  
21 pre-defined inclusion criteria; 4) patients with any primary psychiatric illness, except  
22 for Anxiety/Depression; 5) patients with Dementia, Epilepsy, Cancer, or Multiple  
23 Sclerosis; 6) patients with neurological or neurodegenerative conditions, except for  
24 Stroke/Neurovascular; 7) reviews of any kind; 8) questionnaire validation studies; 9)  
25 case studies; 10) randomised controlled trials (RCTs); 11) paediatric studies (samples  
26 that include patients under the age of 18 years); 12) studies assessing the  
27 effectiveness of medication; 13) protocol papers; 14) studies with retrospective  
28 design; 15) studies that have less than one-year follow-up period; and 16) theses and  
29 dissertations.  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

### 47 **Information sources and search strategy**

48  
49  
50

51 A comprehensive search of peer-reviewed literature from six electronic databases will  
52 be conducted from their inception through to May 2021. The following medical and  
53 health sciences databases will be included: PubMed (NLM), Embase (Elsevier), APA  
54 PsycInfo (EBSCOhost), Scopus(Elsevier), Web of Science (Clarivate) and  
55  
56  
57  
58  
59  
60

1  
2  
3 CINAHL(EBSCOhost). A preliminary search string to support the development of the  
4  
5 research question and pre-set inclusion and exclusion criteria, was conducted in  
6  
7 February- March 2021. The search strategy was developed by a medical librarian who  
8  
9 is specialized in the conduct of systematic reviews (LÖ). PubMed and PubMed's  
10  
11 MeSH was used to systematically identify relevant search terms and synonyms for  
12  
13 review and further suggestions by a subject specialist (SS). The pre-search in PubMed  
14  
15 will later be adapted to, and performed in, all six selected databases. All keywords will  
16  
17 be searched in a combination of the fields: "title", "abstract," and in  
18  
19 "MeSH"/"thesaurus". We will limit the search to English papers only. No additional  
20  
21 filters or geographical limitations will be used to ensure the best possible literature  
22  
23 inclusion. Systematic hand screening of the reference lists of the included papers  
24  
25 identified by the search will be conducted independently by two reviewers. A search  
26  
27 log, with search technical specifications, as well as results and notes for all databases  
28  
29 included in the search, will be appended to the review to support the appraisal and  
30  
31 reproduction of the search. The literature search will be repeated before completing  
32  
33 the data extraction, and potential new studies published during the work process will  
34  
35 be added to the result. The details of the preliminary search performed in PubMed is  
36  
37 available in the online Supplementary Material file 2.  
38  
39  
40  
41  
42  
43  
44  
45  
46

## 47 **Data management**

48  
49  
50  
51 The result from the database search will be uploaded to the systematic review  
52  
53 software, Covidence<sup>36</sup>. Automatic de-duplication and screening will be conducted in  
54  
55 the software. The finally selected references will be exported to a reference  
56  
57 management software to enable manuscript preparation. Covidence will also support  
58  
59  
60

1  
2  
3 the update of the search before publishing by a re-upload and de-duplication of the  
4 complete result from all databases. This will ensure blinded screening of all additional  
5 back-file and new records added since the initial search in May 2021.  
6  
7  
8  
9  
10

### 11 12 13 **Selection of studies** 14

15  
16  
17 All unique records identified in the database search will be screened for eligibility  
18 against the pre-defined inclusion and exclusion criteria by four independent reviewers,  
19 as follows: TA and HA will conduct the initial title and abstract screening. TCM and IG  
20 will screen the papers selected for full-text review. After each screening module,  
21 eventual conflicts identified by the software will be resolved by a fifth reviewer (SS).  
22 All stages of the screening and selection processes in Covidence follow the PRISMA  
23 workflow<sup>32</sup>. The screening processes and blinding will be pre-defined in the software  
24 settings based on the authors' responsibilities.  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38

39 The search result, de-duplication, screening and selection process, including reasons  
40 for study exclusion, will be documented in a PRISMA (2020) flow diagram. Cabells  
41 Predatory Reports<sup>37</sup> will be consulted to verify that eventual Open Access papers  
42 selected are not published in possible predatory journals.  
43  
44  
45  
46  
47  
48  
49  
50

### 51 **Data extraction** 52

53  
54  
55 An extraction template will be used to extract relevant data from each of the included  
56 studies. The template will be developed by the team statistician (RS) and the principal  
57  
58  
59  
60

1  
2  
3 investigator (SS). The data extraction template will be piloted on five articles initially  
4 and adjusted, if necessary. Information about population characteristics, length of  
5  
6 follow-up, depression scale used, time of screening for depression, Stroke disability  
7  
8 ratings, rehabilitation length of stay, mobility status as well as QOL scales and scores  
9  
10 will be documented. The effect size/measure of association between PSD screening  
11  
12 and the outcome variables of interest, along with 95% confidence intervals (95% CIs)  
13  
14 will also be extracted. Two reviewers will extract the information independently and  
15  
16 any discrepancies will be resolved by the primary study investigator (SS).  
17  
18  
19  
20  
21  
22  
23

### 24 **Quality assessment of individual studies**

25  
26  
27  
28  
29 Two reviewers will independently assess the quality of evidence and the risk of bias  
30  
31 of all eligible studies using the Newcastle Ottawa Scale. Eventual disagreements  
32  
33 between the reviewers will be discussed with the principal investigator (SS) until a  
34  
35 consensus is reached.  
36  
37  
38  
39  
40

### 41 **Data analysis and synthesis**

42  
43  
44  
45  
46 The systematic review will identify and report the number of qualifying articles and  
47  
48 provide an overall summary. Information surrounding the sample size, population,  
49  
50 and outcomes of interest will be compared across the studies. Articles that contain  
51  
52 appropriate statistical information for meta-analysis will be assessed by the team  
53  
54 statistician (RS). The meta-analysis will calculate a pooled prevalence/odds/hazard  
55  
56 ratio and 95% CI for each outcome variable of interest. Specific outcomes that will be  
57  
58  
59  
60



1  
2  
3 evaluated in the present study will include Stroke disability scales (Barthel index [BI],  
4 Modified Rankin Scale [MRS], Rivermead Mobility Index [RMI]), Quality of Life (Short  
5 Form 36 [SF-36]; Stroke-Specific Quality of Life [SS-QOL], Euro-Quality of Life  
6 [Euro-QOL]), and Mortality (dichotomous). The lower bound of studies to be included  
7 in any given meta-analysis is two<sup>38</sup>. Analyses will, however, include as many studies  
8 that meet our pre-defined inclusion/exclusion criteria. Finally, we will perform meta-  
9 regression to account for the influence of Stroke severity (NIH Stroke Severity  
10 [NIHSS], Glasgow Coma Scale [GCS]), type of Stroke (ischemic vs. hemorrhagic),  
11 and length of follow-up (months).  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

26 To account for potential sources of heterogeneity, we will use random effects models  
27 in all analyses. Both a narrative and pooled prevalence will be reported. A forest plot  
28 will be used to provide a visual summary of the point estimate and 95% confidence  
29 interval for each study and the overall pooled effect. Visual inspection of funnel plots,  
30 with trim and fill as well as Egger's test of asymmetry, will be used to identify sources  
31 of bias. Individual study influence will be evaluated via leave-one-out jackknife  
32 sensitivity analysis, whereby the overall pooled effect is calculated while omitting  
33 each study in turn.  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

47 Analyses will be conducted using the package metafor<sup>39</sup> in the R Statistical  
48 Computing Environment<sup>40</sup> by the team statistician (RS). We will assess confidence in  
49 estimates by evaluating sources of bias in the main patient outcomes. We will follow  
50 the Grading of Recommendations Assessment, Development, and Evaluation  
51 (GRADE) guidelines<sup>40</sup>.  
52  
53  
54  
55  
56  
57  
58  
59  
60

### **Strengths and limitations:**

The strength of the protocol is the study design including the longitudinal cohort design to focus on early post-Stroke period. Our review will also employ comprehensive search strategies, compliance to PRISMA guidelines for systematic reviews and our protocol is also registered with the international database, PROSPERO. We also acknowledge the following limitations. First, we will not include grey literature sources. However, our comprehensive search strategy covers six major databases that will provide relevant, published, high-quality papers. Although RCTs and retrospective studies can provide additional insight, we decided not to include these in our review for the following reasons. First, when we evaluated our pilot searches, we found that the range of interventions studied in RCTs was extremely variable. Moreover, controlling for outcomes are difficult. Furthermore, RCTs are typically shorter time-framed which is not aligned with our aim of investigating the early depression symptoms and its impact on long-term Stroke outcome(s). We excluded retrospective studies, due to bias associated with these types of studies including selection and recall bias. Furthermore, it is difficult to ascertain temporal relationships between Depression and Stroke outcomes with retrospective studies.

### **Review status**

A preliminary search was performed in PubMed in February 2021 and the result was updated in May 2021 (see Supplementary Material file 2). The review is set to start in May 2021.

## Potential amendments

To avoid reporting bias of the review, we do not intend to modify the protocol. However, if necessary, any changes to the timeframe or process of the review will be reported through updates in the online registered PROSPERO protocol (CRD42021235993).

## Patient and public involvement

No patients or members of the public are involved in this study.

## Ethics and dissemination

Our institutional ethics board policies exempts ethical approval for systematic reviews. The review results will be published in a peer-reviewed journal and disseminated through abstracts, posters and oral presentations at relevant scientific conferences.

**Authors' contributions:** The protocol draft was prepared by LÖ, TA & SS. The search will be performed by LÖ and the title and abstract screening will be conducted by TA & HA. The full-text screening will be completed by TCM & IG. Data extraction will be completed by TA & MF and overseen by the team statistician, RS. The data analytic strategy was designed by TA, RS & SS. SeSa, SS & JB conceptualized the research questions and the study design.

## Funding

This research received no specific grant from any funding agency in public, commercial or not-for-profit sectors. The publication cost for the protocol paper was covered by the National Medical Library at the United Arab Emirates University.

**Competing interest:** None declared.

**Word Count:** 3106

## References

1. Towfighi A, Ovbiagele B, El Hussein N, et al. Poststroke Depression: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 2017;48(2):e30-e43. doi: 10.1161/STR.000000000000113
2. Robinson RG, Price TR. Post-stroke depressive disorders: a follow-up study of 103 patients. *Stroke* 1982;13(5):635-41.
3. Ayerbe L, Ayis S, Wolfe CD, et al. Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. *Br J Psychiatry* 2013;202(1):14-21. doi: 10.1192/bjp.bp.111.107664
4. Hadidi N, Treat-Jacobson DJ, Lindquist R. Poststroke depression and functional outcome: a critical review of literature. *Heart & Lung* 2009;38(2):151-62.
5. Chemerinski E, Robinson RG, Kosier JT. Improved recovery in activities of daily living associated with remission of poststroke depression. *Stroke* 2001;32(1):113-17.
6. Singh RDS, Pandhi A, Alexandrov AV. Post Stroke Depression. *Cerebrovascular Diseases: IntechOpen* 2019.
7. Carod-Artal FJ, Egido JA. Quality of life after stroke: the importance of a good recovery. *Cerebrovasc Dis* 2009;27 Suppl 1:204-14. doi: 10.1159/000200461
8. Carod-Artal J, Egido JA, Gonzalez JL, et al. Quality of life among stroke survivors evaluated 1 year after stroke: experience of a stroke unit. *Stroke* 2000;31(12):2995-3000. doi: 10.1161/01.str.31.12.2995
9. Eriksson M, Glader EL, Norrving B, et al. Poststroke suicide attempts and completed suicides: a socioeconomic and nationwide perspective. *Neurology* 2015;84(17):1732-8. doi: 10.1212/WNL.0000000000001514
10. Bartoli F, Pompili M, Lillia N, et al. Rates and correlates of suicidal ideation among stroke survivors: a meta-analysis. *J Neurol Neurosurg Psychiatry* 2017;88(6):498-504. doi: 10.1136/jnnp-2017-315660

11. Fuller-Thomson E, Tulipano MJ, Song M. The association between depression, suicidal ideation, and stroke in a population-based sample. *Int J Stroke* 2012;7(3):188-94. doi: 10.1111/j.1747-4949.2011.00702.x
12. Santos CO, Caeiro L, Ferro JM, et al. A study of suicidal thoughts in acute stroke patients. *J Stroke Cerebrovasc Dis* 2012;21(8):749-54. doi: 10.1016/j.jstrokecerebrovasdis.2011.04.001
13. Kutlubaev MA, Hackett ML. Part II: predictors of depression after stroke and impact of depression on stroke outcome: an updated systematic review of observational studies. *Int J Stroke* 2014;9(8):1026-36. doi: 10.1111/ij.12356
14. Paolucci S, Iosa M, Coiro P, et al. Post-stroke Depression Increases Disability More Than 15% in Ischemic Stroke Survivors: A Case-Control Study. *Front Neurol* 2019;10:926. doi: 10.3389/fneur.2019.00926
15. van de Weg FB, Kuik DJ, Lankhorst GJ. Post-stroke depression and functional outcome: a cohort study investigating the influence of depression on functional recovery from stroke. *Clin Rehabil* 1999;13(3):268-72. doi: 10.1191/026921599672495022
16. Subramanian SK, Chilingaryan G, Sveistrup H, et al. Depressive symptoms influence use of feedback for motor learning and recovery in chronic stroke. *Restor Neurol Neurosci* 2015;33(5):727-40. doi: 10.3233/RNN-150508
17. Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. *Neurology* 2012;79(18):1862-5. doi: 10.1212/WNL.0b013e318271f848
18. Schmid AA, Kroenke K, Hendrie HC, et al. Poststroke depression and treatment effects on functional outcomes. *Neurology* 2011;76(11):1000-5. doi: 10.1212/WNL.0b013e318210435e
19. Hackett ML, Kohler S, O'Brien JT, et al. Neuropsychiatric outcomes of stroke. *Lancet Neurol* 2014;13(5):525-34. doi: 10.1016/S1474-4422(14)70016-X
20. Prabhakaran S, Zarah E, Riley C, et al. Inter-individual variability in the capacity for motor recovery after ischemic stroke. *Neurorehabil Neural Repair* 2008;22(1):64-71. doi: 10.1177/1545968307305302
21. Zeiler SR, Krakauer JW. The interaction between training and plasticity in the poststroke brain. *Curr Opin Neurol* 2013;26(6):609-16. doi: 10.1097/WCO.0000000000000025
22. Ward NS. Restoring brain function after stroke - bridging the gap between animals and humans. *Nat Rev Neurol* 2017;13(4):244-55. doi: 10.1038/nrneurol.2017.34
23. Herrmann N, Seitz D, Fischer H, et al. Detection and treatment of post stroke depression: results from the registry of the Canadian stroke network. *Int J Geriatr Psychiatry* 2011;26(11):1195-200. doi: 10.1002/gps.2663
24. Ayerbe L, Ayis S, Crichton S, et al. The natural history of depression up to 15 years after stroke: the South London Stroke Register. *Stroke* 2013;44(4):1105-10. doi: 10.1161/STROKEAHA.111.679340
25. Dowrick C, Buchan I. Twelve month outcome of depression in general practice: does detection or disclosure make a difference? *BMJ* 1995;311(7015):1274-6. doi: 10.1136/bmj.311.7015.1274
26. Williams JW, Jr., Mulrow CD, Kroenke K, et al. Case-finding for depression in primary care: a randomized trial. *Am J Med* 1999;106(1):36-43. doi: 10.1016/s0002-9343(98)00371-4

- 1  
2  
3 27. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with  
4 depression and chronic illnesses. *N Engl J Med* 2010;363(27):2611-20. doi:  
5 10.1056/NEJMoa1003955
- 6  
7 28. Cai W, Mueller C, Li YJ, et al. Post stroke depression and risk of stroke  
8 recurrence and mortality: A systematic review and meta-analysis. *Ageing Res*  
9 *Rev* 2019;50:102-09. doi: 10.1016/j.arr.2019.01.013
- 10  
11 29. Sibolt G, Curtze S, Melkas S, et al. Poststroke dementia is associated with  
12 recurrent ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2013;84(7):722-6.  
13 doi: 10.1136/jnnp-2012-304084
- 14  
15 30. Ayerbe L, Ayis S, Crichton S, et al. The long-term outcomes of depression up to  
16 10 years after stroke; the South London Stroke Register. *J Neurol Neurosurg*  
17 *Psychiatry* 2014;85(5):514-21. doi: 10.1136/jnnp-2013-306448
- 18  
19 31. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic  
20 review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*  
21 2015;4:1. doi: 10.1186/2046-4053-4-1
- 22  
23 32. Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D.,  
24 Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J.,  
25 Grimshaw, J. M., Hróbjartsson A, Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E.,  
26 McDonald, S., ... Moher, D. (2021). The prisma 2020 statement: an updated  
27 guideline for reporting systematic reviews. *BMJ (Clinical Research Ed.)*, 372, 71.  
28 <https://doi.org/10.1136/bmj.n71>
- 29  
30 33. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic  
31 Reviews of Interventions. 2nd ed. Chichester (UK): John Wiley & Sons 2019.
- 32  
33 34. Meader N, Moe-Byrne T, Llewellyn A, et al. Screening for poststroke major  
34 depression: a meta-analysis of diagnostic validity studies. *J Neurol Neurosurg*  
35 *Psychiatry* 2014;85(2):198-206. doi: 10.1136/jnnp-2012-304194
- 36  
37 35. Covidence systematic review software [program]. Melbourne, Australia: Veritas  
38 Health Innovation, 2021.
- 39  
40 36. Report CP. Cabells Predatory Report Beaumont, Texas, USA, 2021.
- 41  
42 37. Valentine JC, Pigott TD, Rothstein HR. How Many Studies Do You Need?: A  
43 Primer on Statistical Power for Meta-Analysis. *Journal of Educational and*  
44 *Behavioral Statistics* 2010;35(2):215-47. doi:  
45 <https://doi.org/10.3102/1076998609346961>
- 46  
47 38. Viechtbauer W. Conducting Meta-Analyses in R with the metafor Package.  
48 *Journal of Statistical Software* 2010;36(1):1-48. doi: 10.18637/jss.v036.i03
- 49  
50 39. R: A language and environment for statistical computing. R Foundation for  
51 Statistical Computing [program]. Vienna, Austria.
- 52  
53 40. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, et al.  
54 GRADE guidelines: 4. Rating the quality of evidence—study limitations  
55 (risk of bias). *J Clin Epidemiol* 2011;64(4):407-15.

## Supplementary Materials file 1: PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist

**Title:** Early screening for post-stroke depression, and the effect on functional outcomes, quality of life and mortality: a protocol for a systematic review and meta-analysis

**Authors:** Dr. Sudhakar Selvaraj; Dr. Teresa Arora; Ms. Tahani Casameni Montiel; Dr. Ian Grey; Ms. Hind Alfraih; Ms. Melissa Fadipe; Dr. Rob Suchting Sean Savitz; Dr. Jennifer Beauchamp and Ms. Linda Östlundh

Section and topic	Item No	Checklist item	Reported on page
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	<b>1</b>
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<b>N/A</b>
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	<b>4 and 8</b> (PROSPERO nr. CRD42021235993)
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	<b>1</b>
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<b>16</b>
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	<b>N/A</b>
Support:			
Sources	5a	Indicate sources of financial or other support for the review	<b>17</b>
Sponsor	5b	Provide name for the review funder and/or sponsor	<b>N/A</b>
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<b>N/A</b>
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	<b>5-7</b>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference	



		to participants, interventions, comparators, and outcomes (PICO)	<b>7-8</b>
<b>METHODS</b>			
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	<b>9-10</b>
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	<b>10-11</b>
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<b>10-11 and Supplementary Materials file 2</b>
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<b>11-12</b>
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)	<b>12</b>
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	<b>13</b>
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	<b>13-14</b>
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<b>13-14</b>
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	<b>13</b>
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<b>13-14</b>
	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 $\tau$ )	<b>13-14</b>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	<b>13-14</b>



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<b>13-14</b>
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	<b>14</b>
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	<b>14</b>

**\* 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.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

12

## Supplementary Materials file 2: preliminary search strategy

**Source:** PubMed

**Search date:** 2021-05-21

**Search specifications:** All search terms are searched in the search fields “title”, “abstract” and in MeSH (when available). A filter for English language is applied.

**Result:** 1,421

### Preliminary search strategy:

Search notes	Search string	Results
<b>Search no. 1:</b> “Stroke” and relevant synonyms.	("Stroke"[Mesh] OR Stroke*[Title/Abstract] OR "Cerebrovascular Accident"[Title/Abstract] OR CVA[Title/Abstract] OR CVAs[Title/Abstract] OR "Cerebrovascular Apoplexy"[Title/Abstract] OR "Brain Vascular Accident"[Title/Abstract])	<b>286,552</b>
<b>Search no. 2:</b> “Depression” and relevant synonyms.	(depression*[Title/Abstract] OR depressed[Title/Abstract] OR depressive[Title/Abstract] OR "Depression"[Mesh] OR "post-traumatic stress disorder"[Title/Abstract] OR "PSD"[Title/Abstract] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "Depressive Disorder"[Mesh:NoExp] OR "Depressive Disorder, Major"[Mesh])	<b>501,507</b>
<b>Search no. 3:</b> “Screening” and relevant synonyms.	("Mass Screening"[Mesh:NoExp] OR screen*[Title/Abstract] OR diagnos*[Title/Abstract] OR "Diagnosis"[Mesh:NoExp] OR "hospital anxiety and depression scale"[Title/Abstract] OR "HADS-D"[Title/Abstract] OR "CES-D"[Title/Abstract] OR "HDRS"[Title/Abstract] OR "geriatric depression scale"[Title/Abstract] OR "GDS"[Title/Abstract] OR "Patient Health Questionnaire"[Title/Abstract] OR "PHQ-9"[Title/Abstract] OR "Patient Health Questionnaire"[Mesh] OR "Beck depression inventory"[Title/Abstract] OR "stroke aphasia depression questionnaire"[Title/Abstract] OR "Aphasia depression rating scale"[Title/Abstract] OR "International Classification of Diseases"[Mesh] OR "ICD-10"[Title/Abstract] OR "International Classification of Diseases"[Title/Abstract] OR "ICD-9"[Title/Abstract])	<b>2,871,536</b>
<b>Search no. 4:</b> Study types.	(prospective[Title/Abstract] OR "follow-up"[Title/Abstract] OR followup[Title/Abstract] OR longitudinal[Title/Abstract] OR "long-term"[Title/Abstract] OR cohort[Title/Abstract] OR "Cohort Studies"[Mesh:NoExp] OR "Follow-Up Studies"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Prospective Studies"[Mesh])	<b>2,986,835</b>
<b>Search no. 5:</b> Combination of search no.: (1 AND 2 AND 3 AND 4)	((("Stroke"[Mesh] OR Stroke*[Title/Abstract] OR "Cerebrovascular Accident"[Title/Abstract] OR CVA[Title/Abstract] OR CVAs[Title/Abstract] OR "Cerebrovascular Apoplexy"[Title/Abstract] OR "Brain Vascular Accident"[Title/Abstract]) AND (depression*[Title/Abstract] OR depressed[Title/Abstract] OR depressive[Title/Abstract] OR "Depression"[Mesh] OR "post-traumatic stress disorder"[Title/Abstract] OR "PSD"[Title/Abstract] OR "Stress Disorders, Post-Traumatic"[Mesh] OR "Depressive Disorder"[Mesh:NoExp] OR "Depressive Disorder, Major"[Mesh])) AND ("Mass Screening"[Mesh:NoExp] OR screen*[Title/Abstract] OR diagnos*[Title/Abstract] OR	<b>1,421</b>

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	"Diagnosis"[Mesh:NoExp] OR "hospital anxiety and depression scale"[Title/Abstract] OR "HADS-D"[Title/Abstract] OR "CES-D"[Title/Abstract] OR "HDRS"[Title/Abstract] OR "geriatric depression scale"[Title/Abstract] OR "GDS"[Title/Abstract] OR "Patient Health Questionnaire"[Title/Abstract] OR "PHQ-9"[Title/Abstract] OR "Patient Health Questionnaire"[Mesh] OR "Beck depression inventory"[Title/Abstract] OR "stroke aphasia depression questionnaire"[Title/Abstract] OR "Aphasia depression rating scale"[Title/Abstract] OR "International Classification of Diseases"[Mesh] OR "ICD-10"[Title/Abstract] OR "International Classification of Diseases"[Title/Abstract] OR "ICD-9"[Title/Abstract])) AND (prospective[Title/Abstract] OR "follow-up"[Title/Abstract] OR followup[Title/Abstract] OR longitudinal[Title/Abstract] OR "long-term"[Title/Abstract] OR cohort[Title/Abstract] OR "Cohort Studies"[Mesh:NoExp] OR "Follow-Up Studies"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Prospective Studies"[Mesh])	
---	---	--