**SUPPLEMENTARY MATERIALS**

**Supplementary 1: Grade Tables**

**GRADE Tables**

|  |  |  |  |
| --- | --- | --- | --- |
| **Quality criteria** | **Rating** (circle one for each criterion) | **Footnotes**(explain reasons for up- or downgrading) | **Quality of the evidence** (Circle one per outcome) |
|  **Outcome # 1: Pre-stroke depression prevalence** |
| **Risk of bias** | serious (-1) | **All studies were graded as having a risk of bias in at least one category of the ROB assessment.** | HighModerateLowVery Low |
| **Inconsistency** | very serious (-2) | **Very high I-squared and variability in reported rates.** |
| **Indirectness** | serious (-1) | **Majority of studies did not have a specific interest in assessing pre-stroke depression.** |
| **Imprecision** | No | **Confidence intervals are narrow.** |
| **Publication Bias** | Unlikely | **No reason to base publication on basis of reported pre-stroke depression prevalence rate.** |
| **Large effect** | NA | **NA** |
| **Dose-response gradient** | No | **NA** |
| **Plausible confounding would change the effect** | No | **NA** |

|  |  |  |  |
| --- | --- | --- | --- |
| **Quality criteria** | **Rating** (circle one for each criterion) | **Footnotes**(explain reasons for up- or downgrading) | **Quality of the evidence** (Circle one per outcome) |
|  **Outcome #2: Risk association with post-stroke depression** |
| **Risk of bias** | serious (-1) | **Most studies had potential sources of bias in primary ROB categories. All studies were at risk of bias based upon possible variations in care pathway.** | HighModerateLowVery Low |
| **Inconsistency** | No | **Vast majority of studies suggest similar sized odds ratios.** |
| **Indirectness** | serious (-1) | **Pre-stroke depression was assessed as a covariate in a number of regression models and hence was not a primary variable of interest.** |
| **Imprecision** | No | **Confidence intervals are narrow.** |
| **Publication Bias** | very likely (-2) | **Studies often do not provide odds ratios if not significant.** |
| **Large effect** | Large (+1) | **>3 odds ratio** |
| **Dose-response gradient** | No | **NA** |
| **Plausible confounding would change the effect** | No | **Confounders such as care pathway could conceivably increase or decrease effect size.** |

|  |  |  |  |
| --- | --- | --- | --- |
| **Total studies that describe the association between pre-stroke depression and post-stroke depression** | **Studies that reported a *significant (p<0.05)* association between pre-stroke depression and post-stroke depression** | **Studies that assessed pre-stroke depression/post-stroke depression association using multiple regression analysis** | **Studies that report a significant association between pre-stroke depression and post-stroke depression using multiple regression analysis** |
| McCarthy et al., 2016; Schottke & Giabbiconi, 2015; De Ryck et al., 2013; White et al., 2014; Aben et al., 2006; Prisnie et al., 2016; Tang et al., 2011; Zhang et al., 2010; Bara et al., 2016; Cairo et al., 2006; Gillen et al., 2001; Hackett et al., 2006; Jorgensen et al., 2016; Kim et al., 2014; Kootker et al., 2016; Liu et al., 2017; Ng et al., 1995; Paolucci et al., 2006; Pohjasvarra et al., 1998; Sienkiewicz-Jarosz et al., 2010; Singh et al., 2000; Tang et al., 2005; Tse et al., 2017; Verdelho et al, 2004 | McCarthy et al., 2016; De Ryck et al., 2013; Prisnie et al., 2016; Tang et al., 2011; Zhang et al., 2010; Caeiro et al., 2006; Gillen et al., 2001; Kim et al., 2014; Ng et al., 1995; Paolucci et al., 2006; Pohjasvarra et al., 1998; Verdelho et al., 2004 | McCarthy et al., 2016; Schottke & Giabbiconi, 2015; De Ryck et al., 2013; White et al., 2014; Aben et al., 2006; Tang et al., 2011; Zhang et al., 2010; Bara et al., 2016; Cairo et al., 2006; Hackett et al., 2006; Jorgensen et al., 2016; Ng et al., 1995; Paolucci et al., 2006; Pohjasvarra et al., 1998; Verdelho et al, 2004 | McCarthy et al., 2016; De Ryck et al., 2013; Tang et al., 2011; Zhang et al., 2010; Cairo et al., 2006; Hackett et al., 2006; Jorgensen et al., 2016; Ng et al., 1995; Paolucci et al., 2006; Pohjasvarra et al., 1998; Verdelho et al, 2004 |

**Supplementary 2: Table of included Studies that reported on the association between pre-stroke depression and post-stroke depression**

**Supplementary 3: Reference list of included studies that reported on the association between pre-stroke depression and post-stroke depression**

Aben I, Lodder J, Honig A, et al. Focal or generalized vascular brain damage and vulnerability to depression after stroke: a 1-year prospective follow-up study. International Psychogeriatrics 2006;**18**(1):19-35

Bara M, Evensen GSH, Valberg BT. Cues and clues predicting presence of symptoms of depression in stroke survivors. Journal of Clinical Nursing 2016;**26**:546-556

Caeiro L, Ferro JM, Santos CO, et al. Depression in acute stroke. J Psychiatry Neurosci 2006;**31**(6):377-383

Castellanos-Pinedo F, Hernandez-Perez JM, Zurdo M, et al. Influence of Premorbid Psychopathology and Lesion Location on Affective and Behavioral Disorders After Ischemic Stroke. The Journal of Neuropsychiatry and Clinical Neurosciences 2011; **23**(3): 340 –347

De Ryck A, Fransen E, Brouns R, et al. Psychosocial problems associated with depression at

18 months poststroke. International Journal of Geriatric Psychiatry 2013; **29**(2):144-152

Dou J, Tang J, Chu-Hong L, et al. A study of suicidal ideation in acute ischaemic stroke patients. Health and Quality of Life Outcomes 2015; 13(7) doi: 10.1186/s12955-014-0198-9

Gillen R, Tennen H, McKee TE, et al. Depressive Symptoms and History of Depression Predict Rehabilitation Efficiency in Stroke Patients. Arch Phys Med Rehabil 2001;**82**:1645-1649

Hackett ML, Anderson CS. Frequency, Management, and Predictors of Abnormal Mood After Stroke The Auckland Regional Community Stroke (ARCOS) Study, 2002 to 2003. Stroke. 2006;**37**:2123-2128

Jorgensen TSH, Wium-Andersen IK,Wium-Andersen MK, et al. Incidence of Depression After Stroke, and Associated Risk Factors and Mortality Outcomes, in a Large Cohort of Danish Patients. *JAMA Psychiatry*. 2016;**73**(10):1032-1040

Kim JM, Stewart R, Kang HJ, et al. A Prospective Study of Statin Use and Poststroke Depression. Journal of Clinical Psychopharmacology 2014;**34**: 72-79

Kocer E, Kocer A, Degirmenci Y, et al. Long-term depression is a stroke risk factor. Acta Neuropsychiatrica 2011; **23**: 292–296

Kootker JA, van Mierlo ML, Hendricks JC, et al. Risk factors for symptoms of depression and anxiety one year poststroke: a longitudinal study. Archives of physical medicine and rehabilitation 2016; **97**:919-28

Liu R, Yingying Y, Haitang J, et al. A risk prediction model for post-stroke depression in Chinese stroke survivors based on clinical and socio-psychological features. [Oncotarget](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5609889/). 2017;**8**(38): 62891–99

McCarthy MJ, Sucharew HJ, Alwell K, et al. Age, subjective stress, and depression after ischemic stroke. Journal of Behavioral Medicine 2016;**39**(1):55-64 doi: 10.1007/s10865-015-9663-0[published Online First: Epub Date]|.

Ng KC, Chan KL, Straughan PT. A study of post-stroke depression in a rehabilitative center. Acra Psychiatr Scand 1995;**92**:75-79

Paolucci S, Gandolfo C, Provinciali L, et al. The Italian multicenter observational study on post-stroke depression (DESTRO). J Neurol 2006;**253**:556–562

Pohjasvarra T, Leppavuori A, Siira I, et al. Frequency and Clinical Determinants of Poststroke Depression. Stroke 1998;**29**:2311-2317

Prisnie JC, Fiest KM, Coutts SB, et al. Validating screening tools for depression in stroke and transient ischemic attack patients. The International Journal of Psychiatry in Medicine 2016;**51**(3) 262–277

Schottke H, Giabbiconi CM. Post-stroke depression and post-stroke anxiety: prevalence

and predictors. International Psychogeriatrics 2015; **27**(11):1805–1812

Sienkiewicz-Jarosz H, Milewska D, Bochynska A, et al. Predictors of depressive symptoms in patients with stroke – a three-month follow-up. Neurologia i Neurochirurgia Polska 2010; **44**(1):13–20

Singh A, Black SE, Hermann N, et al. Functional and Neuroanatomic Correlations in Poststroke Depression The Sunnybrook Stroke Study. Stroke 2000;**31**:637-644

Slater K, McClure AJ, Mahon H, et al. Adherence to Canadian Best Practice Recommendations for Stroke Care: Assessment and Management of Poststroke Depression in an Ontario Rehabilitation Facility 2012. Topics in Stroke Rehabilitation;**19**(2):132-140

Tang KW, Chang SSM, Chiu HFK, et al. Poststroke depression in Chinese patients: frequency, psychosocial, clinical, and radiological determinants. J Geriatr Psychiatry Neurol 2005;**18**:45-51

Tang WK, Lu JY, Chen YK, et al. Association of Frontal Subcortical Circuits Infarcts in Poststroke Depression: A Magnetic Resonance Imaging Study of 591 Chinese Patients With Ischemic Stroke. Journal of Geriatric Psychiatry and Neurology 2011;**24**(1) 44-49

Tse T, Douglas J, Lentin P, et al. Reduction in retained activity participation is associated with depressive symptoms 3 months after mild stroke: an observational cohort study. J Rehabil Med 2017;49:120–127

Verdelho A, Henon H, Lebert F, et al. Depressive symptoms after stroke and relationship with dementia A three-year follow-up study. Neurology 2004;**62**:905–911

Vermeer J, Rice D, McIntyre A, et al. Correlates of depressive symptoms in individuals

attending outpatient stroke clinics. Disability and Rehabilitation 2017;39(1):43-49

White JH, Attia J, Sturm J, et al. Predictors of depression and anxiety in community dwelling stroke survivors: a cohort study. Disability and rehabilitation 2014;**36**(23):1975-82

Zhang T, Wang C, Liu L, et al. A prospective cohort study of the incidence and determinants of post-stroke depression among mainland Chinese patients. Neurological research 2010; **32**(4):347-352 doi: 10.1179/016164110x12656393665125

**Supplementary 4: Table of Pre-stroke depression/post-stroke depression risk association study heterogeneity**

|  |  |  |  |
| --- | --- | --- | --- |
| **Study** | **Pre-stroke depression assessment method** | **Post-stroke depression assessment method** | **Covariates controlled for** |
| Aben et al. (2006) | SCID\* | SCID | Sex; Somatic comorbidity; family history of depression |
| Barra et al. (2016) | Medical records | HADS$ | Age; sex; mRSD; previous stroke. |
| Caiero et al. (2006) | Semi-structured clinical interview | MADRS^ (Cut-off 7) | Age; sex; aphasia. |
| De Ryck et al. (2013) | 1)Self-report 2)Medical records/charts3)Screening (CSD%) | CSD and MADRS  | BIE; NIHSSF; mRS; GFIM; HMMSE; ISIS |
| Hackett et al. (2006) | Self-report  | GHQ-28+ | Sex; age; comorbidity; BI; premorbid dependency; loss of consciousness. |
| Jorgensen et al. (2016) | Medical records | Medical records | Age; sex; education; cohabitation status; diabetes. |
| Mcarthy et al. (2016) | Medical records and self-report | CESD# | Sex; race; marital status; education; NIHSS; mRS; age;  |
| Ng et al. (1995) | Clinical Interview | Clinical interview (DSMIIIB) and HDRSA | Age; sex; Lesion type; functional status. |
| Paolucci et al. (2006) | Self-report | BDI (>10) or “sad face” on VAMS | Sex; prev stroke; mRS; aphasia; BI. |
| Pohjasvarra et al. (1998) | Medical records | Neuropsychiatric inventory (DSMIII and ICD10C) | Dependence; BI; Stroke severity scale. |
| Schottke et al. (2015) | SCID | SCID | Life-time anxiety disorders. |
| Tang et al. (2011) | Medical records and self-reports | SCID | Sex; lesion location; education; NIHSS; Social network; Life events. |
| Verdelho et al. (2004) | Medical Records and self-reports | CAMDEX£ and MADRS | Sex; prev stroke; prev dementia; stroke characteristics; mRS; Orgozo score; post-stroke dementia. |
| White et al. (2014) | Medical records | HADS | Time; age; mRS; social support; Sex; activities; anxiety; baseline depression.  |
| Zhang et al. (2010) | CIDI! | CIDI | Gender; marital status; Hypertension; mRS; HDRS. |

\*SCID= Structured clinical interview for depression; $HADS= Hospital Anxiety Depression questionnaire; %CSD=Cornell scale for depression; ^MADRS= Montgomery and Asberg Depression Rating Scale; +GHQ28= General Health Questionnaire; #CESD= Centre for Epidemiological Studies Depression scale; £CAMDEX= Cambridge Mental Disorders of the Elderly Examination; !CIDI= Composite International Diagnostic Interview; AHDRS= Hamilton Depression Rating Scale; BDSMIII= Diagnostic and Statistical Manual of mental disorders; CICD10= International Statistical Classification of Diseases; DmRS= modified Rankin Scale; EBI= Barthel Index; FNIHSS= National Institutes of Health Stroke Scale; GFIM= Functional Independence Measure; HMMSE= Mini Mental State Examination; ISIS= Stroke Impact Scale.

**Supplementary 5: Risk of Bias (ROB) assessment rationale**

Prevalence:-

Specifically, studies were assessed based upon 1) whether the study had a particular focus upon assessment of pre-stroke depression, 2) if the studies cohort was recruited in an acceptable way, 3) if the study population’s stroke diagnosis was consistent with WHO criteria, 4) risk of over/under estimation in reported pre-stroke depression rates, and 5) the generalisability of their study population:

1) A study was required to explicitly state intention to investigate pre-stroke depression (or at least pre-stroke psychological functioning) as a primary variable of interest (either to determine prevalence or association with a post-stroke outcome) to be considered to have a particular focus on pre-stroke depression. If a study assessed pre-stroke depression simply to control for it as a covariate, it was not deemed to have a particular focus on pre-stroke depression.

2) Recruitment was required to be based upon consecutive admissions to a given setting; i.e. a non-pre-selected stroke population. Studies that failed to do this would be scored as being high risk of bias.

3) Stroke diagnosis was considered to be consistent with WHO if explicitly stated, or if diagnosis was described in sufficient detail as to be likely to be consistent with WHO. If no information was given regarding how the stroke was defined, studies were classified as being of unclear risk of bias. If diagnosis was inconsistent with WHO, it was deemed to be at high risk of bias.

4) Risk of over/underestimation was based upon means of assessment and restriction placed within those assessments. For instance, if studies assessed pre-stroke depression using medical records, they were deemed to be at risk of underestimating pre-stroke depression since receiving a formal diagnosis of depression requires patients to seek help for their depression, which not everyone will do. Similarly, self-report methods that asked patients if they had ever been diagnosed with depression suffer in this same way, but with added recall or social desirability influences that could further affect reported rates. Informant questionnaires were limited in that they require an informant to know about the patient’s prior psychiatric history; and screening tools are liable to overestimate cases of depression. On this basis, assessment via a comprehensive clinical interview that established cases of depression based on reported symptoms meeting DSM criteria-- rather than simply existent diagnosis, evidence of treatment for depression, or symptoms not well defined enough to establish DSM criteria (e.g. screening tool cut-offs) -- was deemed to be the only method that minimised bias to an acceptable level and as such would be scored as low-ROB. All other assessment methods were scored as high-ROB. Studies in which the assessment method was unclear were scored as unclear ROB.

5) Since our exclusion criteria rejected studies with particularly poor population generalisability, generalisability assessments in the ROB review were predominantly based upon the exclusion of patients whose issues may affect reported pre-stroke depression rates. For example, pre-stroke dementia, pre-stroke disability, first ever strokes only, concurrent psychiatric disorders, previous alcohol or drug misuse were deemed as being high risk of bias; age restrictions or exclusion of TIA’s were deemed unclear risk of bias due to reduced overall generalisability of population. Studies were also scored as having a high risk of bias in this category if there was uncertainty regarding the overall generalisability of their inclusion criteria.

Model assessment:-

Of the covariates controlled for, the most commonly cited variable associated with post-stroke depression across four systematic reviews was ‘post-stroke functional impairment’ or ‘stroke severity’. [1-4] As post-stroke functional impairment and stroke severity are highly linked [5], we required all studies to control for one of these variables to achieve a positive ROB review in this category. The ‘event-covariate ratio’ category required studies to have 10 events (i.e. cases of PSD) per covariate controlled for in their model [6,7]. For ‘collinearity control’, studies were deemed to meet this criterion if they ran their multiple regression using stepwise measures or alternatively ran explicit collinearity tests. We also judged the quality of the statistical model based upon control for changes in care pathway. Altered care-pathway has been demonstrated to be a potential consequence of detection of pre-stroke depression in clinical practice. Specifically, reports suggest that patients with pre-stroke depression are more likely to be administered prophylactic (preventative) treatment for post-stroke depression, in addition to an increased likelihood to be referred for psychological consult [8,9]. We felt that both of these variables could impact any reported associations between pre-stroke depression and post-stroke depression, but were unlikely to be controlled for in studies (via records of post-stroke care accessed by each patient). As such, it was included as a secondary attribute for RoB assessment.

**Sub group categorisation details**

*Assessment method classification:*

Assessment methods were classified as follows: ‘self-report’ (any method that simply required a patient to inform as to a prior diagnosis of- or treatment for- depression, as part of a questionnaire or non-clinical interview), ‘medical records’ (hospital charts, admin records etc.), ‘clinical interview’ (both structured, semi-structured and unstructured in depth interviews conducted by a clinician; or alternatively, by a researcher using a tool such as the Structured Clinical Interview for Depression), ‘informant report’ (any assessment method in which *only* the informant was asked for pre-stroke depression information), ‘screening tool’ (validated tools for assessing depressive symptoms, such as the CESD). Where studies utilised more than one assessment method, we classified the assessment type via the method that we felt was most likely to have identified the highest number of pre-stroke depression cases reported in each study’s sample. Generally, Clinical Interviews took precedence over all other assessment types apart from screening tools. Based on findings from previous research [10], medical records took precedence over self-reports. A breakdown of the methods of assessment utilised in included studies can be seen in Table 3.

**Supplementary 6: Risk of Bias (ROB) assessment rationale references**

1.De Ryck A, Brouns R, Geurden M, et al. Risk factors for poststroke depression: Identification of inconsistencies based on a systematic review. Journal of geriatric psychiatry and neurology 2014;**27**(3):147-58Hackett et al 2005

2.Hackett ML, Yapa C, Parag V, et al. Frequency of depression after stroke: A systematic review of observational studies. Stroke 2005;**36**:1330–40

3.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. International Journal of Stroke 2014;**9**(8):1026-36 doi: 10.1111/ijs.12356[published Online First: Epub Date]|

4.Robinson RG, Jorge RE. Post-stroke depression: A review. American Journal of Psychiatry 2016;**173**(3):221-31

5.Mok VCT, Wong A, Lam WWM, et al. Cognitive impairment and functional outcome after stroke associated with small vessel disease Journal of Neurology, Neurosurgery & Psychiatry 2004;**75:**560-566.

6.Peduzzi P, Concato J, Feinstein AR, et al. Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. J Clin Epidemiol 1995;**48**:1503–1510

7.Peduzzi P, Concato J, Kemper E, et al. A stimulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;**49**:1373– 1379

8.Reid DL, Jia H, Cameon R, et al. Does prestroke depression impact poststroke depression and treatment? AM J Geriatr Psychiatry 2010;**18**:624-23

9.Slater K, McClure AJ, Mahon H, et al. Adherence to Canadian Best Practice Recommendations for Stroke Care: Assessment and Management of Poststroke Depression in an Ontario Rehabilitation Facility 2012. Topics in Stroke Rehabilitation;**19**(2):132-140

10.Wu C-S, Lai M-S, Gau SS-F, Wang S-C, Tsai H-J Concordance between Patient Self-Reports and Claims Data on Clinical Diagnoses, Medication Use, and Health System Utilization in Taiwan. PLoS ONE 2014;**9**(12): e112257. doi:10.1371/journal.pone.0112257

**Supplementary 7: Specific Search strategy**

Pre-stroke depression focus search:

1. pre-stroke.mp.

2. prestroke.mp.

3. premorbid.mp.

4. 1 or 2 or 3

5. Mood Disorder Questionnaire/ or mood change/ or "Profile of Mood States"/ or mood/ or mood stabilizer/ or mood.mp. or mood disorder/ or mood disorder assessment/

6. depression/

7. 5 or 6

8. 4 and 7

9. limit 8 to human

10. (depressi$ adj2 "before the stroke").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

11. (depressi$ adj2 "history of").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. 1 or 2 or 3 or 10 or 11

13. 12 and 7

14. limit 13 to human

15. stroke/

16. 14 and 15

**Supplementary 8: Sensitive search strategy**

Post-stroke depression search:

1. exp Cerebrovascular Disorders/

2. stroke\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

3. poststroke\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

4. cerebrovascular\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

5. cerebral vascular.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

6. 2 or 3

7. 4 or 5

8. infarct\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

9. isch?emi\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

10. thrombo\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

11. emboli\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

12. apoplexy.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

13. 8 or 9 or 10 or 11 or 12

14. cerebral.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

15. intracerebral.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

16. intracranial.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

17. brain\*.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

18. cerebellar.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

19. vertebrobasilar.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

20. 14 or 15 or 16 or 17 or 18 or 19

21. h?emorrhage.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

22. bleed.mp. [mp=ti, ot, ab, nm, hw, ui, an, tc, id, sh, tn, dm, mf]

23. 21 or 22

24. 13 and 20

25. 20 and 23

26. 1 or 6 or 7 or 24 or 25

27. Depression/

28. Depressive Disorder/

29. 27 or 28

30. 26 and 29

31. limit 30 to human