Post-Stroke Depression: Addressing the Giant Iceberg in the Room

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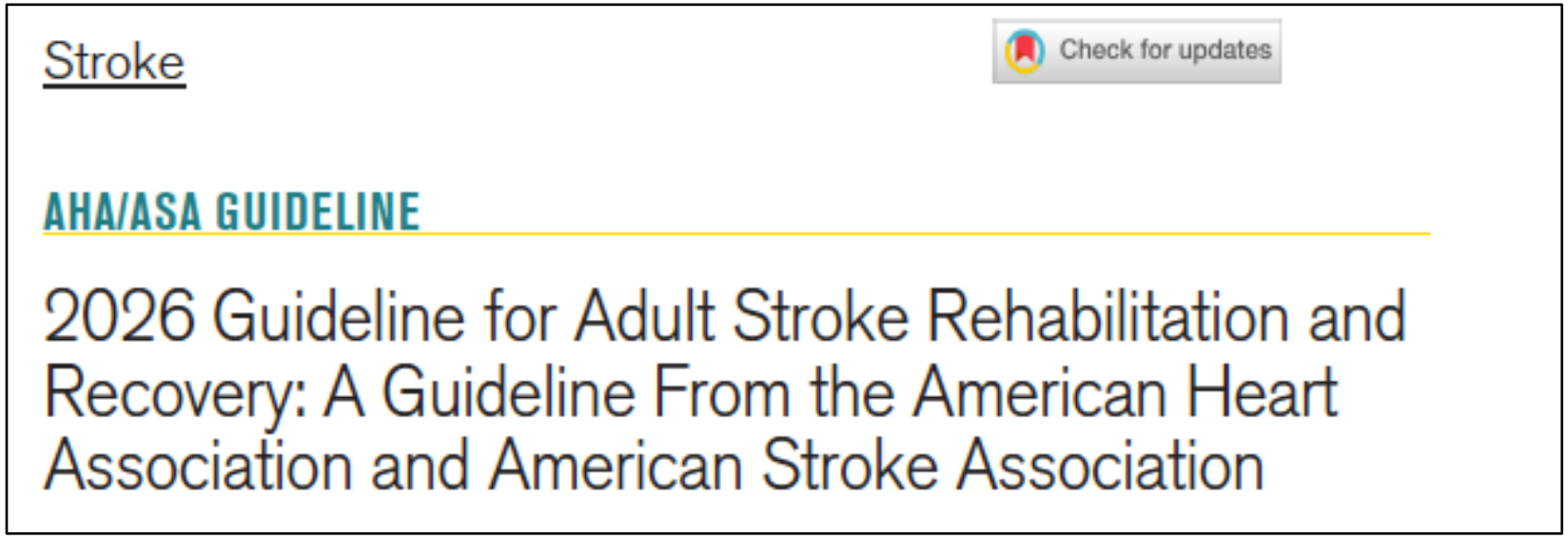
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Objectives

1. Review the prevalence, mechanisms, and impact of post-stroke depression across the recovery continuum.

2. Discuss best practices for identifying and diagnosing post-stroke depression in medically and neurologically complex stroke survivors.

3. Evaluate current treatment strategies for post-stroke depression and their role in optimizing rehabilitation participation and long-term outcomes.

Post-Stroke Depression (PSD)



- Post-Stroke Depression (PSD) is the most frequent neuropsychiatric consequence of stroke affecting as high as 33% of stroke survivors.
- Depression is often perceived as a natural reaction to stroke rather than a disease diagnosis of PSD.



- Although prevalence estimates vary considerably depending on assessment method and timing, this far exceeds rates of depression in the general population (8.3%).
- Complicated by overlapping physical symptoms of stroke such as cognitive impairment and communication difficulties.

Consequence of Post-Stroke Depression

- It is associated with increased **mortality** and **poor functional outcomes**.
- Individuals suffering from stroke have rates of suicide attempts **twice** as high as the general population.
- The detrimental effects of mental health issues are well-documented and include **reduced independence, social engagement, therapy participation, adherence to medication, and quality of life**.
- PSD is also associated with **increased risk for stroke recurrence** and mortality.

DSM-V Criteria for Post-Stroke Depression

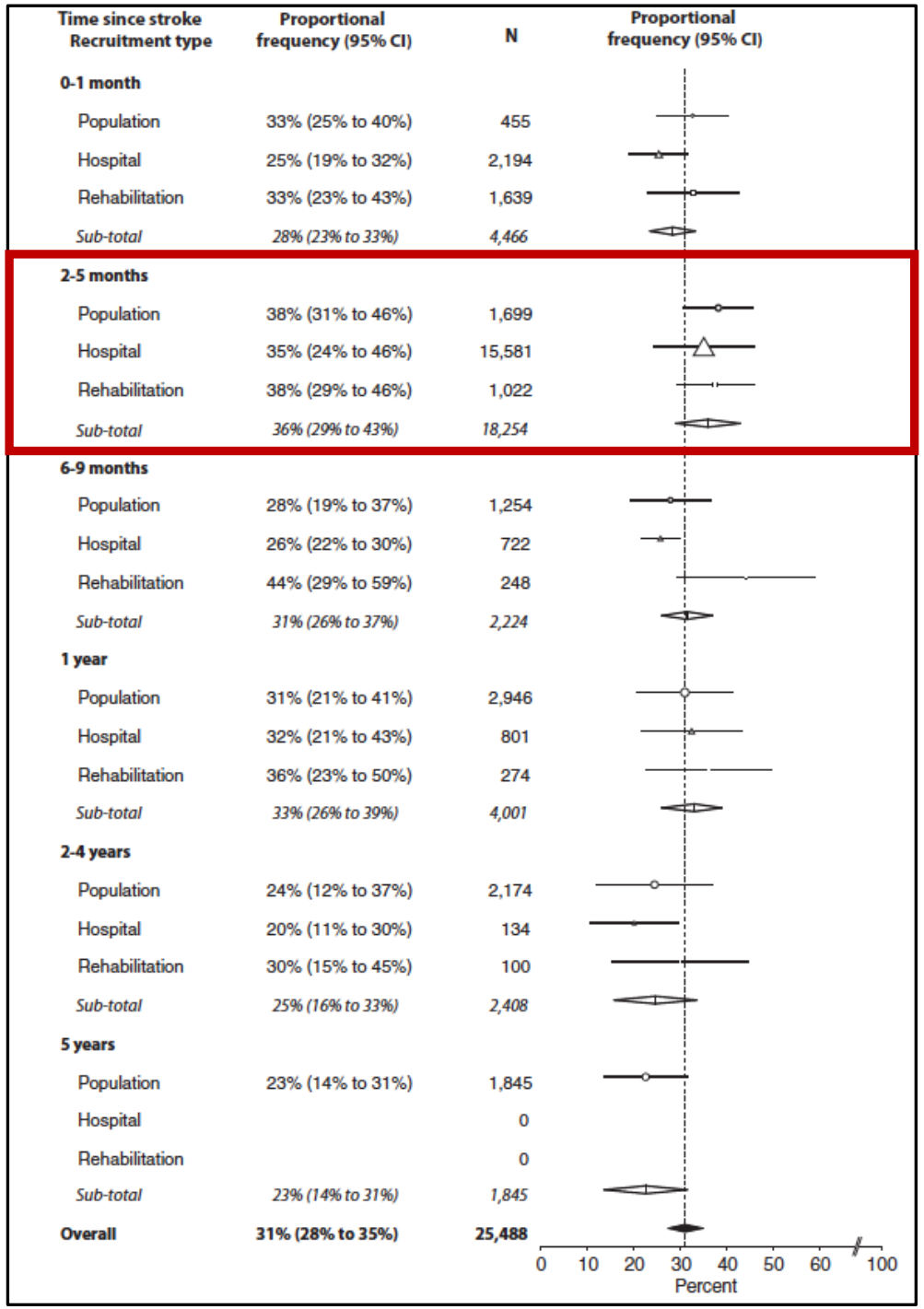
- **Mood disorder due to stroke with depressive features (minor):** must have depressed mood or loss of interest or pleasure and 2-4 symptoms of depression, lasting two or more weeks.

- **Mood disorder due to stroke with a major depression-like episode (major):** must have depressed mood or loss of interest or pleasure and 5-7 symptoms of major depression, lasting two or more weeks.

Symptoms of Post-Stroke Depression

- Impaired mood for most of the day
- Reduced interest of pleasure in various activities (anhedonia)
- Weight loss
- Insomnia
- Fatigue or loss of energy
- Reduced self-esteem of self-worth
- Inappropriate feelings of guilt
- Reduced ability to think or concentrate
- Recurrent thoughts of death, suicidal ideation, or suicide attempts

TIME


Time since stroke
Recruitment type
Proportional frequency (95% CI)
N
Proportional frequency (95% CI)
0-1 month
Population 33% (25% to 40%) 455
Hospital 25% (19% to 32%) 2,194
Rehabilitation 33% (23% to 43%) 1,639
Sub-total 28% (23% to 33%) 4,466
2-5 months
Population 38% (31% to 46%) 1,699
Hospital 35% (24% to 46%) 15,581
Rehabilitation 38% (29% to 46%) 1,022
Sub-total 36% (29% to 43%) 18,254
6-9 months
Population 28% (19% to 37%) 1,254
Hospital 26% (22% to 30%) 722
Rehabilitation 44% (29% to 59%) 248
Sub-total 31% (26% to 37%) 2,224
1 year
Population 31% (21% to 41%) 2,946
Hospital 32% (21% to 43%) 801
Rehabilitation 36% (23% to 50%) 274
Sub-total 33% (26% to 39%) 4,001
2-4 years
Population 24% (12% to 37%) 2,174
Hospital 20% (11% to 30%) 134
Rehabilitation 30% (15% to 45%) 100
Sub-total 25% (16% to 33%) 2,408
5 years
Population 23% (14% to 31%) 1,845
Hospital 0
Rehabilitation 0
Sub-total 23% (14% to 31%) 1,845
Overall 31% (28% to 35%) 25,488
0 10 20 30 40 50 60 100
Percent

Pathogenesis

Mechanism: The cause of poststroke depression is poorly understood but is likely the result of a complex dynamic interaction between biological, psychological, and social factors that change over time.

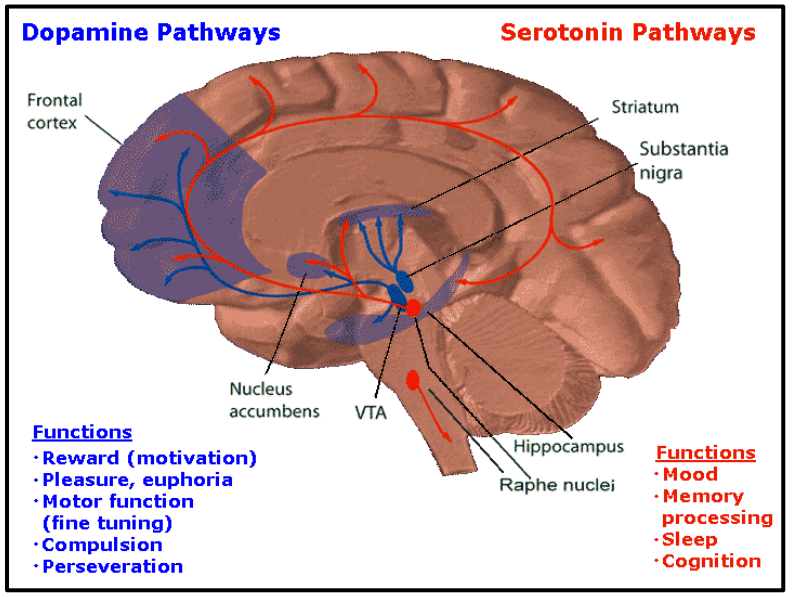
- **Psychological concept-**assumes that depression occurs as a reaction to the illness, often associated with disability (akin to depression linked to other chronic illnesses, including CVD, cancer).

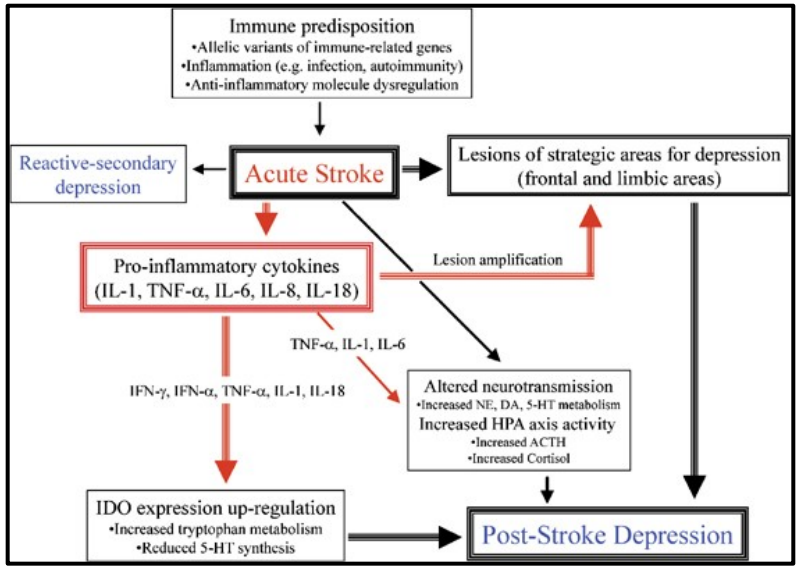
- **Social Stressors-**related to personal life, work, financial concerns, limited social support, and increased social isolation after stroke may also contribute to depression

- **Organic concept:** a consequence of damage to brain areas involved in mood regulation (i.e. left dorsolateral prefrontal cortex).

Pathogenesis Cont.

- **Biogenic Amine Concept:** Alterations in ascending monoamine systems secondary to results in decreased neurotransmission (5-HT, Dopa, NE).
- **Neuroinflammation** is increasingly recognized as a factor in PSD, with elevated pro-inflammatory cytokines, such as IL-6and TNF-alpha, correlating with depressive symptoms.
- **Other contributing factors** certain medications used for stroke recovery can exacerbate depressive symptoms.



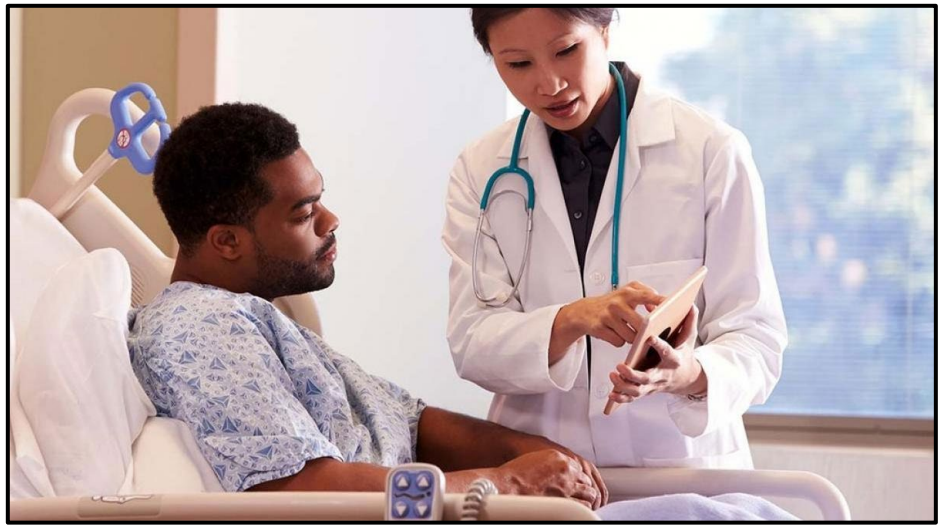


Pathogenesis Cont.

- Stroke severity
- Severe disability/High mRS
- Cognitive impairment
- Previous stroke
- History of depression
- Family history of psychiatric disorder
- Diabetes
- Female Sex
- Apathy or Lachrymosity in the acute stage

Screening for PSD

Regular screening and early identification of depression in stroke survivors are critical for timely and appropriate intervention.



Recommendations for Mental Health Assessment and Treatment of Poststroke Depression and Anxiety, Including Emotional and Behavioral State
Referenced studies that support recommendations are summarized in the online data supplement.

COR	LOE	Recommendations
1	A	1. In persons with stroke, early screening using a valid screening instrument for poststroke depression (PSD; from 3 days to 3 months poststroke) is recommended to identify individuals in need of further evaluation and treatment.[1–3]
1	B-NR	2. In persons with stroke, periodic screening of depression, anxiety, and other psychiatric symptoms using valid measurement instruments (at 3 and 6 months, and throughout the lifespan) should be performed to improve detection and access to treatment.[3]
1	C-LD	3. In persons with stroke who experience impaired communication, screening for depression, anxiety, and other psychiatric symptoms should be performed using a valid measurement instrument or appropriate supported communication strategies designed for this population to improve detection and access to treatment.[4]

Symptoms of Post-Stroke Depression

- Impaired mood for most of the day
- Reduced interest of pleasure in various activities (anhedonia)
- Weight loss
- Insomnia
- Fatigue or loss of energy
- Reduced self-esteem of self-worth
- Inappropriate feelings of guilt
- Reduced ability to think or concentrate
- Recurrent thoughts of death, suicidal ideation, or suicide attempts

Screening for PSD

Patient Health Questionnaire (PHQ-2)

Patient Name _____ Date of Visit _____

Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not At all	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3

Patient Health Questionnaire (PHQ-9)

		Not at all	Several days	More than half the days	Nearly every day
1.	Little interest or pleasure in doing things	0	1	2	3
2.	Feeling down, depressed, or hopeless	0	1	2	3
3.	Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4.	Feeling tired or having little energy	0	1	2	3
5.	Poor appetite or overeating	0	1	2	3
6.	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7.	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8.	Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9.	Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Score	Depression Severity
0 - 4	None – Minimal
5 - 9	Mild
10 - 14	Moderate
15 - 19	Moderately Severe
20 - 27	Severe

Table 3. Anxiety and Depression Assessments Validated for Use in Persons With Stroke

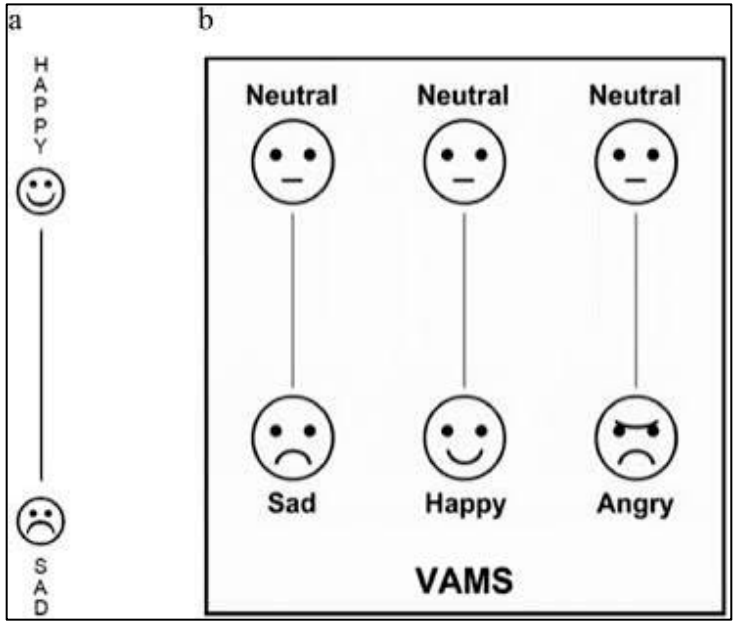
Measure	Description	Cutoff	Notes
BDI-II[85,183]	21 self-report items Proxy version available	Mild, 11–16; borderline, 17–20; moderate, 21–30; severe, 31–40; extreme, >40	May not be appropriate for persons with cognitive or communication impairments without modifications
PHQ[84,86] PHQ-2,[86] PHQ-9[84]	Self-report depression measure on the presence and/or severity of symptoms over the past 2 weeks 2-item: 2 hallmark symptoms of depression: depressed mood and anhedonia; used as a screen 9-item: severity of depressive symptoms over the previous 2 weeks	≥1 (Yes/No) ≥2 or 3 (multiple choice) ≥10 Mild, 4–9; moderate, 10–14; moderate-severe, 15–19; severe, 20+	PHQ-9 includes suicide item May not be appropriate for persons with cognitive or communication impairments without modifications
GDS[87,88]	15 or 30 items, "Yes/No" response format Does not include somatic symptoms	>11 (30-item) >5 (15-item)	Geared toward older adults; response format may be useful for persons with impaired communication
HDRS[85,89]	17-item, clinician rated depression measure May replace structured interviews based on diagnostic criteria	Mild, 8–16; moderate, 17–23; severe, 24	Screens suicide May not be appropriate for persons with cognitive or communication impairments without modifications
MADRS[85,90]	10-item, clinical interview (self-report available) Less reliant on physical symptoms	Mild, 7–19; moderate, 20–34; severe, 35–60	Assesses suicide
HADS[91,92]	14 self-report items (7 depression, 7 anxiety), rated based on severity of symptoms over the past week HADS-A is the most commonly used measure of PSA	≥8 or 11 for HADS-Total; ≥4, 5, or 7 for HADS-D; ≥5 for HADS-A	May not be appropriate for persons with cognitive or communication impairments without modifications
BOA[93]	10 self-report and carer-rated versions of observable behaviors related to anxiety	≥13/14 Mild, 7–13; moderate, 14–17; severe, 18+	Potential for use with persons unable to self-report anxiety
VAMS[94] D-VAMS[95]	Indicate mood state on a vertical line Bipolar scales used to report mood by modifying facial expression images using a slider on a tablet	Based on normative data	Developed and validated for persons with aphasia
SADQ[96]	10 items of observable behaviors related to depression	≥15	

BDI-II indicates Beck Depression Inventory-II; BOA, Behavioural Outcomes of Anxiety scale; GDS, Geriatric Depression Scale; HADS, Hospital Anxiety and Depression Scale; HDRS, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale; PHQ-2/PHQ-9, Patient Health Questionnaire (2-item and 9-item versions); SADQ, Stroke Aphasia Depression Questionnaire; and VAMS/D-VAMS, Visual Analog Mood Scale/Dynamic Visual Analog Mood Scales.

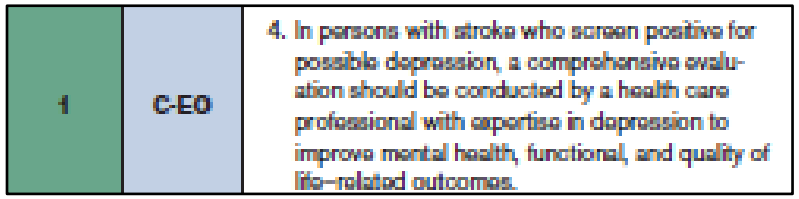
Screening for PSD: Aphasia

VAMS[84] D-VAMS[85]	Indicate mood state on a vertical line Bipolar scales used to report mood by modifying facial expression images using a slider on a tablet	Based on normative data	Developed and validated for persons with aphasia

Visual Analog Mood Scale



Diagnostic Evaluation



1	C-EO	4. In persons with stroke who screen positive for possible depression, a comprehensive evaluation should be conducted by a health care professional with expertise in depression to improve mental health, functional, and quality of life–related outcomes.

- Diagnosis is based on a **structured interview and scales** that allow quantitative assessment of depression and tracking of its course over time.

- Symptoms should not result from direct exposure to a substance (medication, drugs) or a medical condition(e.g., hypothyroidism) and should not be attributed to grief (e.g., loss of a loved one, etc.)

- If the diagnosis is unclear, a trial of antidepressants is recommended.

Management



- **Patient Education** about stroke is recommended

- **Counseling:** Patients should be provided with information, advice, and the opportunity to talk about the impact of the illness on their lives

2a	B-R	9. In persons with PSD, psychoeducation about the effects of stroke on mental health, dyadic and family-oriented approaches, and peer support can be useful treatment components to reduce PSD.[19-22]

Only a minority of PSD patients achieve spontaneous remission without pharmacologic treatment

Management

2a	A	6. In persons with PSD, use of antidepressants can be beneficial to reduce depressive symptoms.[7–12]

- Early and effective treatment of PSD can have a significant positive impact on the course of recovery, with SSRIs reducing depression and anxiety and improving neurological deficit.

Table 1. FDA-Approved SSRIs

Generic	Trade Name	Approved Uses
Citalopram	Celexa	Depression
Escitalopram	Lexapro	Depression, generalized anxiety
Fluoxetine	Prozac	Depression, OCD, bulimia, panic disorder
	Sarafem	PMDD
Fluvoxamine	Luvox	OCD
Paroxetine	Paxil	Depression, OCD, generalized anxiety, panic disorder, social anxiety, PTSD
Sertraline	Zoloft	Depression, OCD, panic disorder, social anxiety, PTSD, PMDD
Vilazodone	Viibryd	Depression

OCD: obsessive-compulsive disorder; PMDD: premenstrual dysphoric disorder; PTSD: posttraumatic stress disorder; SSRI: selective serotonin reuptake inhibitor.

Selective serotonin reuptake inhibitors (SSRIs)

- SSRIs inhibit the reuptake of serotonin into nerve endings, thereby increasing the amount of serotonin in the synaptic left, which acts on postsynaptic receptors.

- SSRIs have little or no affinity for cholinergic, histaminergic, and various adrenergic and dopaminergic receptors.

Management

2a	A	6. In persons with PSD, use of antidepressants can be beneficial to reduce depressive symptoms.[7–12]

- Clinical improvement typically **begins within 2-4 weeks**, although full therapeutic effects may take longer; if the patient does not respond after 3 weeks, consider increasing the dose.

- Treatment should be continued for at least 6 months to prevent relapse.

Don’ts with SSRIs

- Do not administer SSRIs to patients treated with monoamine oxidase inhibitors (MAOIs) ⇒ risk of serotonin syndrome.
- MAOIs should not be started within 7 days after discontinuing an SSRI.
- Prophylactic use of SSRIs in stroke patients is not recommended.

3-No Benefit	A	15. In persons with stroke, prophylactic use of antidepressants is not recommended for routine prevention of PSD.[8-11,34-38]

Management: Other Pharmacologic



- **Trazodone-**Serotonin antagonist and reuptake inhibitor (SARI)
- **Venlafaxine-**Selective serotonin/norepinephrine reuptake inhibitors (SNRI)
- **Bupropion-**Selective catecholamine and dopamine reuptake inhibitor (DNRI)
- **Nortriptyline; Amitriptyline:** Tricyclic/Tetracyclic Antidepressant



Management: Other Pharmacologic



- **Mirtazapine-** Antagonizes alpha-2-adrenergic and serotonin 5HT2 receptors (tetracyclic)

- **Methylphenidate-** Inhibits the dopamine transporter (DAT) and norepinephrine transporter (NET), reducing presynaptic reuptake.



Behavioral Approaches

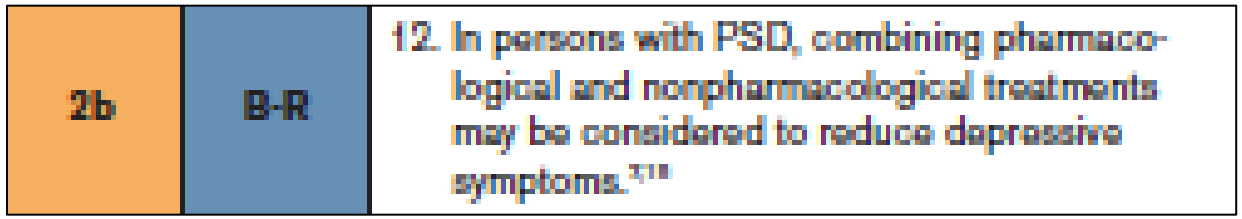
- Cognitive Behavioral Therapy
- Acceptance and Commitment Therapy
- Exercise
- Repetitive transcranial magnetic stimulation (rTMS)
- Acupuncture; Music Therapy; Meditation; Mindfulness

Recommendations for Mental Health Assessment and Treatment of Poststroke Depression and Anxiety, Including Emotional and Behavioral State (Continued)

COR	LOE	Recommendations
2a	A	10. In persons with PSD, an exercise program at least 3 times per week can be beneficial for reducing depressive symptoms.[34,35]
2b	B-R	11. For persons with PSD, use of rTMS may be considered to reduce depressive symptoms.[7,36,37]
2b	B-R	12. In persons with PSD, combining pharmacological and nonpharmacological treatments may be considered to reduce depressive symptoms.[7,18]
2b	B-R	13. In persons with PSD or anxiety, acceptance and commitment therapy (ACT) may be considered to reduce depressive and/or anxiety symptoms.[13,38–40]
2b	B-R	14. In persons with PSD or anxiety, the use of music therapy, acupuncture, and mindfulness-based interventions may be considered to reduce depressive and/or anxiety symptoms.[13,21–23]

Best Practice

- Management necessitates a multidisciplinary approach to effectively treat PSD.
- Mainstay of treatment includes **SSRIs + psychotherapy and early intensive rehabilitation.**
- The combination of pharmacological and non-pharmacological treatments offers synergistic effects



2b	B-R	12. In persons with PSD, combining pharmacological and nonpharmacological treatments may be considered to reduce depressive symptoms.[7,18]

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Questions?

Thanks!!