

Post-Stroke Depression: A Review

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Based in part on:

Dr Schmitz, Neuroscience Institute, Minneapolis; Am J Psychiatry 2016 Review; Canadian Best Practice Recommendations for Stroke Care: 2008.



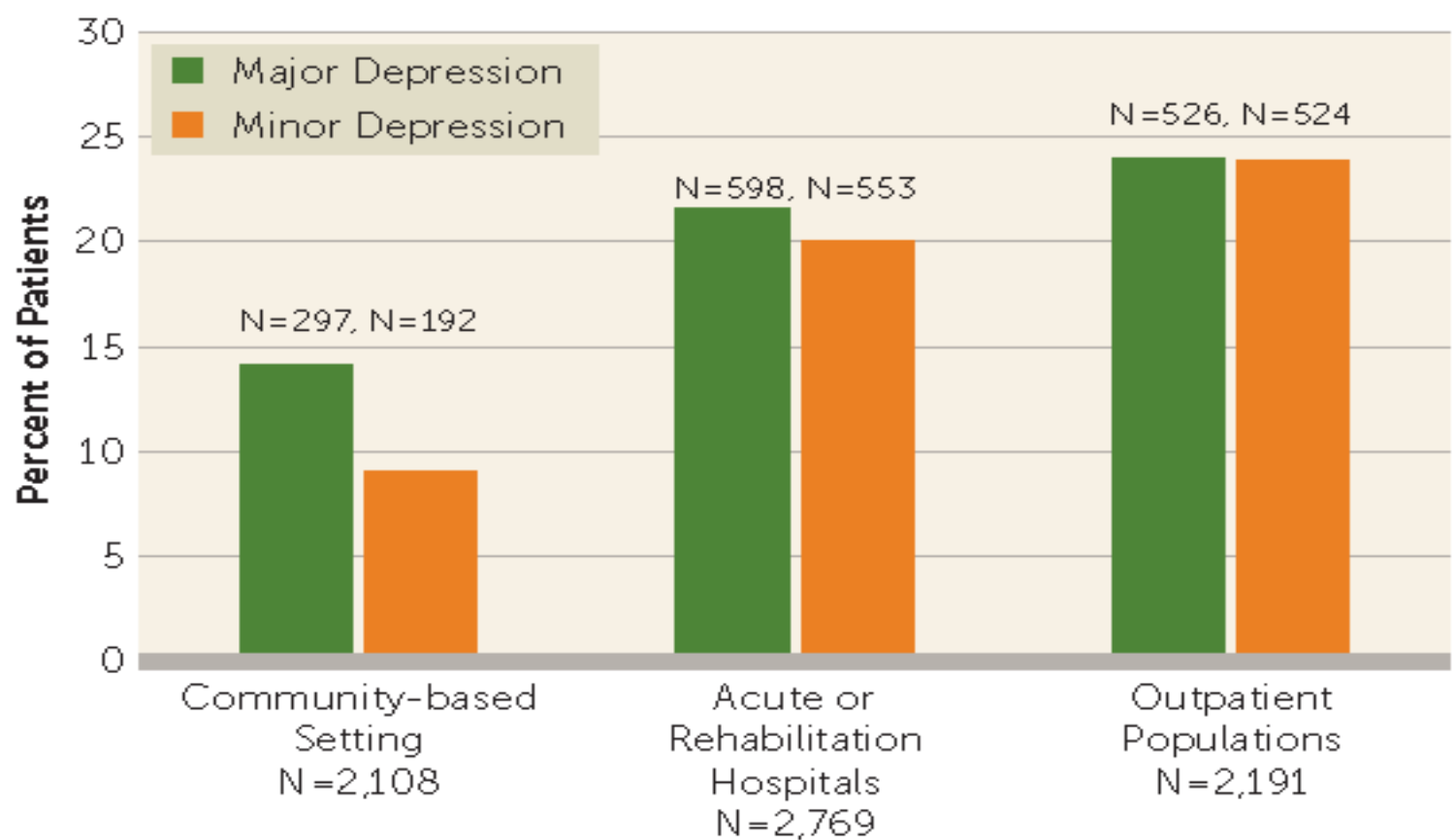
Goals of presentation

- Describe etiology and incidence of post-stroke depression (PSD).
- Outline treatment options and strategies for PSD.

Incidence of PSD.

- Approximately 1/3 of persons will experience clinically significant depression at some point following a stroke. Hackett, et al., 2005
- Robinson found that 19.3% and 18.5% of stroke survivors had major depression or minor depression, respectively, in acute care rehabilitation settings. Robinson, RB, 2003
- No significant difference in incidence between hemorrhagic and infarct strokes

FIGURE 1. The Prevalence of Depression in Various Clinical Settings Following Stroke^a



^a Patients were examined using a standardized mental status examination and DSM-IV diagnostic criteria for depression following stroke with major depressive-like features or minor depression defined as more than two but less than five symptoms of major depression. Meta-analyses stating that the prevalence of poststroke depression is 31% miss these important clinical variables.



PSD associated with:

- ❑ Poor functional recovery – may delay recovery by 2 years.
- ❑ Poor social outcomes
- ❑ Reduced quality of life
- ❑ Reduced rehabilitation treatment efficiency
- ❑ Increased cognitive impairment
- ❑ Increased mortality Morris, et al., 1993



A biopsychosocial model of PTSD

□ **Biological factors**

Location of stroke – left cortical and subcortical lesions risk is controversial

Exact neuroanatomical mechanism unknown

Presumed disruption in amine pathways



A biopsychosocial model of PSD

- **Psychosocial factors**
 - Pre-stroke history of depression
 - Personality and coping style
 - Inadequate social support, particularly significant other.
 - Level of disability

Early Predictors of PSD Carota, et al. (2005)

- Low Barthel Index score

<http://www.strokecenter.org/trials/scales/barthel.pdf>

- Age <68 years

- Crying in first few days

- Pathological crying (not associated with PSD)
- Emotionalism (41% developed PSD)
- Catastrophic reaction (63% developed PSD)

Distinguishing types of crying:

- **Pathological crying** linked to infarct in basis of pontis and corticobulbar pathways and occurs in response to mood incongruent cues.
- **Emotionalism** is crying that is congruent with mood (sadness) but patient is unable to control crying as they would have before stroke.
- **Catastrophic reaction** is crying or withdrawal reaction triggered by a task made difficult or impossible by a neurologic deficit (e.g. moving a hemiplegic arm)

Emotionalism and catastrophic reaction

Evidence for neurobiological basis over situational psychological factors

- Catastrophic reactions occur more with left hemispheric lesions and aphasia
- Greater in strokes involving structures heavily connected to the amygdala and paralimbic regions
- May be seen as abnormal reflexes rather than conscious responses evoked by lesion related damage, hypoperfusion and edema in acute phase of stroke



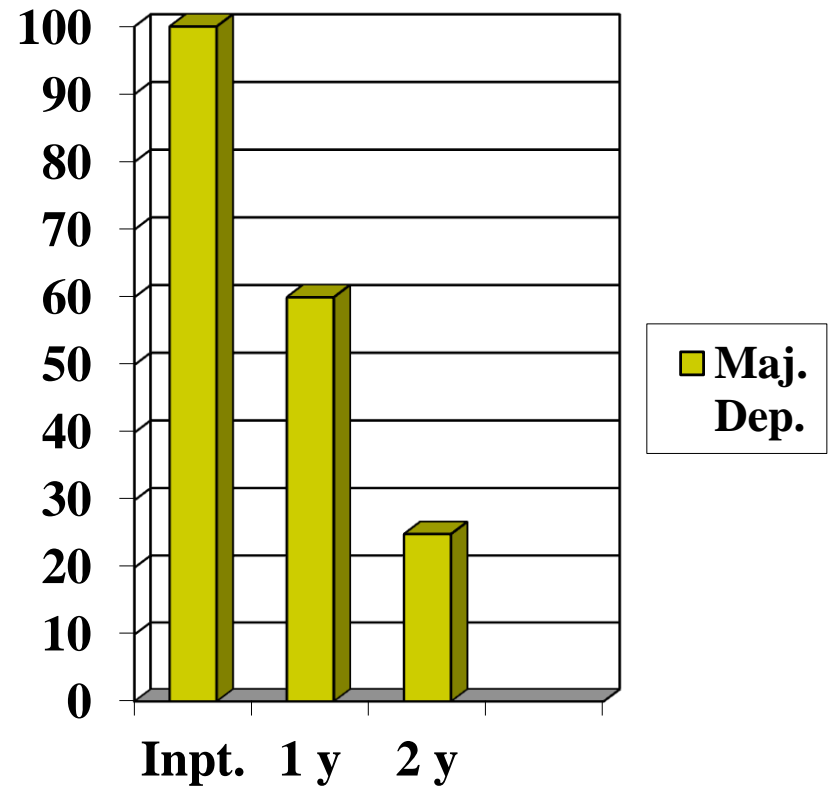
Course of PSD

- About 40% of those with PSD will develop symptoms within 3 months.
- 30% of nondepressed patients become depressed upon discharge from the hospital.
- At 6 months, a majority of patients with PSD continued to have symptoms.
- Course of PSD different for major and minor depression

Major PSD

- Recovery significantly better in major PSD than minor PSD with nearly 75% resolution in symptoms after two years.

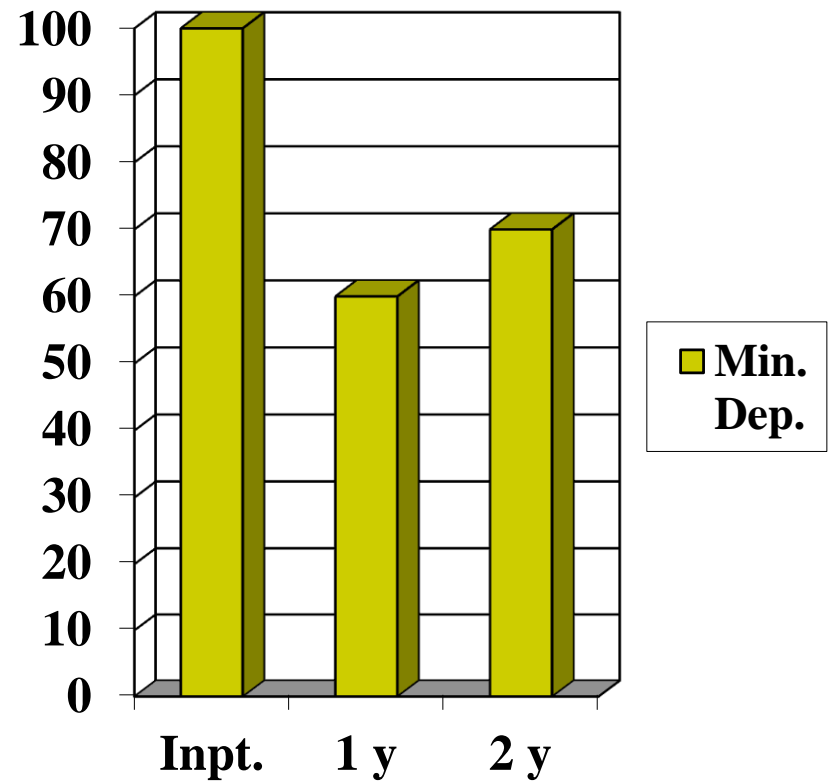
Chemerinski & Robinson, 2000.



Minor PSD

- Prognosis worse in patients with minor depression.

Chemerinski & Robinson, 2000

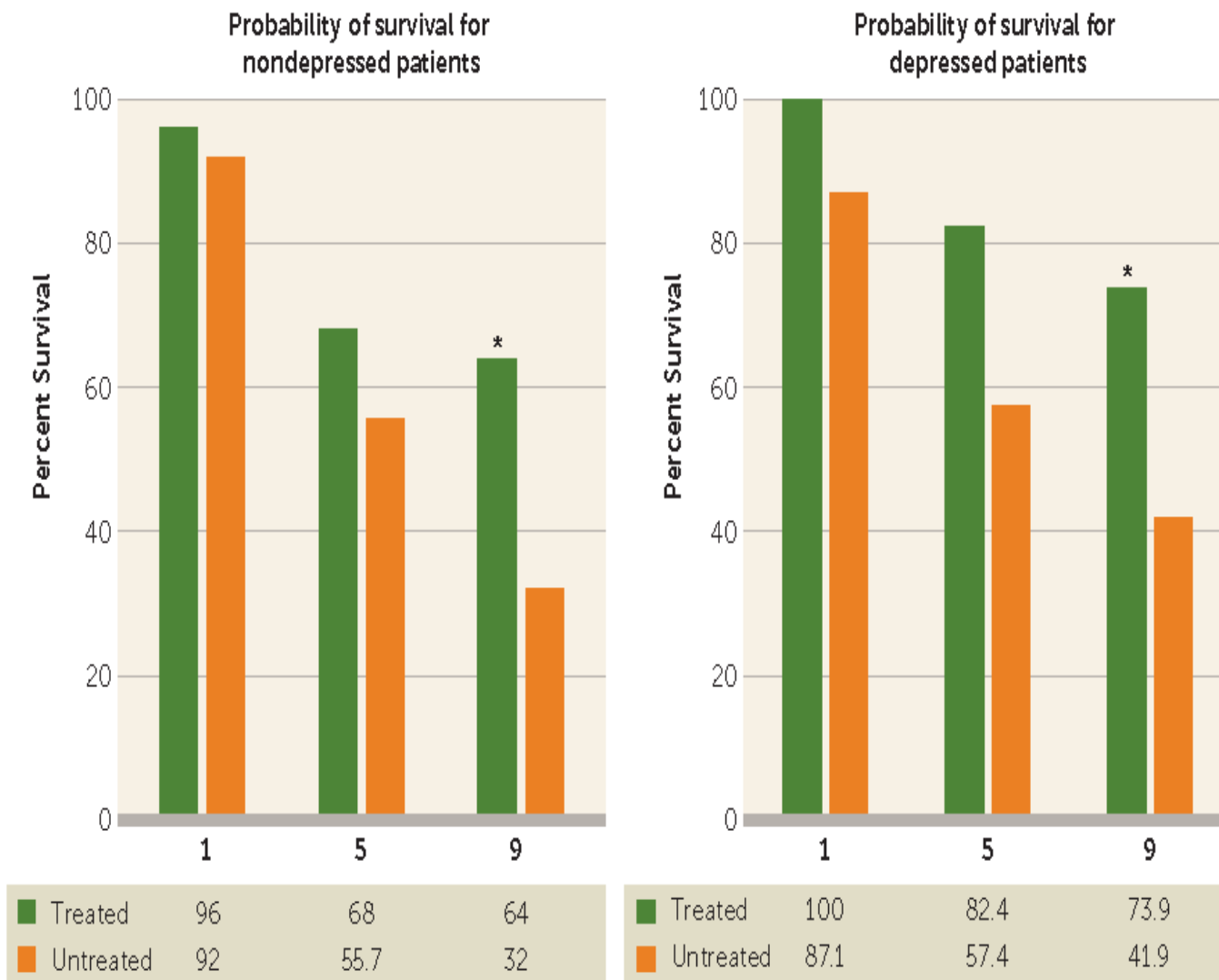


PSD and mortality

Morris, et al., 1993

- Patients with either Major or Minor PSD are 3.4 times more likely to die during a 10 year period poststroke than nondepressed patients.
- Patients with PSD and few social contacts have an even increased mortality rate: 90% died in Morris et al cohort.

FIGURE 2. Survival Rate for Patients Who Were Depressed and Nondepressed at 3 Months Followed Over 9 Years^a



^a Patients were randomly assigned to nortriptyline (100 mg/day), fluoxetine (40 mg/day), or placebo for 3 months. The survival rate of patients given antidepressants was almost twice that of those given a placebo.

* p=0.004.

Diagnosis of PSD

- Difficult to reliably diagnose
- Post-stroke depression under-diagnosed by non-psychiatric physicians in 50-80% of cases. Shuebert, et al. 1992
- Widespread belief that depression is simply an understandable psychological reaction or grief response.

Overlapping Neurological impairment presents diagnostic challenges

Gaete, et al., 2008

- Cognitive deficits
- Fatigue
- Apathy – motivational disorder found in 23-57% of patients with stroke.
 - Not correlated with depression
 - Depression correlated with memory and executive functioning deficits
- Anosognosia – lack of awareness, denial or underestimate of sensory, cognitive or affective impairment (60% in R-CVA, 24% L-CVA)

DSM-IV Diagnostic criteria for major depression

Five or more of the following present during two week period and representing a change in function, one symptom must be either depressed mood or loss of interest

- Depressed mood most of the day for most days.
- Marked reduction in interest or pleasure in most activities
- Significant weight loss or gain, significant increase or decrease in appetite
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness; inappropriate guilt
- Reduced ability to think or concentrate
- Recurrent thoughts of death or suicide



Assessment of PSD:

- ❑ Clinical interview and history
- ❑ Collateral information from family and caregivers
- ❑ Observational standardized screening measure
- ❑ Self-reports standardized screening measure when appropriate



Treatment for Post-stroke Depression

- Tricyclic antidepressants
- SSRI and SSNRI Antidepressants
- Psychostimulants
- Counseling and Psychotherapy

Effectiveness of antidepressant treatment of PSD

- Meta-analysis of studies of antidepressant therapy conclude that this treatment modality may be beneficial to patients with PSD

Chen, Y, et al, 20006

- Tricyclic antidepressants are as effective as newer generation selective serotonin reuptake inhibitors (SSRI) but with greater side effects reported..

Effectiveness of antidepressant treatment of PSD

- SSRIs have been the most widely studied class of antidepressants
- Citalopram (Celexa) is the single most widely studied agent in PSD
- No evidence that one SSRI preferential over another.
- Selective serotonin/norepinephrine reuptake inhibitors such as venlafaxine and duloxetine are also increasingly utilized.

TABLE 1. Double-Blind Placebo-Controlled Treatment Studies of Poststroke Depression^a

Study	N	Medication (N and Maximum Daily Dose)	Duration	Evaluation Measure	Results	Response Rate	Completion Rate
Lipsey et al. (6)	34	Nortriptyline (N 14; 100 mg/day) Placebo (N 20)	6 weeks	HAM-D; Zung Depression Scale	Intent to treat and efficacy: Nortriptyline> placebo	Completers: nortriptyline, 100%; placebo, 33%;	11 of 14 nortriptyline; 15 of 20 placebo
Reding et al. (83)	27	Trazodone (N 7; 200 mg/day); placebo (N 9)	Mean 32 days (SD=6)	Zung Depression Scale	Efficacy: trazodone> placebo on Barthel Activities of Daily Living Index for patients with abnormal dexamethasone suppression test	NR	
Andersen et al. (72)	66	Citalopram (N 33; 20 mg/day, 10 mg for patients >65 years); placebo (N 33)	6 weeks	HAM-D; Melancholia Scale	Intent to treat: citalopram>placebo	Completers: citalopram, 61%; placebo, 29%	26 of 33 citalopram
Grade et al. (84)	21	Methylphenidate (N 10; 30 mg/day); placebo (N 11)	3 weeks	HAM-D	Intent to treat: methylphenidate> placebo	NR	9 of 10 methylphenidate; 10 of 11 placebo
Robinson et al. (85)	56	Fluoxetine (N 23; 40 mg/day); nortriptyline (N 16; 100 mg/day); placebo (N 17)	12 weeks	HAM-D	Intent to treat: nortriptyline> fluoxetine placebo	Fluoxetine, 14%; nortriptyline, 77%; placebo, 31%	14 of 23 fluoxetine; 13 of 16 nortriptyline; 13 of 17 placebo
Wiat et al. (86)	31	Fluoxetine (N 16; 20 mg/day); placebo (N 15)	6 weeks	Montgomery Åsberg Depression Rating Scale	Intent to treat: fluoxetine>placebo	Fluoxetine, 62%; placebo, 33%	14 of 16 fluoxetine; 15 of 15 placebo
Fruehwald et al. (87)	54	Fluoxetine (N 28; 20 mg/day); placebo (N 26)	12 weeks	Beck Depression Inventory, HAM-D	HAM-D score >15; fluoxetine placebo; HAM-D scores < 13; fluoxetine placebo	HAM-D score <13: fluoxetine, 69%; placebo, 75%	26 of 28 fluoxetine; 24 of 26 placebo
Rampello et al. (88)	31	Reboxetine (N 16; 4 mg/day); placebo (N 15)	16 weeks	Beck Depression Inventory, HAM-D	Reboxetine>placebo for intellectually challenged depressed patients	NR	NR
Choi-Kwon et al. (89)	152	Fluoxetine (N 76; 20 mg/day); placebo (N 76)	3 months	Beck Depression Inventory	Fluoxetine placebo	NR	15 of 76 fluoxetine; 12 of 76 placebo

^a HAM-D=Hamilton Depression Rating Scale, NR=not reported.

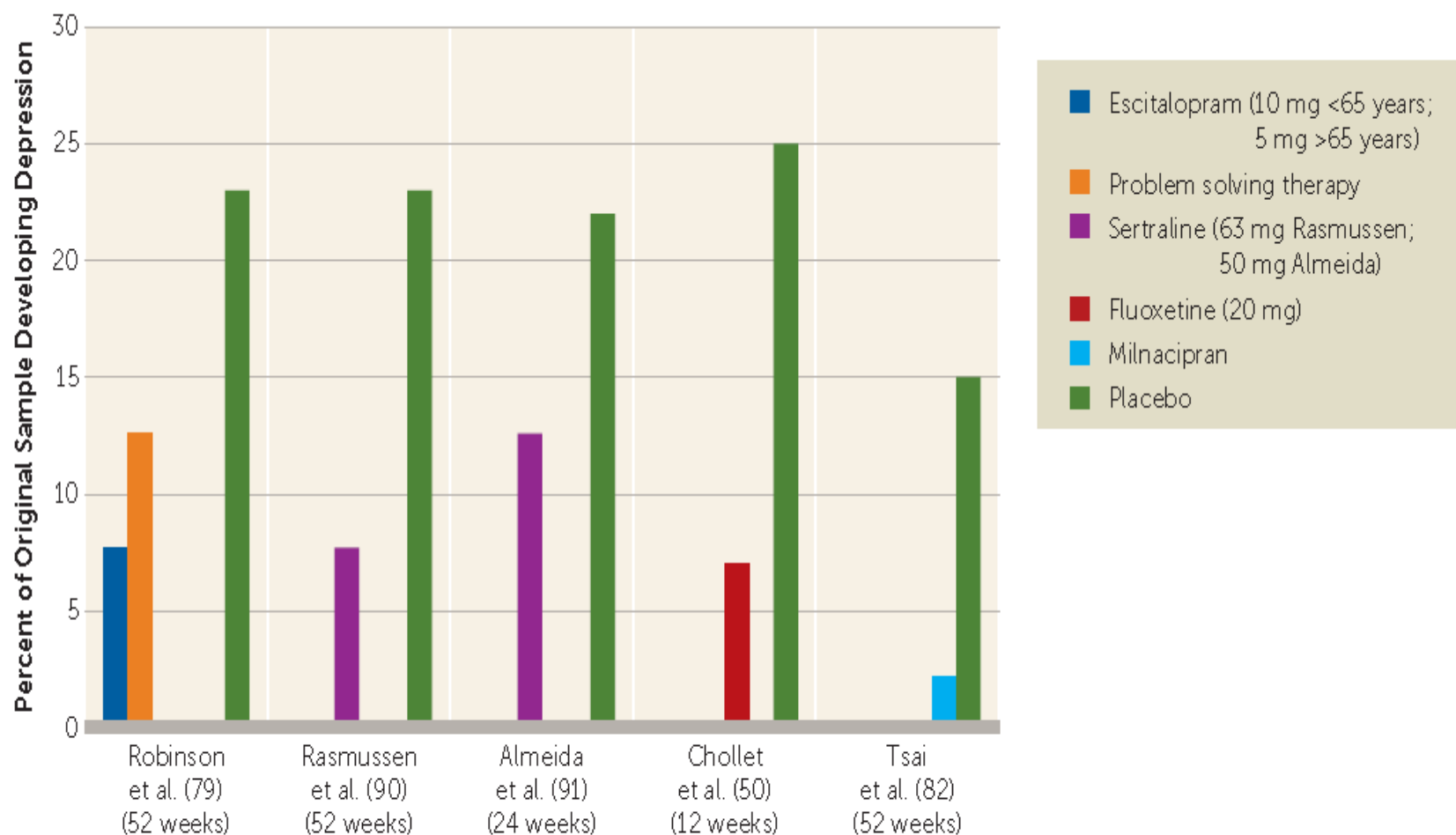
Considerations for treatment with antidepressant medication

- Goal is to choose agent with least potential for side effects and titrate slowly to improve tolerability and compliance with treatment.
- Some agents, such as mirtazapine, may be preferential to treat poor appetite or other vegetative symptoms in some patients.
- In patients with apathy and significant psychomotor retardation, consider initiating treatment with psychostimulant and then convert to SSRI/SSNRI.

Prophylactic treatment to prevent PTSD

- Mirtazapine has shown promise in as acute treatment for prevention of PTSD Niedermaier et al., 2005
- Sertraline has shown promise in the prevention of PTSD as well as in treatment of PTSD symptoms. Poulsen, et al, 2003

FIGURE 3. Randomized Controlled Trials for Evaluation of Preventative Treatments for Poststroke Depression^a



Completers	134	67	56	88	56
Randomized	176	137	92	113	111

^a Although the trials show very similar results in the percent of patients developing depression with placebo or pharmacological treatment, the Robinson et al. (79), Tsai et al. (82), and Chollet et al. (50) trials had sufficient power to demonstrate statistical significance.

Psychostimulant as treatment for PSD

- Limited research regarding use of psychostimulants in PSD
- Increasing clinical use reported, especially in patients with marked vegetative symptoms, apathy, and lethargy.
- Masand, et al psychostimulant study results
 - Primary stimulants used were methylphenidate (Ritalin) and Dextroamphetamine
 - 82% of patients improved with 77% showing marked improvement
 - 51% responded in one day, an additional 34% by the second day
 - Only 2% relapse during treatment
 - 15% incidence of side effects
 - No cases of anorexia, appetite improved with mood.



Non-pharmacological Interventions

- ❑ Counseling and psychotherapy have show little efficacy early in the coarse of PSD.
- ❑ Psychotherapy more effective as adjustment issues emerge later in post-stroke recovery.
- ❑ Early intervention with structured group problem-solving interventions effective in improving quality of life and functioning in both patients and significant others (SO).
- ❑ Psychotherapy with SO shown to significantly improve functional outcomes for patients and may reduce PSD.



Non-pharmacological Intervention

- ❑ Psychotherapy most helpful in patients with milder cognitive and functional impairments.
- ❑ Psychotherapy more effective in patients with minor depression.
- ❑ Research is mixed on effectiveness of community based outreach and support programs.

Canadian Best Practice Recommendations for Stroke Care: 2008

Recommendation 6: Selected Topics in Stroke Management



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Réseau canadien contre
les accidents cérébrovasculaires

6.2 Identification and Management of Post-Stroke Depression

- ❑ All patients with stroke should be considered to be at high risk for depression. At time of the first assessment, the team should determine whether the patient has a history of depression or risk factors for depression.
- ❑ All patients with stroke should be screened for depression using a validated tool.
- ❑ Screening should take place at all transition points and whenever clinical presentation indicates.

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