

# Post-stroke depression

Primary Care & Stroke Prevention Clinic Update  
March 20<sup>th</sup>, Donald Gordon Conference Centre,  
Kingston

Dr. Maria Hussain, MD FRCPC  
Geriatric Psychiatrist  
Assistant Professor  
Department of Psychiatry  
Queen's University

Emily St. Denis, MD MSc  
PGY4 Psychiatry Resident  
Department of Psychiatry  
Queen's University

## Presenter Disclosure



**Faculty: Maria Hussain MD FRC PC  
Emily St. Denis MD MSc**

### **Relationships with commercial interests:**

- Grants/Research Support: None**
- Speakers Bureau/Honoraria: None**
- Consulting Fees: None**
- Other: None**

**At the end of this session the participant will be able to:**

- **Understand the prevalence and impact of Post Stroke Depression (PSD)**
- **Understand the utility of various screening tools for PSD**
- **Develop an approach to management of PSD, with a focus on outpatient management**

# Prevalence of PSD



- 62 000 people with stroke and TIA are treated in Canadian hospitals every year
- PSD: Most frequent psychiatric complication following stroke
- Pooled prevalence of depression at any time after stroke
  - In population studies 22%
  - In hospital studies 30%
  - In rehabilitation studies 30%

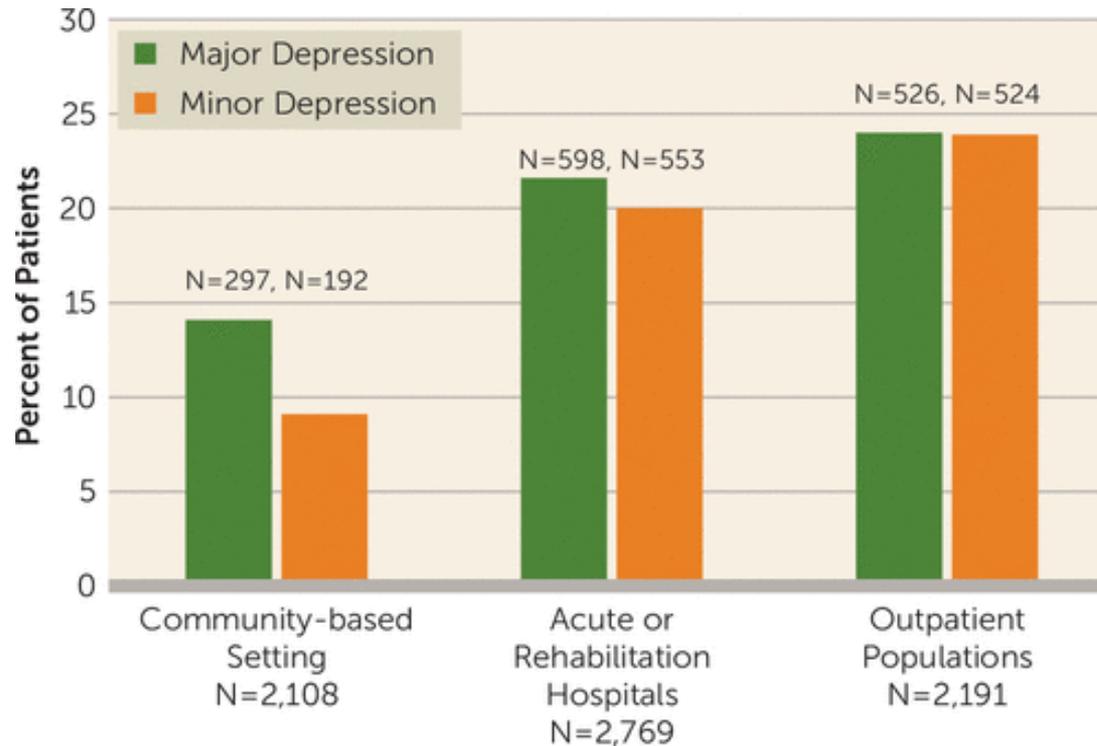
# Risk factors for PSD



- Increased post stroke impairment
- History of depression predating stroke
- Cognitive impairment
- Anxiety
- Social Isolation
- Risk increases exponentially if more than one risk factor is present
- Associated lesions (inconsistent data):
  - Greatest risk with left frontal strokes and left basal ganglia lesions
- Depression itself is a risk factor for the occurrence of stroke with a prospective population based cohort study reflecting a RR=1.73

Ayerbe Stroke 2011  
Morrison J Psychosom Res 2005  
Caeiro J Psychiatry Neurosci 2006  
Jonas Psychosomatic Medicine 2000  
Allan BJPsych 2013

## Why assess and treat?



# Why assess and treat?



- Poorer functional recovery
- Increased risk for dependence
- Poorer cognitive function
- Reduced social participation
- Increased hospital visits, length of stay in hospital
- Increased depression in family and caregivers (30- 60%)
- Suicidal ideation; suicidal death
- Increased mortality risk

# Screening of PSD



- All patients with stroke should be screened for depression using a validated tool (Evidence Levels A)
- Screening should take place at various stages throughout the continuum of stroke care [Evidence Level C]:
  - during acute care stay
  - following hospital discharge to an outpatient or community-based healthcare setting
  - throughout rehabilitation
  - periodically, following discharge to the community

- Major depressive disorder:
  - 5 or more symptoms nearly every day for 2+ weeks:
    - One symptom must be: 1) **Depressed mood** or 2) **loss of interest**
      - Depressed mood most of the day
      - Markedly diminished interest or anhedonia
      - Significant weight loss (unintentional)
      - Insomnia (typical) or hypersomnia (atypical)
      - Psychomotor agitation or slowing
      - Fatigue
      - Feelings of worthlessness or excessive / inappropriate guilt
      - Diminished ability to think, concentrate, make decisions
      - Recurrent thoughts of death or suicidal ideation

# DSM-5 Diagnosis



- Depressive disorder due to another medical condition:
  - Prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all, or almost all, activities
    - With depressive features, major depression-like episode, mixed
  - Onset can be acute or weeks to months after CVA

- Patients with PSD more likely to have:
  - Later age of onset
  - Greater cognitive impairment
  - Less family and personal history of depression
  - Greater physical impairment
- Patients with PSD and executive dysfunction have poor response to treatment with antidepressants and a more chronic and relapsing clinical course



## Differential diagnosis

- Adjustment disorder
  - Number and quality of depressive symptoms will be less
- Post stroke apathy syndrome
  - Will not have mood component
- Post stroke emotional lability (pseudobulbar affect)
  - Can be mistaken for delirium, bipolar disorder
  - Will not have associated happiness or sadness
- Hypoactive delirium, dementia

# Screening and assessment tools



- All patients with stroke should be screened for depression
- Screening complicated by aphasia, cognitive deficits, somatic stroke-related symptoms
- Clinical history, patient interview, mental status examination, collateral from caregivers
- Recommended first line screening tools:
  - Geriatric Depression Scale (GDS)
  - Hospital Anxiety and Depression Scale (HADS)
  - Patient Health Questionnaire – 9 (PHQ-9)
- Consider for aphasic patients:
  - Stroke Aphasic Depression Questionnaire – 10
  - Aphasia Depression Rating Scale



## PSD assessment

	PHQ-9	HADS	GDS	SADQ-10
Rater	Self-Rated or Interviewer Administered	Self-Rated or Interviewer Administered	Self- Rated or Interviewer Administered	Observer/ Caregiver Rated
Time in minutes	2-4	2-5	8-10	2-4
Population	Adults Older adults	Adults Older adults	Developed in Older adults	Stroke Population
Cost	Free	\$	Free	Free
Misc	Based DSM-IV	Both D + A	Possible use aphasia	Rater: Family vs. health professional



### The Patient Health Questionnaire (PHQ-9)

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
3. Trouble falling asleep, 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're 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

Column Totals \_\_\_\_\_ + \_\_\_\_\_ + \_\_\_\_\_

Add Totals Together \_\_\_\_\_

10. If you checked off any problems, how difficult have those problems made it for you to Do your work, take care of things at home, or get along with other people?

- Not difficult at all    Somewhat difficult    Very difficult    Extremely difficult

### Total Score Depression Severity

- 0-4 None
- 5-9 Mild depression
- 10-14 Moderate depression
- 15-19 Moderately severe depression
- 20-27 Severe depression



## The Patient Health Questionnaire-2 (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

- First step approach
- Quick, simple to administer, showed promising results when evaluated in patients with non aphasic stroke
- Cut off score of 3 for depressive disorders
  - Positive screen should be further evaluated with a PHQ-9

Please indicate how often in the last week the patient has shown the following behaviours:

Does he/she have weeping spells?	Sometimes	Rarely	Never
Does he/she have restless disturbed nights?	Sometimes	Rarely	Never
Does he/she avoid eye contact when you talk to him/her?	Sometimes	Rarely	Never
Does he/she burst into tears?	Sometimes	Rarely	Never
Does he/she complain of aches and pains?	Sometimes	Rarely	Never
Does he/she get angry?	Sometimes	Rarely	Never
Does he/she refuse to participate in social activities?	Sometimes	Rarely	Never
Is he/she restless and fidgety?	Sometimes	Rarely	Never
Does he/she sit without doing anything?	Sometimes	Rarely	Never
Does he/she keep him/herself occupied during the day?	Sometimes	Rarely	Never

Sutcliffe Clin Rehab 1998

### SADQ-10

- Scores range from 0-30
- Scores  $\geq 15$  may represent presence of depression (Leeds et al., 2004)

- Non-pharmacological and Adjunct Treatments
- Pharmacotherapy

# Canadian Best Practice Guidelines for Stroke Care: Psychological Management



Queen's  
UNIVERSITY

- Patients should be given information and advice about the impact of stroke, and the opportunity to talk about the impact on their lives [Evidence Level B].
- Patients and their caregivers should have their psychosocial and support needs reviewed on a regular basis as part of long-term stroke management [Evidence Level A].

- There is inadequate evidence at present to support the use of psychotherapy as monotherapy in the treatment of PSD [Evidence Level C].
- Reasonable to consider these therapies as one of the first line treatments for depressive disorders post-stroke, given demonstrated efficacy in primary depressive disorders (Evidence Level A).
- May be used as adjunctive therapies (Evidence Level B)

- Cochrane review: no evidence of effectiveness of psychotherapy to treat depression after stroke
- Since Cochrane review, some encouraging RCTs:
- CALM study:
  - Behavior therapy in aphasic stroke patients offered for 3 months up to 20 sessions
  - maximizing mood-elevating activities
  - education, activity monitoring, activity scheduling, and graded task assignments
  - resulted in improvement in mood as compared to usual care

- 8-week adjunctive nurse-delivered brief psycho-social behavioral intervention in addition to antidepressant
  - Stroke Recovery materials provided
  - Medication diary
  - Education around PSD in sessions
  - Increased pleasant social and physical activity
  - Individualized Problem Solving strategies
- found to be effective as compared to antidepressant alone for remission of PSD at all time points (9wks,6mths,1yr)

# Canadian Best Practice Guidelines for Stroke Care: Antidepressants



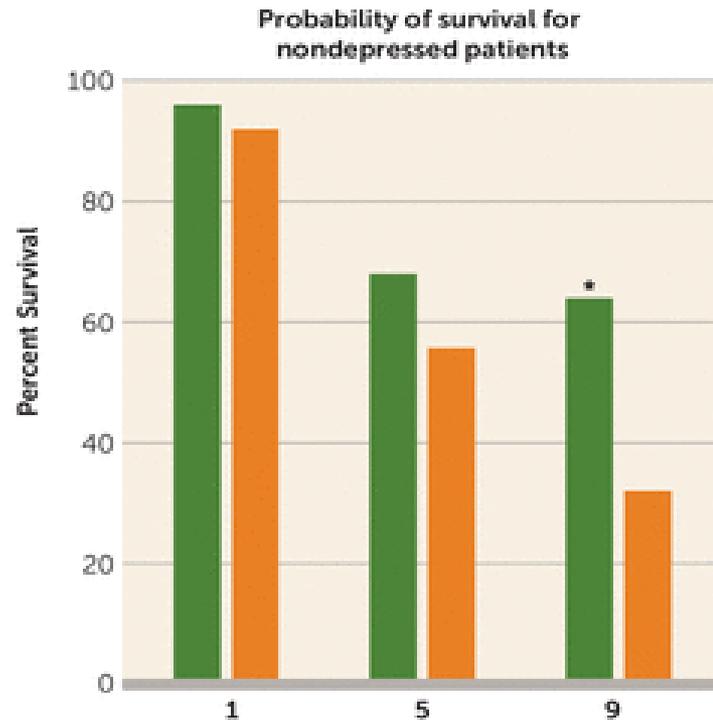
- Patients diagnosed with a depressive disorder should be given a trial of antidepressant medication, if no contraindication exists. [Evidence Level A].
- Treatment should be monitored; should continue for a **minimum of six months** if a good response is achieved [Evidence Level A].

- Meta-analysis of antidepressants for post-stroke depression (10 studies)
  - 8 SSRIs, 2 TCAs, 1 trazodone
  - Recovery or remission of depression: OR: 2.58 (1.56 – 4.26,  $p=0.002$ )
- Cochrane
  - A small but significant effect of pharmacotherapy on treating depression and reducing depressive symptoms was found, as was a significant increase in adverse events.
- Recent meta-analysis replicated finding

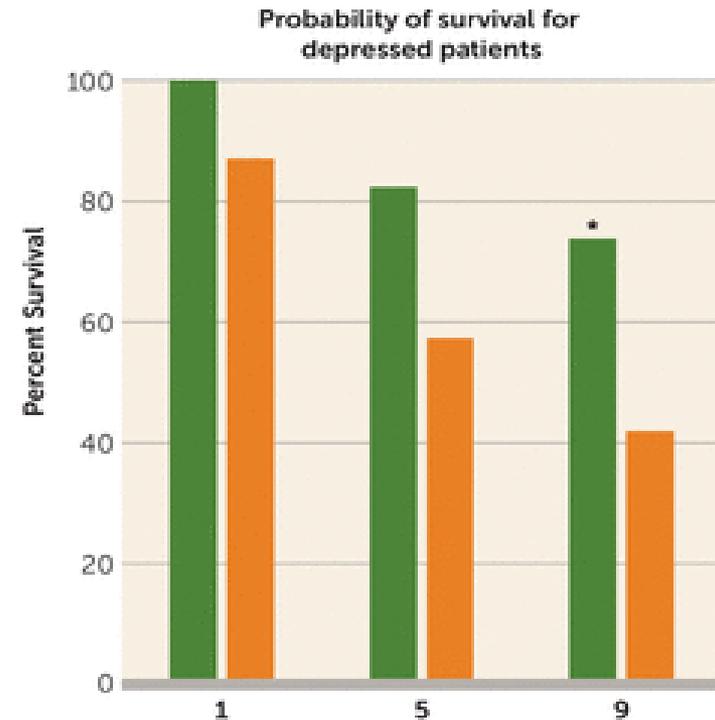
Price, J Neurol Neurosurg Psychiatry, 2011

Hackett, Cochrane, 2008

Xu, Medicine, 2016



Treated	96	68	64
Untreated	92	55.7	32



Treated	100	82.4	73.9
Untreated	87.1	57.4	41.9

- Both TCAs and SSRIs effective for PSD
- Relatively little comparative information on how to make the choice of one AD over another
- SNRIs:
  - Duloxetine vs. Citalopram and Sertraline
  - Duloxetine more effective in reducing symptoms of depression and anxiety

1. Paolucci, Neuropsychiatr Dis Treat. 2008
2. Karaiskos, J Neuropsychiatry Clin Neurosci 2012

# Antidepressants and Risk of Intracerebral Hemorrhage



- Antidepressants increase the risk of bleeding related adverse events:
  - Upper GI bleeds, perioperative bleeding
  - Mediated through anti-platelet aggregation effects of serotonergic antidepressants
- Risk of intracerebral hemorrhage with SSRIs:
  - RR: 1.42 (95% CI: 1.23 – 1.65)
  - RR: 1.5 for antidepressants combined with oral anticoagulants (above anticoagulants alone)
  - Absolute risk: 1/10,000 treated for 1 year

# Antidepressants for Stroke Recovery



- Cochrane review of 52 RCTs<sup>2</sup>
  - Reduced dependency, neurological deficits, depression
  - No benefit in cognitive status and death
  - Insufficient evidence to recommend routine use
- Routine use of prophylactic antidepressants is not recommended in post-stroke patients at this time [Evidence Level A]

# Antidepressants for Stroke Recovery



- RCT of fluoxetine (20 mg daily) vs. placebo for adults with acute ischemic stroke (5-10 days post stroke) treated for 3 months, all patients received physiotherapy
  - Excluded patients with depression
  - Fluoxetine group had significant improvement in motor recovery effect only observed at 90 days
- RCT of problem solving therapy vs. escitalopram in prevention of depression demonstrated cognitive benefit of escitalopram

# Prevention of Post Stroke Depression



- Antidepressants
  - No clear effect of pharmacological therapy on the prevention of depression in a Cochrane review
  - AD prophylaxis was associated with a significant reduction in the occurrence rate of newly developed post stroke depression in another meta-analysis
- PST adapted for use in stroke population, 12 sessions, found to be effective

Hackett, Cochrane, 2008

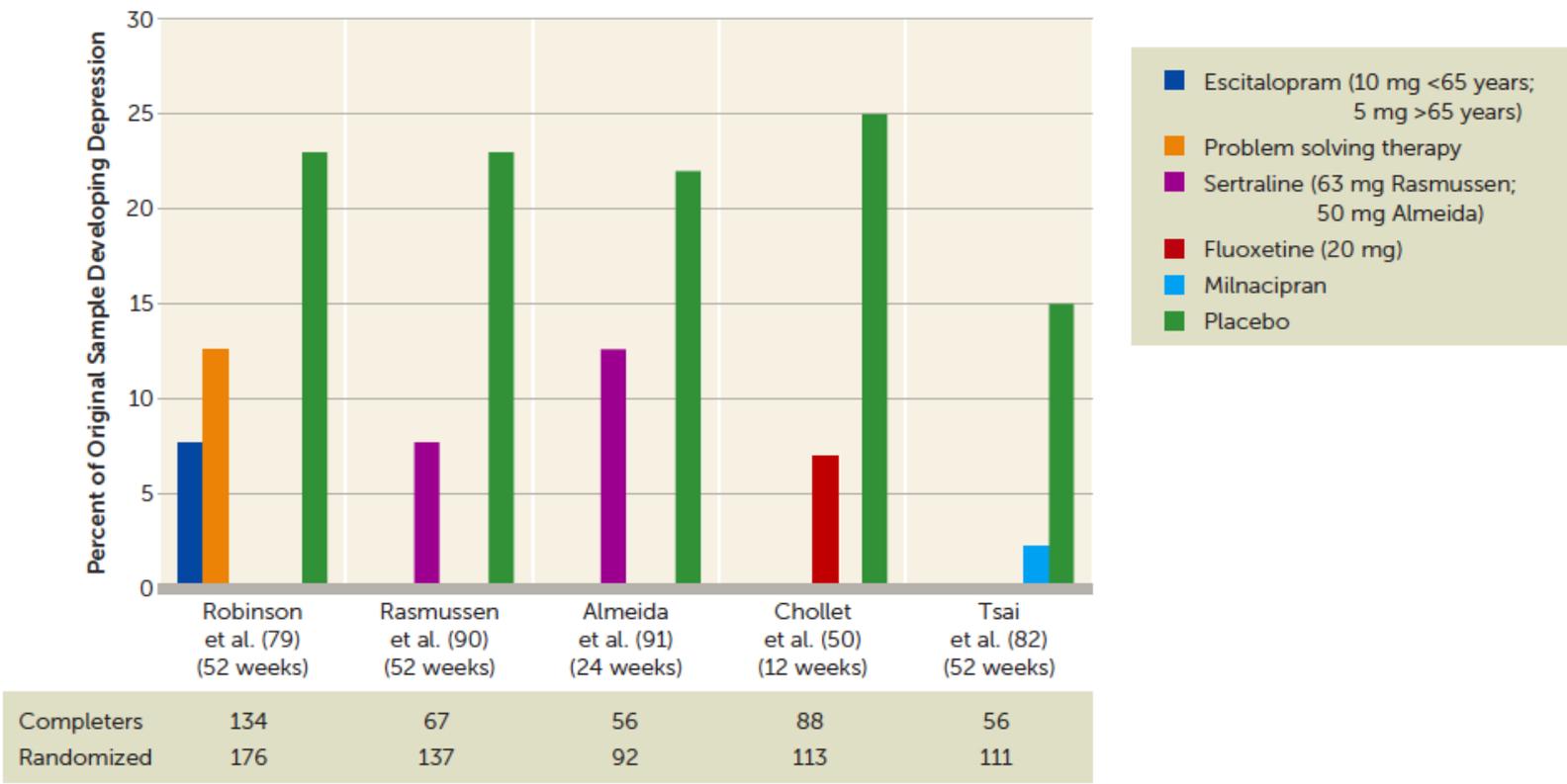
Chen, Int Clin Psychopharmacology 2007

Robinson, JAMA, 2008

# Prevention of Post Stroke Depression



FIGURE 3. Randomized Controlled Trials for Evaluation of Preventative Treatments for Poststroke Depression<sup>a</sup>



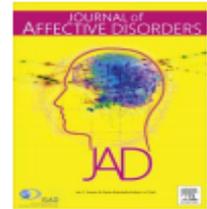
# PSD: Other Treatment Options



Contents lists available at ScienceDirect

## Journal of Affective Disorders

journal homepage: [www.elsevier.com/locate/jad](http://www.elsevier.com/locate/jad)



### Review article

## Repetitive transcranial magnetic stimulation for the treatment of post-stroke depression: A systematic review and meta-analysis of randomized controlled clinical trials



XinYi Shen<sup>a,1</sup>, MingYi Liu<sup>a,1</sup>, Yu Cheng<sup>a,1</sup>, Cui Jia<sup>b,1</sup>, XinYue Pan<sup>a</sup>, QingYun Gou<sup>a</sup>, XinLian Liu<sup>b</sup>, Hui Cao<sup>b</sup>, LuShun Zhang<sup>b,c,\*</sup>

<sup>a</sup> Department of Clinical Medicine, Chengdu Medical College, Chengdu 610500, China

<sup>b</sup> Department of Pathology and Pathophysiology, Chengdu Medical College, Chengdu 610500, China

<sup>c</sup> Development and Regeneration Key Laboratory of Sichuan Province, Department of Neurobiology, Chengdu Medical College, Chengdu 610500, China

### ARTICLE INFO

#### Keywords:

Post-stroke depression

Transcranial magnetic stimulation

Meta-analysis

### ABSTRACT

**Background:** Every year, more than fifteen million people worldwide experience a stroke, nearly 30% of stroke survivors are likely to experience post-stroke depression (PSD). Repetitive transcranial magnetic stimulation (rTMS) is one of the emerging techniques which assist in targeting rehabilitation after stroke. Although deterioration of PSD greatly affects the recovery and quality of life of stroke sufferers, the effect of rTMS therapy has not been systematically studied.

**Objective:** A systematic review and meta-analysis was conducted to determine the effect of rTMS on PSD.

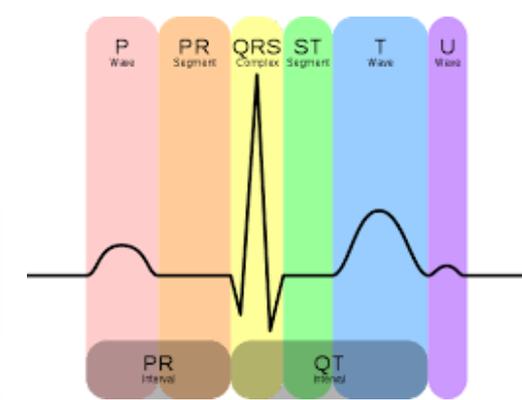
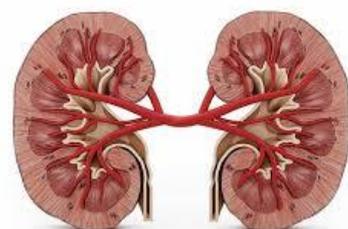
**Methods:** We carried out a systematic review and meta-analysis of randomized controlled trials (RCTs) of rTMS for the treatment of PSD. Primary outcome was severity of depression measured by the Hamilton Depression Rating Scale (HAM-D). Secondary outcomes were response rates, remission rates, stroke severity and ability to perform daily activities.

**Results:** 22 RCTs studies (n=1764 patients) were included. The results demonstrated that rTMS was beneficial on PSD using three scales: HAM-D (MD=-6.09, 95% CI: -7.74, -4.45,  $P < 0.001$ ); response rates (OR=3.46, 95% CI: 2.52, 4.76,  $P < 0.00001$ ); remission rates (OR 0.99, 95% CI: 0.56, 1.75,  $P < 0.00001$ ); National Institutes of Health Stroke Scale (NIHSS) (MD=-2.74, 95% CI: -3.33, -2.15,  $P < 0.001$ ); Activities of daily living (ADL) (SMD=-1.20, 95% CI: 0.68, 1.72,  $P < 0.001$ ); Montgomery-Asberg Depression Scale (MARDE) (MD=-6.21; 95% CI: -9.34, -3.08;  $P=0.0001$ );

**Conclusion:** In present meta-analysis, the positive findings suggest rTMS has beneficial effects on PSD. However, those findings should be treated with caution because of heterogeneity and potential biases.

# Practical tips around choosing pharmacotherapy

- Principles:
  - Evidence
  - Individual factors
    - Comorbidities
    - Drug-Disease Interactions
    - Drug-Drug Interactions
    - Past trials
  - Older adults:
    - start slow, go slow (but go!)
    - Overall dose lower than younger adults



- SSRIs:
  - Least Drug-Disease and Drug-Drug Interaction with Escitalopram, Citalopram and Sertraline
  - Higher drug-drug interactions with Paroxetine, Fluvoxamine and Fluoxetine
  - ↑ QTc: Escitalopram and Citalopram (Max dose 10mg and 20mg respectively in older adults)
- SNRIs:
  - Venlafaxine: Dose adjustment may be needed with eGFR <30
  - Duloxetine: Avoid in severe renal impairment and chronic liver disease

- **Depression is common following stroke and associated with significant disability**
- **All stroke patients should be screened across the continuum of care**
- **There is limited evidence for psychotherapy in PSD at the present time**
- **Antidepressants are effective for PSD, and may also provide cognitive and functional benefit for individuals without depression**

- Geriatric Psychiatry Outreach Programs and Mood Disorder Program through Providence Care Hospital
- Canadian Coalition for Seniors Mental Health
  - [www.ccsmh.ca](http://www.ccsmh.ca)
- Canadian Stroke Best Practices website (healthcare provider information and patient information):
  - [www.strokebestpractices.ca](http://www.strokebestpractices.ca), particularly:
  - <http://www.strokebestpractices.ca/cognition-mood/post-stroke-depression/>
- [www.strokingengine.ca](http://www.strokingengine.ca)



Queen's  
UNIVERSITY

# *Taking Charge of Your Stroke Recovery*

A SURVIVOR'S GUIDE TO THE CANADIAN STROKE  
BEST PRACTICE RECOMMENDATIONS

BE INFORMED | BE INVOLVED | TAKE ACTION



HEART &  
STROKE  
FOUNDATION

CANADIAN  
**Stroke**  
**BEST PRACTICE**  
RECOMMENDATIONS

## Selected References/ Academic Resources



- Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue Following Stroke practice guidelines, update 2015; International Journal of Stroke
- Towfighi, A., Ovbiagele, B., El Husseini, N., Hackett, M. L., Jorge, R. E., Kissela, B. M., ... & Williams, L. S. (2017). Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, 48(2), e30-e43.
- Robinson, R. G., & Jorge, R. E. (2015). Post-stroke depression: a review. *American Journal of Psychiatry*
- Price A, Rayner L, Okon-Rocha E, et al. Antidepressants for the treatment of depression in neurological disorders: a systematic review and meta-analysis of randomized controlled trials. *J Neurol Neurosurg Psychiatry*. Vol 82.2011:914-923.
- Ayerbe, L., Ayis, S., Wolfe, C. D., & Rudd, A. G. (2013). Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. *The British Journal of Psychiatry*, 202(1), 14-21.
- Chollet et al. Fluoxetine for motor recovery after acute ischemic stroke (FLAME): a randomised placebo-controlled trial. *Lancet Neurology* 2011;10:123-130

Thank you



Maria Hussain MD FRCPC

Email: [hussainm@providencecare.ca](mailto:hussainm@providencecare.ca)