Why Am I Blue?
Depression in Stroke: Prevalence, Recognition, and Treatment

Linda Williams, MD
VA HSR&D Stroke QUERI
Indiana University
Regenstrief Institute, Inc.
Overview

• What is PSD and how common is it?
• What is the impact of PSD?
• How do you identify PSD?
• How do you treat PSD?
• Can you prevent PSD?
How many stroke survivors develop PSD?

- 700,000 new strokes yearly in the US
- 595,000 of these ischemic
- **25-30% (175,000)** of all stroke survivors develop PSD
- It is not clear how much “PSD” truly develops *de novo* post-stroke
- **Worse outcomes:** functional, risk factor management, health care utilization, mortality
How can we best identify PSD?
DSM definition of depression

• At least one of these two symptoms:
  1. Depressed mood (feeling down, blue)
  2. Loss of interest in usual activities

• At least three of these symptoms:
  1. Change in sleep
  2. Fatigue
  3. Change in appetite
  4. Feeling worthless
  5. Irritability/anger
  6. Trouble concentrating
  7. Thoughts of death

• These symptoms are present most of the time for at least two weeks
Depression screening tools

• Many symptom-based screening tools
  – Scores generally indicate severity of symptoms
  – Typically validated against a standard clinical interview
  – Various strategies employed to address the issue of screening in patients with multiple medical symptoms

• Fewer tools establish depression diagnosis
  – E.g. differentiate major from minor depression
PSD tools validated in stroke

**Symptom tools**
- Beck Depression Inventory*
- Centers for Epidemiologic Study-Depression Scale
- General Health Questionnaire
- Geriatric Depression Scale
- Hamilton Depression Rating Scale*
- Hospital Anxiety and Depression Scale*
- Kessler-10*
- Montgomery Asberg Rating Scale*
- Post-stroke Depression Scale
- SCL-90

**Diagnostic tools**
- Patient Health Questionnaire-9*
- Zung Depression Scale

*These scales have performed well compared to structured interview (Turner A et al, Stroke 43:1000-5; Kang HJ et al, J Affect Disord 2012)
# Screening and diagnosis: PHQ-9

During the last two weeks, how often have you been bothered by... (not at all = 0, several days = 1, more than half the days = 2, nearly every day = 3)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Little interest or pleasure in doing things.</td>
</tr>
<tr>
<td>2.</td>
<td>Feeling down, depressed, or hopeless</td>
</tr>
<tr>
<td>3.</td>
<td>Trouble falling or staying asleep...or sleeping too much.</td>
</tr>
<tr>
<td>4.</td>
<td>Feeling tired or having little energy.</td>
</tr>
<tr>
<td>5.</td>
<td>Poor appetite...or overeating.</td>
</tr>
<tr>
<td>6.</td>
<td>Feeling bad about yourself, or that you are a failure or have let your family down.</td>
</tr>
<tr>
<td>7.</td>
<td>Trouble concentrating on things, such as reading the newspaper or watching television.</td>
</tr>
<tr>
<td>8.</td>
<td>Moving or speaking so slowly that other people could have noticed...or the opposite, being so fidgety or restless that you were moving around a lot more than usual.</td>
</tr>
<tr>
<td>9.</td>
<td>Feeling that you might be better off dead or of hurting yourself in some way.</td>
</tr>
</tbody>
</table>
PHQ-9 diagnosis of major depression after stroke

Compared to standardized structured clinical interview

PHQ-9 accuracy for PSD

Compared the PHQ-9 to structured psychiatric interview in 200 patients within 1 month of stroke onset:

<table>
<thead>
<tr>
<th></th>
<th>PHQ-9 $\geq$ 10</th>
<th>PHQ-2 $\geq$ 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>91%</td>
<td>83%</td>
</tr>
<tr>
<td>Specificity</td>
<td>87%</td>
<td>84%</td>
</tr>
</tbody>
</table>

PSD is often poorly managed

• **Under-recognized**
  – Epidemiologic studies that do population screening suggest that < 50% of those with PSD are diagnosed
  – Patients and providers misattribute symptoms, natural poststroke focus on other management

• **Under-treated**
  – Lack of diagnosis, assessed as “natural reaction”
  – Many studies show at least 50% with PSD symptoms are untreated; some evidence that treatment is increasing over time

• **Inadequate treatment**
  – 1/3 of patients treated for depression stop meds in the first few weeks
  – Lack of maintenance, treatment adjustments, ongoing monitoring
Can we effectively increase PSD screening and diagnosis?

• Quasi-experimental 2-site study VA HSR&D study comparing the proportion of patients screened and treated for PSD to the rates at these sites in the 12 months prior to the study

• Intervention:
  – **System intervention** at both sites—focus on modifying existing annual depression screening system for all Veterans in Primary Care to target veterans within 6 months of stroke)
  – Based on Chronic Care Model components

*Williams LS et al. J Gen Intern Medicine 2011;26:852-857*
## Menu of system intervention choices

<table>
<thead>
<tr>
<th>Model component</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Resources</td>
<td>Depression symptom pamphlets to stroke survivors</td>
</tr>
<tr>
<td>Decision Support</td>
<td>Provider evidence review session(s)—(nurse and MD)</td>
</tr>
<tr>
<td>Decision support</td>
<td>Provider pocket cards, electronic reminder of depression guidelines</td>
</tr>
<tr>
<td>Delivery system</td>
<td>Dedicated clinic forms to flag stroke patients</td>
</tr>
<tr>
<td>Delivery system</td>
<td>Identification of local champion(s)</td>
</tr>
<tr>
<td>Delivery system</td>
<td>Nurse training for intake interviews to identify veterans with stroke and screen for depression</td>
</tr>
<tr>
<td>Information system</td>
<td>Local CPRS-based automated reminders for PSD screening and treatment</td>
</tr>
</tbody>
</table>
**PSD screening reminder**

Templated screening with all 9 items

Manual scoring triggers provider treatment reminder

---

***This patient has recently suffered a stroke, please complete the PHQ-9 Depression Screen below.***

Over the last 2 weeks, how often have you been bothered by any of the following problems?

1. Little interest or pleasure in doing things.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

2. Feeling down, depressed, or hopeless.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

3. Trouble falling or staying asleep, or sleeping too much.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

4. Feeling tired or having little energy.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

5. Poor appetite or overeating.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

6. Feeling bad about yourself— or that you are a failure or have let yourself or your family down.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

7. Trouble concentrating on things, such as reading the newspaper or watching television.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (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.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

9. Thoughts that you would be better off dead or of hurting yourself in some way.
   - Not at all (0)
   - Several days (1)
   - More than half the days (2)
   - Nearly every day (3)

Was the patient’s total score 10 or GREATER?

- No
- Yes

Stroke education packets are available in clinic. Please provide one to any patient with a history of stroke within the last 6 months.
Provider treatment reminder triggers on positive screen

Reminder Resolution: P-DEPRESSION SCREEN (CVA)

This patient has recently suffered a stroke and also screened positive for depression using the PHQ-9 Depression Severity Scale.

Can see patient responses

Click here to see answers from the PHQ-9 Depression Severity Scale

Below are the Chronic Care Model Interventions available locally. Below are resources and information to help promote guideline-based treatment of post-stroke depression. Please consider providing available educational materials to patients and caregivers, and initiating or modifying antidepressant medications in this patient.

*** Community Resources:

- Check here to order Stroke Specific PESC Referral

*** Decision support for post-stroke depression treatment.

- Depression Increases Negative Outcomes: Depression after stroke is associated with decreased functional recovery and increased mortality.
- Treatments for Post-Stroke Depression: Commonly-used antidepressants in guideline-adherent doses are effective in reducing post-stroke depression symptoms.
- Treatment Non-Response: 20-25% of patients non-responsive to an initial antidepressant medication respond to a change in antidepressant class (e.g. changing from an SSRI to an SNRI or an atypical antidepressant).

Click this box to order a Psychiatry consult

A. In accordance with service agreements
B. If unsuccessfully treated with antidepressant medications.

Depression Medications

- Citalopram Hydrobromide
- Fluoxetine 10mg
- Fluoxetine 20mg
- Venlafaxine

All actions taken result in automatically populated orders to sign and text in provider note
Study results: screening

• PSD screening in the first 6 months after stroke increased from 50% in the control group (N = 374) to 86% in the intervention group (N = 278)
  – OR for screening 6.2 (4.2 – 9.3, p < 0.001)
  – Screening most often done using the PSD reminder
  – 43% of the intervention group screened positive
Study results: treatment

• In those that screened positive for PSD, the treatment reminder was associated with a modest increase in treatment:
  – Action taken in 83% of positive screens (85/102) in the intervention group vs. 73% (44/60) in the control group; p = 0.12
  – Adjusting for intervention, site and number of follow-up visits, the intervention was associated with increased treatment (OR 2.45, p = 0.05)
PSD screening: conclusions

• **Systematic PSD screening is necessary** after stroke to identify treatable condition associated with worse outcomes

• Multiple screening tools exist, **choose one that is easy** to do and actionable
  – Electronic screening reminders can increase screening and diagnosis, they may help prompt treatment

• Work still needs to be done to enhance PSD treatment actions, improve reaction to symptom scores
How can we best treat PSD?
Do common antidepressant treatments also work for PSD?

• **Yes:**
  – Several randomized trials, relatively small
  – SSRIs and nortriptyline, also psychotherapy
  – Emerging treatments (not yet proven):
    • Transcranial magnetic stimulation
  – Cochrane analysis of PSD trials concludes that treatment may reduce symptoms but it is not clear that it successfully treats depression
    • Likely a sample size issue, most trials < 200 subjects
AIM intervention RCT
Evidence-based care management intervention

• **Activate** (1 month post-stroke, patient and family)
  – Review symptoms of PSD; focus on benefits for treating symptoms

• **Initiate treatment** (treatment continued for 12 weeks)
  – Nurse care manager used algorithm to suggest antidepressant med to PC provider or neurologist

• **Monitor** (bimonthly phone contact by nurse care manager)
  – Monitor depression symptoms, medication side effects, compliance
  – Antidepressant dose adjustments using algorithm based on PHQ-9 change

*Williams LS et al. Stroke 2007;38:998-1003*
“Usual care” depressed group

• **Attention control:**
  – Same number of phone calls
  – Focus on reviewing stroke symptoms, antiplatelet or anticoagulant medications

• **Depression treatment:**
  – At the discretion of the provider
  – No monitoring, adjustment of treatment

• **Safeguards for suicidality, severe depression**

• **Providers informed of depression screening results**
Providers chose any antidepressant they wanted; algorithm suggested:

- **History of side effects with paroxetine?**
  - *yes* ➔ **Sertraline 50mg qd**
  - *no* ➔ **Paroxetine 20mg qd**

- **6 weeks: Significant improvement in depression?**
  - *yes* ➔ **Continue same medication**
  - *no* ➔ **Change to venlafaxine 75mg**

- **12 weeks: primary outcome assessment**
## Results: Depression Outcomes

<table>
<thead>
<tr>
<th></th>
<th>AIM</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAM-D % remission</td>
<td>40</td>
<td>22</td>
<td>0.04</td>
</tr>
<tr>
<td>% response</td>
<td>44</td>
<td>30</td>
<td>0.01</td>
</tr>
<tr>
<td>12 week</td>
<td>10.6</td>
<td>13.8</td>
<td>0.004</td>
</tr>
<tr>
<td>PHQ-9 % remission</td>
<td>78</td>
<td>53</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>% response</td>
<td>81</td>
<td>56</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>12 week</td>
<td>6.0</td>
<td>9.5</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
AIM Results:
Depression symptom scores

![Graph showing HAM-D score over weeks for Control and Intervention groups.](image)

![Graph showing PHQ-9 score over weeks for Control and Intervention groups.](image)

**HAM-D score**

**PHQ-9 score**

**mean +/- 2 se**
Other PSD Treatments:
Psychosocial intervention

• 101 patients with PSD
• Randomized to 8-week psychosocial-behavioral intervention plus antidepressant vs. antidepressant alone
• Depression scores significantly lower immediately post-intervention and at 12 months in the behavioral plus medication group

Other PSD Treatments:
Transcranial Magnetic Stimulation

• Emerging therapy in non-stroke related depression
• Small studies in PSD
PSD treatment conclusions

• **Patients with PSD should be offered evidence-based depression treatments**
  – Pharmaceutical: SSRIs, SNRIs, atypicals
  – Psychotherapy: with medication may be better than without in post-stroke patients

• **Neurologists or PCPs** can initiate treatment

• **Ongoing monitoring and adjustment of medications** essential to long-term outcomes
  – Coordination of follow-up care is crucial
Does everyone with stroke need treatment to prevent PSD?
Does everyone with stroke need treatment to prevent PSD?

• Not yet:
  – Depressive symptoms immediately after stroke (tearfulness, agitation) do not mean that the stroke survivor will develop depression
  – Conflicting studies, mostly small, possible Type II error
  – Cochrane review (updated 2008) found 14 trials of 1515 participants; no clear effect of pharmacological therapy on prevention of depression, small but significant effect of psychotherapy on improving mood and preventing depression
  – Clinical judgment: prior depression, younger age, other risk factors
PSD prevention studies

- **Rasmussen A et al; Psychosomatics 2003;44:216**
  - 137 pts; sertraline vs. placebo for 12 months
  - **10% PSD in sertraline group vs. 30% placebo (p<.05)**

- **Almeida et al; J Clin Psychiatry 2006;67:1104**
  - 111 pts w/in 2 wks of stroke; sertraline vs. placebo for 6 months (double-blind)
  - **17% PSD in the sertraline group vs. 22% placebo (NS)**

- **Robinson RG et al; JAMA 2008;299:2391**
  - 176 patients within 3 months of stroke; 12 months of escitalopram vs. problem-solving therapy vs. placebo
  - **22% PSD in placebo, 9% in escitalopram, 12% in therapy**
Post-stroke depression conclusions

• **Common** and associated with significant morbidity and mortality

• Easy to **start treatment**
  – Screening plan is key

• **Treatment monitoring** and follow-up are essential and are more challenging to do well
  – Coordinate generalist-specialist care
  – Involve the patient and family in setting f/u plan
  – Automated telephone-based depression management tools
PSD and depression resources

• AIM PSD treatment algorithm brochures (here)
• MacArthur Foundation Initiative on Depression and Primary Care
  – Toolkit, implementation model: http://www.depression-primarycare.org/clinicians/toolkits/

• U. of Michigan Depression Center
  – Patient resources: http://www.depressioncenter.org/health-information/depression-toolkit/