

# Addressing Psychiatric Issues Prior to HCV Treatment



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# Disclosure Information



- Dr Treisman has not relevant financial affiliations to disclose.

# Outline



- Tools to evaluate depression, anxiety disorder, and bipolar disorder
- Timing and frequency of treatment-related depression
- Prophylactic use of antidepressants

**depression  
demoralization  
substance abuse  
cognitive impairment**

**Mental Illness**

**HCV**

**Illness and treatment**

**impulsivity  
depression  
demoralization  
substance abuse  
cognitive impairment**

# Common Psychiatric Conditions in HCV Patients



- Diseases
  - Depression
  - Bipolar disorder (manic-depressive illness)
  - Schizophrenia
- Problems of life experience
  - Demoralization (hopelessness, learned helplessness, frustration)
  - Trust issues
- Dimensional traits (personality and intellectual problems)
- Addictions and behaviors (covered elsewhere)

# Anxiety



- Differential diagnosis includes:
  - Major depression with prominent anxiety features
  - Generalized anxiety disorder
  - Anxious personality types
  - Anxiety-provoking life circumstances
  - Panic disorder (panic attacks)

# Timing and Frequency of Treatment-Related Depression

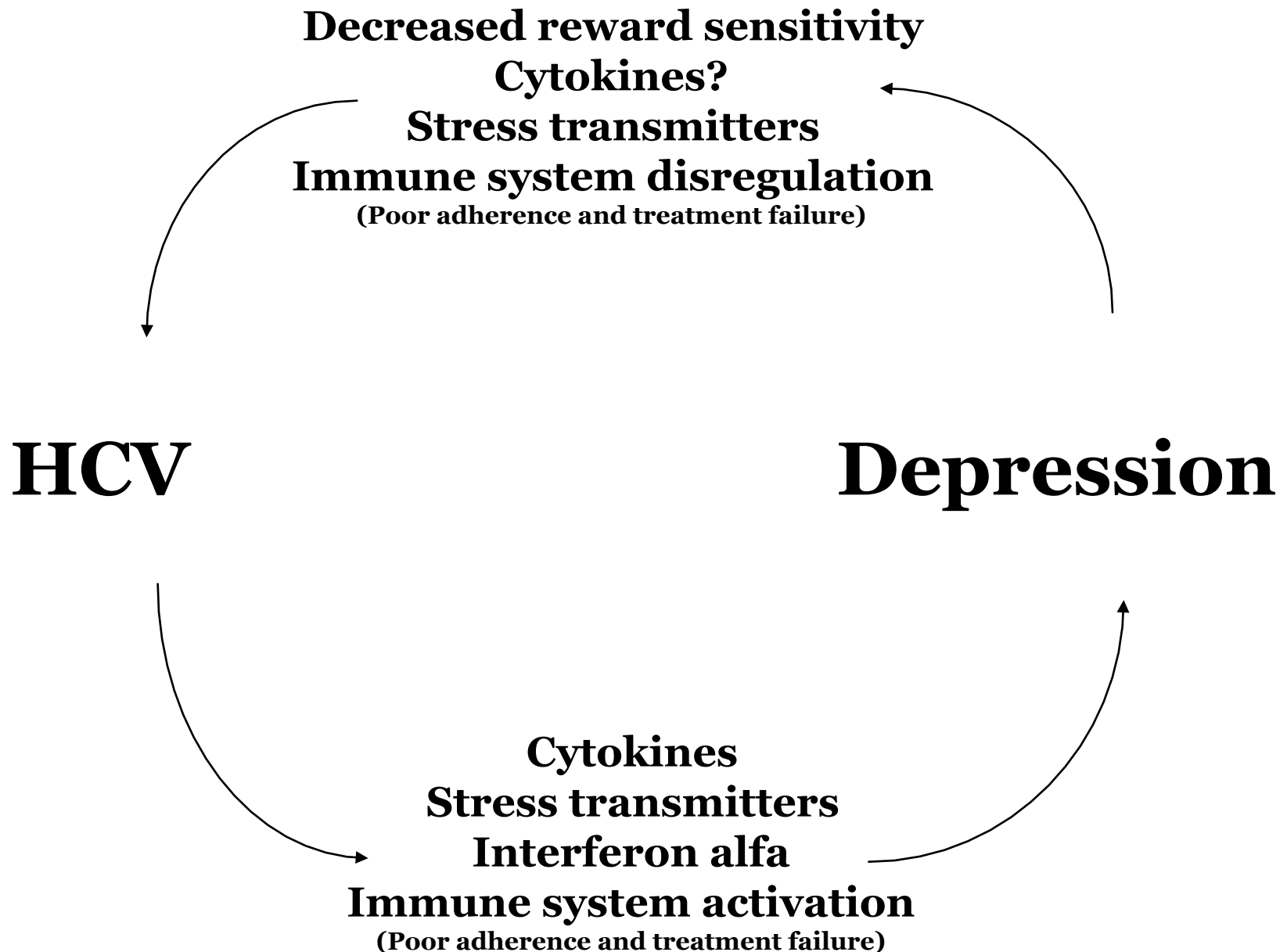


# HCV and Depression

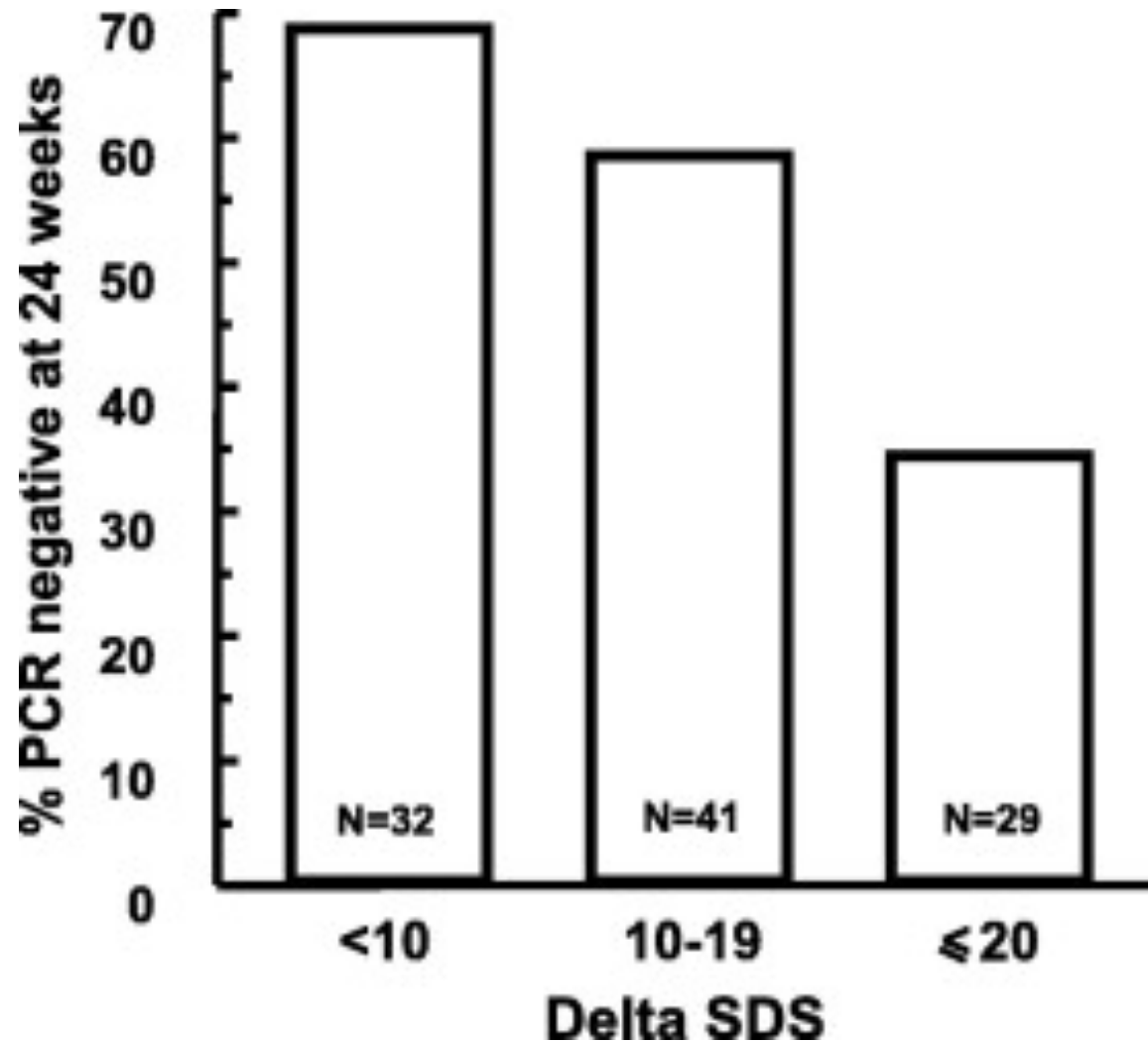


- Depression in 40% to 50%
  - Probably as a consequence of depression-induced risk as well as depression caused by HCV
- Interferon alfa treatment causes depression
- Antidepressant treatment is effective
- Prophylaxis with antidepressants may be effective



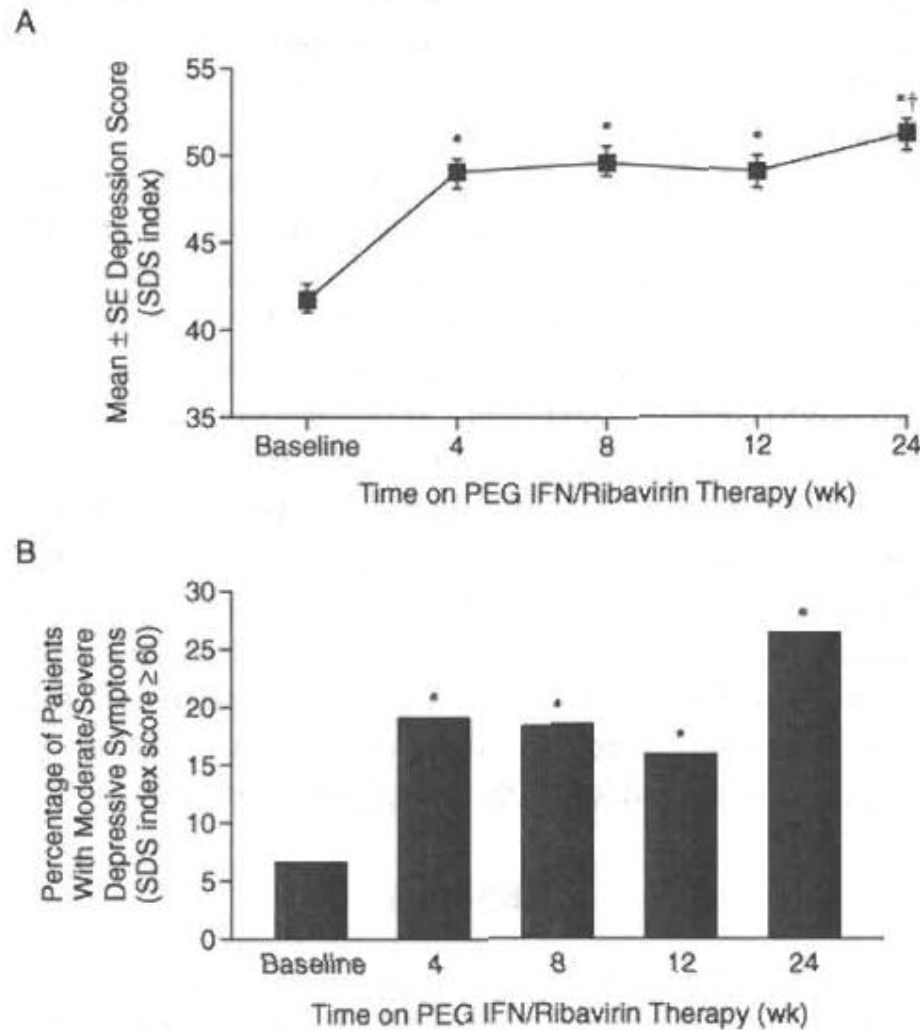


## Depressive Symptoms and Viral Clearance in Patients Receiving Interferon Alfa and Ribavirin for HCV



Raison CL, Broadwell SD, Borisov AS, Manatunga AK, Capuron L, Woolwine BJ, Jacobson IM, Nemeroff CB, Miller AH. *Brain Behav Immun.* 2005 Jan;19(1):23-27.

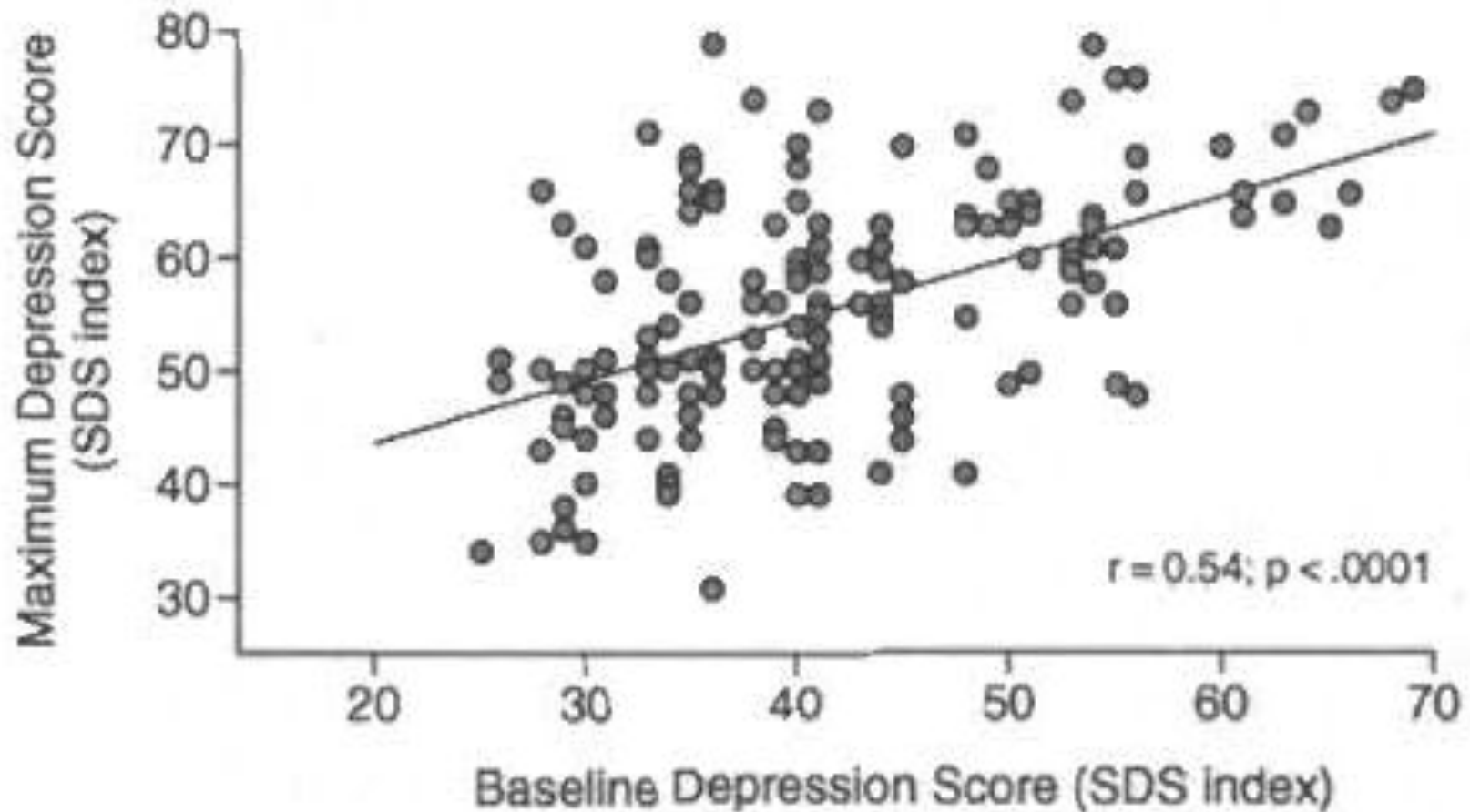
# Depression During Peginterferon Alfa Plus Ribavirin Therapy: Prevalence and Prediction



SDS = Zung Self-Rating Depression Scale

Adapted from Raison CL, Borisov AS, Broadwell SD, Capuron L, Woolwine BJ, Jacobson IM, Nemeroff CB, Miller AH. *J Clin Psychiatry*. 2005 Jan;66(1):41-48

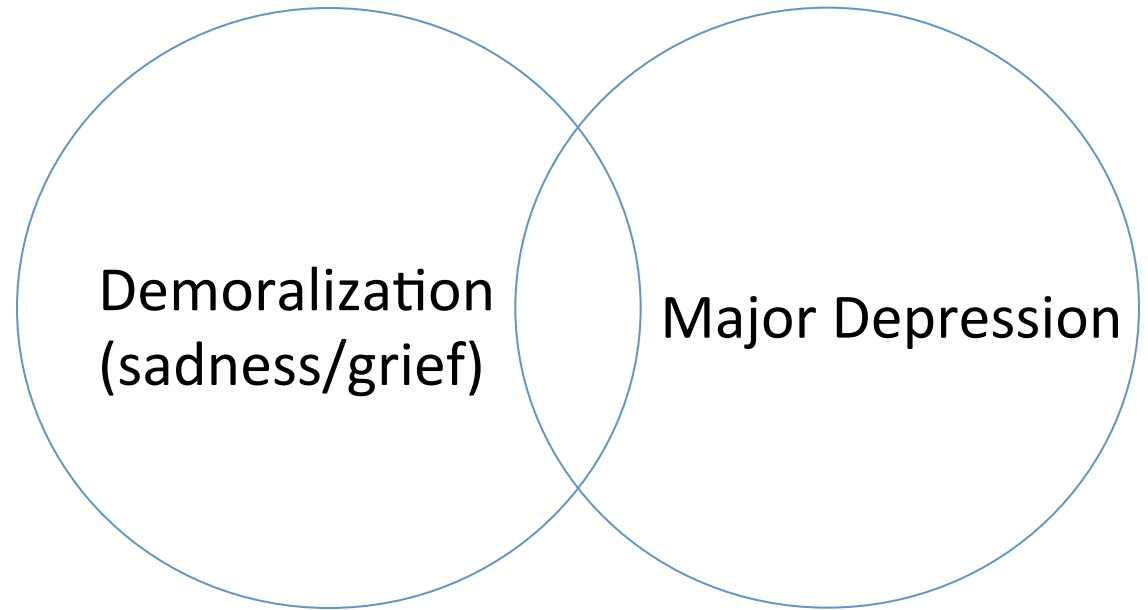
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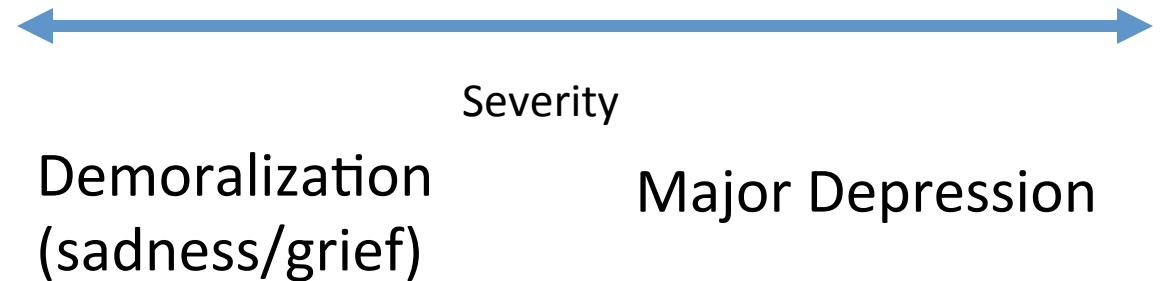
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# Two Ways to Think About Depression

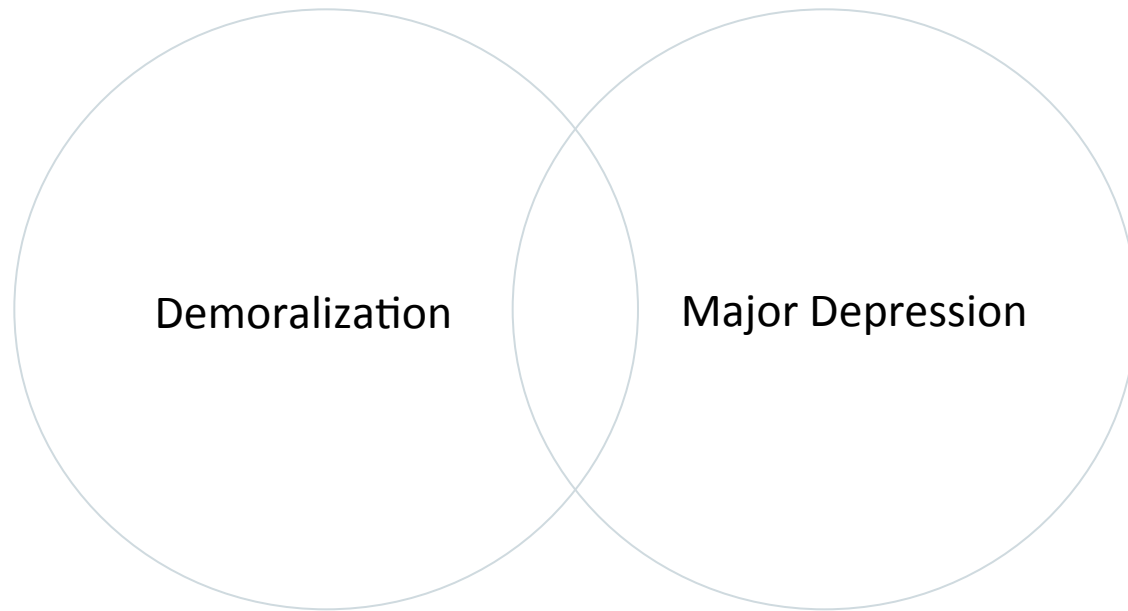
Categorical



Dimensional



# Two Ways to Think About Depression



- **Distractible from loss**  
(Maintains rewards from activity)
- **Initial insomnia**
- **No family history**
- **Unique episode**
- **Stable life course**
- **Responsive to positive events**

- **Anhedonia**  
(Pervasive loss of rewards from activity)
- **AM insomnia**
- **Family history**
- **Similar episodes**
- **Disrupted life course**
- **Unresponsive to positive events**

# Tools to Evaluate Depression, Anxiety Disorder, and Bipolar Disorder



| Screening Instrument  | Administration | Items | Measurements   | Primary Use  |
|---|----------------|-------|--|--------------|
| Beck Depression Inventory (BDI)                             | Self-report    | 20    | Cognitive, somatic subscales   | Clinical     |
| Center for Epidemiological Studies Depression Scale (CES-D) | Self-report    | 20    | Cognitive, somatic subscales<br>(cut scores for clinically relevant symptoms)                                    | Epidemiology |
| Hamilton Rating Scale for Depression (HAM-D)                | Clinician      | 17    | Affective, vegetative subscales  | Research     |
| Hospital Anxiety and Depression Scale (HADS)                | Self-report    | 7     | Screens depression and anxiety; excludes somatic symptoms  | Medical      |
| Patient Health Questionnaire-9 (PHQ-9) Depression Module    | Self-report    | 9     | Keyed to DSM-IV depression diagnostic criteria; also somatic symptoms, anxiety disorders, alcohol and drug abuse | Primary care |



# Validated Tools for Evaluation of Depression and Mental Illness

## Recommended Mental Health Screening Tools From the United States Preventive Services Task Force

| Scale/Assessment  | Number of Questions/Points | Time to Complete |
|---|----------------------------|------------------|
| <b>Depression and Anxiety Disorder</b>                    |                            |                  |
| Beck Depression and Anxiety Inventory (BDI; BAI)          | 21                         | < 10 min         |
| Center for Epidemiologic Studies Depression Scale (CES-D) | 20                         | < 10 min         |
| Hamilton Depression Rating Scale (HAM-D)                  | 21                         | 15 min-20 min    |
| Zung Self-Rated Depression Scale (SDS)                    | 20                         | < 10 min         |
| <b>Dementia and Cognitive Impairment</b>                  |                            |                  |
| Mini-Mental State Exam (MMSE)                             | 0-30                       | 5 min-10 min     |
| HIV Dementia Scale (HDS)                                  | 0-16                       | 5 min-10 min     |

Adapted from Pignone MP, Gaynes BN, Rushton JL, et al. *Ann Intern Med.* 2002;136:765-776; Halverson J. *WMJ.* 2004;103:46-51. 3. Davis HF et al. *AIDS Read.* 2002;12:29-31,38; Power C et al. *J Acquir Immune Defic Syndr Hum Retroviral.* 1995;8:273-278.

Name: \_\_\_\_\_ Marital Status: \_\_\_\_\_ Age: \_\_\_\_\_ Sex: \_\_\_\_\_

Occupation: \_\_\_\_\_ Education: \_\_\_\_\_

**Instructions:** This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

**1. Sadness**

- 0 I do not feel sad.
- 1 I feel sad much of the time.
- 2 I am sad all the time.
- 3 I am so sad or unhappy that I can't stand it.

**2. Pessimism**

- 0 I am not discouraged about my future.
- 1 I feel more discouraged about my future than I used to be.
- 2 I do not expect things to work out for me.
- 3 I feel my future is hopeless and will only get worse.

**3. Past Failure**

- 0 I do not feel like a failure.
- 1 I have failed more than I should have.
- 2 As I look back, I see a lot of failures.
- 3 I feel I am a total failure as a person.

**4. Loss of Pleasure**

- 0 I get as much pleasure as I ever did from the things I enjoy.
- 1 I don't enjoy things as much as I used to.
- 2 I get very little pleasure from the things I used to enjoy.
- 3 I can't get any pleasure from the things I used to enjoy.

**5. Guilty Feelings**

- 0 I don't feel particularly guilty.
- 1 I feel guilty over many things I have done or should have done.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

**6. Punishment Feelings**

- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

**7. Self-Dislike**

- 0 I feel the same about myself as ever.
- 1 I have lost confidence in myself.
- 2 I am disappointed in myself.
- 3 I dislike myself.

**8. Self-Criticalness**

- 0 I don't criticize or blame myself more than usual.
- 1 I am more critical of myself than I used to be.
- 2 I criticize myself for all of my faults.
- 3 I blame myself for everything bad that happens.

**9. Suicidal Thoughts or Wishes**

- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

**10. Crying**

- 0 I don't cry anymore than I used to.
- 1 I cry more than I used to.
- 2 I cry over every little thing.
- 3 I feel like crying, but I can't.

Patient Name: \_\_\_\_\_

Date: \_\_\_\_\_

### Zung Self-Rating Depression Scale (SDS)

Instructions: For each item below, please place a check mark (✓) in the column which best describes how often you felt or behaved this way during the past several days.

| Place check mark (✓) in correct column.                    | A little of the time | Some of the time | Good part of the time | Most of the time |
|--|----------------------|------------------|-----------------------|------------------|
| 1. I feel down-hearted and blue.                           |                      |                  |                       |                  |
| 2. Morning is when I feel the best.                        |                      |                  |                       |                  |
| 3. I have crying spells or feel like it.                   |                      |                  |                       |                  |
| 4. I have trouble sleeping at night.                       |                      |                  |                       |                  |
| 5. I eat as much as I used to.                             |                      |                  |                       |                  |
| 6. I still enjoy sex.                                      |                      |                  |                       |                  |
| 7. I notice that I am losing weight.                       |                      |                  |                       |                  |
| 8. I have trouble with constipation.                       |                      |                  |                       |                  |
| 9. My heart beats faster than usual.                       |                      |                  |                       |                  |
| 10. I get tired for no reason.                             |                      |                  |                       |                  |
| 11. My mind is as clear as it used to be.                  |                      |                  |                       |                  |
| 12. I find it easy to do the things I used to.             |                      |                  |                       |                  |
| 13. I am restless and can't keep still.                    |                      |                  |                       |                  |
| 14. I feel hopeful about the future.                       |                      |                  |                       |                  |
| 15. I am more irritable than usual.                        |                      |                  |                       |                  |
| 16. I find it easy to make decisions.                      |                      |                  |                       |                  |
| 17. I feel that I am useful and needed.                    |                      |                  |                       |                  |
| 18. My life is pretty full.                                |                      |                  |                       |                  |
| 19. I feel that others would be better off if I were dead. |                      |                  |                       |                  |
| 20. I still enjoy the things I used to do.                 |                      |                  |                       |                  |

# Simple Depression Assessment

1. During the past month, have you often been bothered by feeling down, depressed, or hopeless?

☐ Yes

☐ No

2. During the past month, have you often been bothered by having little interest or pleasure in doing things?

☐ Yes

☐ No

If “no” to both, patient is unlikely to have major depression.

If “yes” to either, proceed with the follow-up clinical interview.

# Follow-up Interview for Diagnosis: **SIGECAPSS**

|          |               |   |
|----------|---------------|---|
| <b>S</b> | Sleep         | Disruption in sleep patterns nearly every day?        |
| <b>I</b> | Interests     | Decreased interest and pleasure in usual activities?  |
| <b>G</b> | Guilt         | Feelings of worthlessness or guilt?                   |
| <b>E</b> | Energy        | Decreased energy?                                     |
| <b>C</b> | Concentration | Diminished ability to concentrate?                    |
| <b>A</b> | Appetite      | Change in appetite or weight?                         |
| <b>P</b> | Psychomotor   | Psychomotor retardation or agitation or irritability? |
| <b>S</b> | Suicidal      | Recurrent thought of death or suicide?                |
| <b>S</b> | Sex drive     | Diminished sex drive?                                 |

# Treatment of Depression: SSRIs

| Antidepressant | Approximate Dose   | Advantage/Disadvantage                                |
|----------------|--|---|
| SSRIs          | Easy to use, relatively safe<br>Serotonin syndromes: restlessness, apathy, akathisia<br>Anti-anxiety effects |   |
| Fluoxetine     | 20 mg-40 mg a day*   | Long half life  |
| Sertraline     | 100 mg-200 mg a day*   | Gastrointestinal (GI) activating                      |
| Paroxetine     | 20 mg-60 mg a day*   | Most sedating SSRI<br>Some weight gain                |
| Citalopram     | 20 mg-40 mg a day*   | Black box for QT interval<br>prolongation above 40 mg |
| Escitalopram   | 10 mg-30 mg a day*   | Active isomer of citalopram                           |

\*Doses represent the opinion of Dr Treisman and may differ from the FDA label

# Treatment of Depression: SNRIs

| Antidepressant | Approximate Dose   | Advantage/Disadvantage   |
|----------------|--|--|
| SNRIs          | Similar issues to SSRIs, more GI activation and noradrenergic uptake–related side effects<br>Efficacy in chronic pain<br>Some anti-anxiety effects |  |
| Venlafaxine    | 225 mg-300 mg a day*   | GI activating; I give it BID and use the XR (slow release) formulation |
| Duloxetine     | 60 mg-120 mg a day*  |  |
| Desvenlafaxine | 50 mg-100 mg a day*  |  |
| Milnacipran    | 100 mg-200 mg a day*   | Approved for fibromyalgia but not depression in the USA                |

\*Doses represent the opinion of Dr Treisman and may differ from the FDA label

SNRI = serotonin-norepinephrine reuptake inhibitor



# Treatment of Depression: Others

| Antidepressant                              | Approximate Dose   | Advantage/Disadvantage  |
|---|--|---|
| Bupropion                                   | 300 mg-450 mg a day<br>(I use the XL formulation)            | Most activating; no anti-anxiety effects<br>No weight gain<br>Helpful for smoking cessation |
| Vilazodone (newest antidepressant approved) | 60 mg a day*   | Unclear as of yet   |
| Nefazodone                                  | 200 mg-600 mg a day*   | Rare liver toxicity limits use  |
| Trazodone                                   | 400 mg -600 mg a day*<br>(25 mg-100 mg* for insomnia)        | Quite sedating and mostly used for sleep  |
| Tricyclic antidepressants                   | Expert use but I find them very useful for some HCV patients |   |
| Monoamine oxidase inhibitors                | Expert use but I find them very useful for some HCV patients |   |

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# Bipolar Disorder



- Affective disorder similar to major depression but with episodes of mania as well as depression
- More difficult to treat, expert treatment
- Seen with interferon alfa treatment more rarely than depression but associated
- May not be diagnosed until antidepressants trigger an episode of mania

# Manic Episode: DSM-IV Definition



- A) Abnormally elevated or irritable mood for 1 week and...
- B) 3 or more of the following:
  - Inflated self-esteem or grandiosity
  - Decreased need for sleep
  - More talkative than normal
  - Flight of ideas or racing thoughts
  - Distractibility
  - Increased activity or psychomotor agitation
  - Excess in pleasurable activities with potential for painful consequences
- C) The symptoms MUST cause 1 of the following:
  - Marked impairment in functioning
  - Hospitalization to prevent harm to self or others
  - Psychotic features

# Prophylactic Use of Antidepressants



# **Trials for Prophylaxis of Interferon Alfa–Induced Depression**



- Several positive studies for paroxetine and citalopram (or escitalopram)
- Several failed trials with paroxetine and citalopram (or escitalopram)
- My current recommendation:
  - If the patient has a clear history of major depression that responded to treatment, prophylaxis with that drug
  - If the patient has a clear history of major depression that was severe, prophylaxis with the drug of your choice

# Take-Home Messages



- Screen for depression before treatment and at every visit after starting treatment
- Seeing psychiatric patients more often and treating comorbidity improves outcome
- Collaborative treatment with mental health and addiction specialists improves outcome

# End



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