Didactic Series

Getting to zero *depression* among HIV-infected persons

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Learning Objectives

1) To learn what is needed to diagnose depression
2) How to select an antidepressant
3) Strategies to manage antidepressant treatment
Question 1

What’s the most disabling condition worldwide?
A) Depression
B) Low back pain
C) HIV
### Burden of disease

**Rankings of leading causes of disease burden**

<table>
<thead>
<tr>
<th></th>
<th>Global</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV</td>
<td>Depression</td>
<td>HIV</td>
</tr>
<tr>
<td>YLL</td>
<td># 6</td>
<td># 13*</td>
<td># 26</td>
</tr>
<tr>
<td>YLD</td>
<td># 36</td>
<td># 2</td>
<td># 50</td>
</tr>
<tr>
<td>DALYs</td>
<td># 5</td>
<td># 11</td>
<td># 37</td>
</tr>
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</table>

YLL - Years of Life Lost due to premature mortality  
YLD – Years of Life lived with Disability  
DALYs – Disability Adjusted Life Years  
*Self-harm / Suicide

Depression prevalence

- HIV in the US general population
- Depression in the US general population
- Depression in HIV-infected men and women in the US

Bing et al. 2001; Mimiaga et al. 2015
Question 2:

Which of these symptoms are required to diagnose depression?

A. Depressed mood most of the day, nearly every day
B. Markedly diminished interest or pleasure in activities
C. Feelings of worthlessness or excessive or inappropriate guilt
D. Significant distress or impairment in social, occupational, or other important areas of functioning.
Diagnosis of major depression

5 or more during the same 2-week period:
1. Depressed mood most of the day, nearly every day
2. Markedly diminished interest or pleasure in activities
3. Significant weight loss or decrease or increase in appetite
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation nearly
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive or inappropriate guilt
8. Diminished ability to think or concentrate or indecisiveness
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
Diagnosis of major depression

• Not due to a substance (e.g., a drug of abuse, a medication) or a medical condition (e.g., hypothyroidism)
• Not due to Bereavement
• Not Schizoaffective Disorder or other form of psychosis
• Not Bipolar Disorder: No history of a Manic Episode, a Mixed Episode, or a Hypomanic Episode
• Significant distress or impairment in social, occupational, or other important areas of functioning.

DSM5 2014
**Depression screening tools**

| PHQ-9 | PHQ-2 | BDI-II | CES-D | HAM-D | Etc. |

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

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

<table>
<thead>
<tr>
<th><strong>Problem</strong></th>
<th><strong>Not at all</strong></th>
<th><strong>Several days</strong></th>
<th><strong>More than half the days</strong></th>
<th><strong>Nearly every day</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>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</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**For office coding**

\[
\text{Score} = 0 + \text{___} + \text{___} + \text{___} + \text{___} \\
\text{Total Score: ___}
\]

If you checked off **any** problems, how **difficult** have these 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

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Development of a screening tool: Haiti

- 13 items including 3 idioms of distress were selected:
  - Effect size (Cohen’s $d > 0.3$)
  - Mean difference ($p < 0.1$)
  - Patient comprehension

- Associated with functional impairment
  - Correlated with WHODAS-II scores, $r = .705$ ($p < .001$)

- Acceptable sensitivity and specificity in ROC analysis

Rasmussen et al., 2015
Depression treatment

• Psychotherapies
  – Cognitive behavioral therapy
  – Interpersonal therapy
  – Etc.

• Pharmacotherapies

• Somatic therapies
  – ECT
  – TMS
Antidepressants and HIV

Directly Observed Antidepressant Medication Treatment Study (PI: David Bangsberg, MD, MPH)

• Non-blinded, randomized controlled trial among HIV-infected, homeless or marginally-housed adults in San Francisco

• Treatment group: Directly observed once-weekly fluoxetine for 6 months followed by self-administered once-weekly fluoxetine for 3 months

• Control group: Referral to a nearby community clinic for psychiatric care

R01MH054907
PI: David Bangsberg, MD, MPH
Directly observed fluoxetine

Significant benefit of fluoxetine comparable to other antidepressant trials

Tsai et al. 2013
Directly observed fluoxetine:
Alcohol use

Study month

Grelotti et al. 2016
Directly observed fluoxetine: Drug use

Grelotti et al. 2016
Question 3

Which antidepressant would be considered one of the “first line” choices for a person with uncomplicated MDD and HIV?

A. Sertraline (Zoloft)
B. Once daily bupropion (Wellbutrin XL)
C. Once daily venlafaxine (Effexor XR)
D. Mirtazapine (Remeron)
Question 4

Which antidepressant might be the best first choice for a person with MDD, HIV and neuropathic pain?
A. Sertraline (Zoloft)
B. Once daily bupropion (Wellbutrin XL)
C. Once daily venlafaxine (Effexor XR)
D. Mirtazapine (Remeron)
Question 5

Which antidepressant might be the best first choice for a person with MDD, HIV, and weight loss or difficulty sleeping?

A. Sertraline (Zoloft)
B. Once daily bupropion (Wellbutrin XL)
C. Once daily venlafaxine (Effexor XR)
D. Mirtazapine (Remeron)
Question 6

Which antidepressant might be the best first choice for a person with depression who smokes cigarettes?

A. Sertraline (Zoloft)
B. Once daily bupropion (Wellbutrin XL)
C. Once daily venlafaxine (Effexor XR)
D. Mirtazapine (Remeron)
Depression (uncomplicated)

- **Starting dose**: Zoloft (sertraline) 25 or 50 mg Daily
- **Typical titration**: Increase by 25-50 mg Q4 weeks as needed/tolerated (typical dose 100-200 mg; max 200 mg/day)
- **Side effects**: Nausea, diarrhea, dizziness, headache
- **Caution**: Hepatic impairment
- **Interactions**: No major interactions with common ARVs. Cobicistat and ritonavir may increase sertraline; darunavir and efavirenz may decrease sertraline
Depression and smoking cigarettes

- **Starting dose**: Wellbutrin XL (bupropion ER) 150 mg Daily
- **Typical titration**: Wellbutrin XL 150 mg Daily x 4 weeks and then increase to 300 mg Daily (typical dose 300 mg; max dose 450 mg / day)
- **Side effects**: Insomnia, anxiety, nausea, weight loss, headache
- **Contraindications**: h/o seizures, any concern for an eating disorder
- **Caution**: Hepatic and Renal impairment
- **Interactions**: No major interactions with common ARVs. Ritonavir and efavirenz may decrease bupropion
Depression and [neuropathic] pain

- Starting dose: Effexor XR (venlafaxine ER) 37.5 - 75 mg Daily
- Typical titration: Increase by 37.5 - 75 mg q 4 weeks (typical dose 150 mg, max dose 225 mg)
- Side effects: headache, dizziness, drowsiness, insomnia, and nausea
- Caution: Hepatic and Renal impairment
- Interactions: No major interactions with common ARVs. Cobicistat, ritonavir, and darunavir may increase venlafaxine
Depression and difficulty sleeping and/or weight loss

- Starting dose: Remeron (mirtazapine) 7.5 – 15 mg QHS
- Typical titration: Increase by 7.5 – 15 mg Q4weeks to 15 – 30 mg QHS (typical dose 15-30 mg; max dose 45 mg QHS)
- Side effects: Drowsiness, increased appetite (weight gain), dry mouth, vivid dreams
- Caution: Hepatic and Renal impairment
- Interactions: No major interactions with common ARVs. Ritonavir may increase mirtazapine
Psychiatric prescribing guide

DEPRESSION
• Depression (uncomplicated)
• Depression and smoking cigarettes
• Depression and pain
• Depression and difficulty sleeping and/or weight loss

ANXIETY
• Anxiety disorders
• As needed medication

INSOMNIA

BENZODIAZEPINES

ADHD

NIGHTMARES IN SETTING OF PTSD
Depression Treatment: SLAM-DUNC

- “Measurement-Based Care” (MBC)
- Captures best practice:
  - Treatment algorithms
  - Defined windows for follow up
  - Systematic screening for depressive symptoms and side effects
- Uses a Depression Care Manager to provide data and recommendations to providers

Pence et al. 2012
MBC: Initial visit

Week 0 (Baseline visit)

Baseline visit

PHQ-9 ≥ 10 → MDD confirmed → Bipolar and psychotic disorders ruled out

Not currently on AD → Start AD

Currently on AD, less than adequate trial

SEs tolerable

On AD ≥ 4 wks → Increase dose

On AD < 4 wks → Maintain dose

SEs distressing → Address SEs or switch to new AD

Next phone call in 2 weeks. Return to clinic in 4 weeks.
MBC: Results

- US RCT of MBC (149 patients) vs “usual care” (155 patients)
  - Greater improvement in depression over 6 months
  - Reduction in suicidal ideation
- Cameroon “open” trial
  - 41 patients with depression
  - Amitriptyline was used
  - Significant reduction in depressive symptoms over 4 months
  - 90% of patients achieved remission in 4 months

Pence et al. 2015
Gaynes et al. 2015
MBC Haiti: RCT

• SLAM DUNC was adapted for Haiti and used at GHESKIO (Groupe Haïtien d'Etude du Sarcome de Kaposi et des Infections Opportunistes) using non-specialist health workers

• Participants were randomized to MBC or “enhanced care”
  – 482 patients were screened
  – 21% had confirmed major depression
  – 43 received MBC, 35 received enhanced care
  – Participants were 61% female
  – Mean age was 34.7 years

• Preliminary findings are available for depression symptom severity.

R21MH103054 PI: Jessy Dévieux, PhD
MBC: Haiti

Doz pou n sonje:
- Doz pou komanse tretman an: 10 mg (1/2 grenn) chak maten
- Pi piti doz pou nou bay: 5 mg (1/4 grenn) chak maten
- Pi gwo doz pou nou bay: 60 mg (3 grenn) chak maten

Gid Doz medikaman an pou chak visit (CDP: Critical Decision Points):
- Semèn 0 – Komanse ak 10 mg (1/2 grenn) chak maten
- Semèn 4 – si li nesesè ogmante a 20 mg (1 grenn) chak maten
- Semèn 8 – si li nesesè, ogmante a 40 mg (2 grenn) chak maten
- Semèn 12 – si li nesesè, ogmante a 60 mg (3 grenn) chak maten

Si pasyan an gen anpil efè segondè ak doz li genyen an, bay li doz ki pi piti ke sa lap pran nan moman an:
- Ak 10 mg chak maten, si efè segondè deranje pasyan an twòp, bese doz la a 5 mg chak maten
- Ak 20 mg chak maten, si efè segondè deranje pasyan an twòp, bese doz la a 10 mg chak maten
- Ak 40 mg chak maten, si efè segondè deranje pasyan an twòp, bese doz la a 20 mg chak maten
- Ak 60 mg chak maten, si efè segondè deranje pasyan an twòp, bese doz la a 40 mg chak maten
MBC Haiti: Depression outcomes

Study Month

PHQ 9 score

MBC

Control

P = .023

Jean-Gilles et al. 2016
Summary

• Depression is a highly disabling
• Antidepressant treatment works
• Antidepressant treatment treats depression and likely improves HIV treatment outcomes
Recommendations

1. Screen for depression
2. Start treatment for depression
3. Manage antidepressant treatment or refer to a psychiatrist
References


