Screening for depression in patients with HIV

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High prevalence of psychiatric disorders in PLWHIV

- Retrospective data from the US (n=7834) showed 53% had documented psychiatric condition[1]
  - Mood disorders are the most prevalent[1]
- Substance use is also common: 20–70%[2–5]
- Similar results in developing countries[6]
  - Data from four similar studies in Africa showed that approximately half of PLWHIV had a psychiatric disorder[6]
- Data from face-to-face interviews (n=34,653)[7]
  - HIV more strongly associated with psychiatric disorders in men than in women[7]

PLWHIV: people living with HIV

1. Parhami I, et al. *AIDS Behav* 2013; 17(8):2792–801; 2. Bing E, et al. *Arch Gen Psychiatry* 2001; 58(8):721−728; 3. Kessler RC, et al. *Arch Gen Psychiatry* 2005; 62(6):617−627; 4. Pence BW, et al. *J Acqui Immune Defic Syndr* 2006, 42(3):298-306; 5. Beyer JL, et al. *Psychosomatics* 2007; 48: 31−37;
6. Brandt R. *African J AIDS Res* 2009; 8:123−33; 7. Lopes M, et al. *J Clin Psychiatry* 2012; 73(3):384−391.

Depression in HIV

- **Depression is very prevalent in HIV**

Prevalence (%)	USA[1]		EU[2]
	PLWHIV	Controls	PLWHIV
Major depressive disorder	36	16.6	26
Dysthymia	26.5	2.5	17.3

1. Bing E, et al. *Arch Gen Psychiatry* 2001; 58(8):721−728; 2. Schadé A, et al. *BMC Psychiatry* 2013; 13:35.

High prevalence of psychiatric disorders: Why?

- HIV infection is higher among certain at-risk groups, such as injection drug users and patients with severe mental illness[1] (psychiatric – primary - comorbidity)
- Adjustment reaction to stressful life-events related to HIV infection[2] (psychological)
- Neurologic complications associated with HIV were recognized very early in the epidemic[3] (neurological)
- Medical conditions caused by HIV infection may produce psychiatric symptoms[4] (medical)
- Some HIV treatments can produce psychiatric side-effects[5] (toxic)

1.Beyer JL, et al. *Psychosomatics* 2007; 48:31−37; 2. Patterson TL, et al. *Psychiatry*. 1995;58(4):299–312; 3. Dube B, et al. *J Psychiatry Neurosci* 2005; 30(4):237–246; 4. Neurological Complications of HIV. Available at: http://www.hopkinsmedicine.org /healthlibrary /conditions/nervous_system_disorders/neurological_complications_of_hiv_134,46/ (accessed November 2013).
5. Treisman GJ, Kaplin AI. *AIDS* 2002; 16:1201–1215.

Medical differential diagnosis of HIV related depressive illness

- Substance abuse
- Endocrine abnormalities (thyroid disease, hypogonadism, adrenal insufficiency)
- CNS opportunistic illnesses and cancers
- CNS HIV and HCV cognitive disorders

HIV-related medications that may induce mood disorder symptoms

- Steroids: depression or euphoria
- Interferon: neurasthenia, fatigue syndrome, depression
- Zidovudine: depression or euphoria
- Efavirenz: decreased concentration, depression, nervousness, nightmares

Major depression in persons with comorbid medical illness, including HIV infection, has been associated with:

- Decreased survival
- Impaired quality of life
- Decreased adherence to antiretroviral therapy (ART)
- Increased risk behaviors
- Suicide
- Longer hospital stays and more frequent medical visits (e.g., emergency room and/or medical clinics)
- Higher treatment costs

Depression in HIV Clinics

Depression in HIV patients is underdiagnosed[1]

High prevalence

Depression in HIV is undertreated[1]

Poorer outcome of HIV desease

health costs

quality of life

However: once treated, adherence improves, preventing illness progression = good prognosis[2,3]

1. Rodkjaer L, et al. *HIV Med* 2010; 11(1):46−53
2. Cook JA, et al. *AIDS Care* 2006; 18:93-100;
3. Yun LWH, et al. *J Aquir Immune Defic Syndr* 2005; 38:432−38.

Diagnosing depression in a non psychiatric setting

1. Difficulties related to the health care providers
2. Difficulties related to the patients / illness

Diagnosing depression in a non psychiatric setting

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2. **Difficulties related to the patients / illness**

Diagnosing depression in a non psychiatric setting

- primary care physicians detect clinical cases of depression less than 50% of the time
- Due to:
  - depressed patients may only tend to report somatic symptoms to their physician
  - physicians may feel less comfortable investigating cognitive and affective manifestations of depression
  - unavailability of mental health resources in the medical setting and the short duration of medical consultations
  - common belief that depression is normal or even appropriate in HIV-infected patients

How to solve this problem: screening tools for depression

- it is crucial to provide the health care providers an effective tool to better detect depression so they can offer an appropriate treatment
- the utilization of self-report scales could also improve physicians' and other health care providers‘ ability to screen depression in HIV-seropositive patients.

Diagnosing depression in a non psychiatric setting

1. Difficulties related to the health care providers
2. **Difficulties related to the patients / illness**

Somatic symptoms of depression

- most depression measures contain somatic items that may also represent HIV symptoms (e.g., weight and appetite loss, insomnia, fatigue
- somatic items found in depression measures confound the assessment of depression in HIV-infected patients (Kalichman 1995)
- higher scores on depression scales mainly because they present more HIV related symptoms that mimic depressive symptomatology
- In HIV, it's difficult to differentiate between:
  - major depression (psychiatric)
  - reactive depression (psychological)
  - depression due HIV infection in the brain (secondary)
- in HIV patients these three diagnoses represent a continuum of depressive symptoms rather than three separate categorical diagnoses (Holland 2008)

Diagnostic criteria of MDD: DSM-5

- Depressed mood
- Loss of interest or pleasure
- Decrease in appetite
- Insomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of excessive guilt
- Diminished ability to think or concentrate
- Recurrent thoughts of death, *recurrent suicidal ideation*

American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); Arlington, VA: American Psychiatric Publishing.

Confounding symptoms of depression in HIV

- **Sleep disurbances may be present in up to 97% of PLWHIV vs 33% of the general population[1]**
  - **Multifactorial:[2]**
    - **Psychiatric disorders**
    - **HIV, ART, opportunistic diseases**
    - **Brain injury/dementia**
- **Fatigue: hypogonadism 30%[3]**
  - **Neurocognitive impairment: can resemble depression**
- **Suicide:**
  - **Less prevalent than in the beginning of the epidemics[4]**
  - **Now: still more than 3 times higher than in the general population[5]**
  - **Psychiatric, biological, social vulnerability[6]**

ART, antiretroviral therapy

1. **Low Y et al. AIDS Rev 2014**; 2. **Low Y et al. AIDS Rev 2014**
Omonuwa TS, et al. *J Clin Sleep Med* 2009; **5**(3):251−62.
3. Crum NF, et al. *AIDS Patient Care STDS* 2005; **19**:655–671; 4. Marzuk PM, et al. *JAMA* 1988; **259**(9):1333−1337.
5. Keiser O, et al. *Am J Psychiatry* 2010; **167**:143–150; 6. Carrico AW. *Am J Psychiatry* 2010; **167**:117–119.

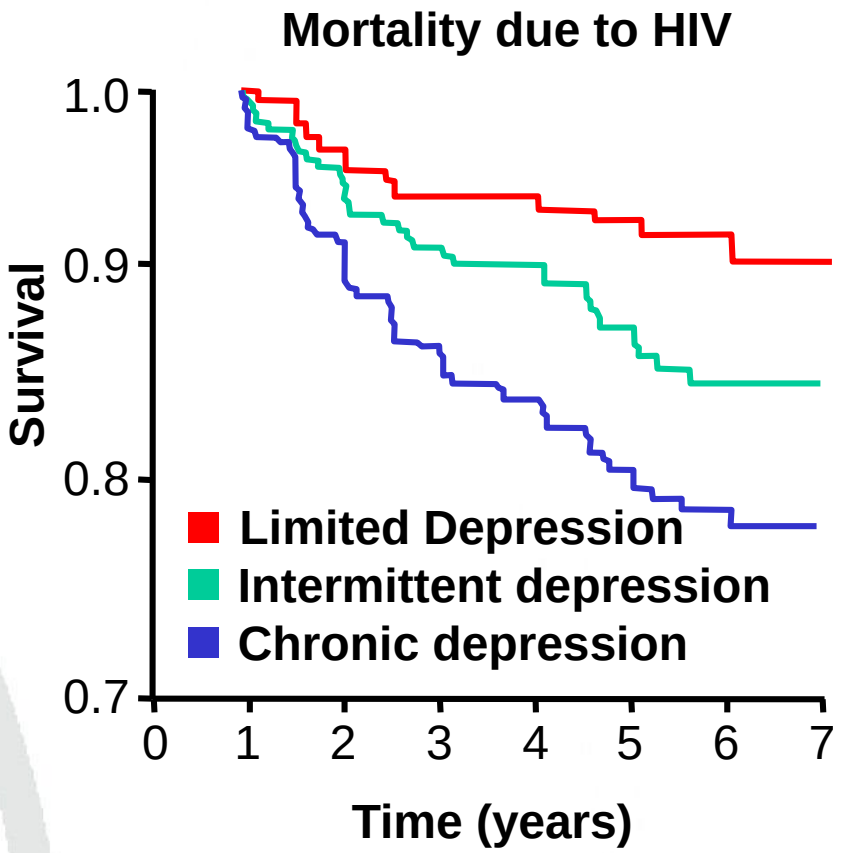
WHO multicenter neuropsychiatric AIDS study

site	symptomatic (AIDS)	asymptomatic	HIV- (controls)
Bangkok	18,4%	9%	1,7%
Kinshasa	4,4%	0%	0%
Munich	4,0%	4,8%	0%
Nairobi	5,5%	0%	0%
Sao Paulo	17,4%	10,9%	7,8%

symptomatic seropositive individuals had higher levels of depression than matched seronegative controls (Maj et al. 1994)

Depression increases mortality in HIV?

- HERS cohort: 765 HIV+ women
- Depression measured by CES-D scale and classified in 3 types: limited, intermittent and chronic
- 2.0 greater risk of mortality in patients with chronic "depression" against patients with limited or without depressive symptoms



Ickovics JR, et al. JAMA 2001;285:1466-1474.

How to solve this methodological problem?

1. **Rule out non psychiatric, non psychological conditions**
2. **Use adequate diagnostic criteria**
   - **to use only nonsomatic items (exclusive approach)**
   - **to take into account symptoms that are clearly caused by depression (etiologic approach)**
   - **to use substitutive criteria (Endicott criteria)**

Diagnosis of MDD

- **An initial screening should include:**
  - **Laboratory tests: glucose, blood cells, electrolytes, liver function, kidney function…**
  - **Thyroid function tests (TSH, T4)**
  - **Testosterone**
  - **Vitamin B12 and folate levels**
  - **Other tests as suggested by history and physical examination**
  - **Screening for drugs in urine**
  - **(Brain imaging)**

TSH: thyroid-stimulating hormone; T4: thyroxine; MDD: major depressive disorder

1. Gallego L, et al. *AIDS Rev* 2011; **13**:171–179.

Depression in HIV: Diagnostic criteria

Somatic symptoms

- Poor appetite or changes in weight
- Loss of energy and fatigue
- Insomnia or hypersomnia
- Diminished ability to think or to concentrate

Endicott's substitutive criteria

- Tearfulness or depressed appearance
- Brooding, self-pity, pessimism
- Social withdrawal
- Lack of reactivity, cannot be cheered up

Endicott J. *Cancer* 1984; **53**:2243–2248.

Screening instruments for patients with depression

Screening Instrument	Administration	Items	Measurements	Primary Use
Beck Depression Inventory (BDI)[1]	Self-report	20	Cognitive, somatic subscales	Clinical
Center for Epidemiological Studies-Depression (CES-D)[2]	Self-report	20	Cognitive, somatic subscales (cut scores for clinically relevant symptoms)	Epidemiologic
Hamilton Rating Scale for Depression (HAM-D)[3]	Clinician	17	Affective, vegetative subscales	Research
Hospital Anxiety and Depression Scale (HADS)[4]	Self-report	7	Screens depression and anxiety; excludes somatic symptoms	Medical
Patient Health Questionnaire-9 (PHQ-9) Depression Module[5]	Self-report	9	Keyed to DSM-IV depression diagnostic criteria; also somatic symptoms, anxiety disorders, alcohol and drug abuse	Primary care

1. Beck AT, et al. *Arch Gen Psychiatry* 1961; **4**(6):561−571; 2. Sawyer Radloff L. *Applied Psychological Measurement* 1977; **1**:385–401;
3. Hamilton M. *J Neurol Neurosurg Psychiatry* 1960; **23**:56–62; 4. Zigmond AS, Snaith RP. *Acta Psychiatr Scand* 1983; **67**: 361–370;
5. Kroenke K, et al. *J Gen Intern Med* 2001; 16:606–613.

Hospital Anxiety and Depression Scale

- self-report scale especially designed to assess anxiety and depression in people affected with a physical illness
- does not comprise any somatic item that can be confused with physical illness symptoms
- the HADS contains 14 four-point items, of which 7 measure depression and 7 assess anxiety.
- accumulating data suggest that the HADS provides a valid and a reliable assessment of depression and anxiety for a wide variety of populations

Review of instruments used to measure depression in HIV (Sherr 2011)

- 21 standardized measures were used for depression
- the most frequently used:
  - Beck Depression Inventory (BDI): 33.3%
  - Hamilton Depression Scale (HAM-D): 23.3%
  - Center for Epidemiological Studies Depression S. (CES-D): 21.1%
  - Profile of mood states (POMS) depression subscale: 16,7%
  - Clinical Global Impression (CGI): 15.5%
  - Hospital Anxiety and Depression Scale (HADS): only 5.5%
- thirty-seven (41.1%) studies included more than one outcome measure
- prevalence rates of depression ranged from 0 to 80%
- measures were diverse and rarely adopted the same cut-off points

Conclusions

- Depression is very prevalent in HIV disease
- Depression has a very negative impact on HIV illness
- Depression is seldom screened and diagnosed
- Differential diagnosis of depression in HIV infected patients is quite difficult.
- Hospital Anxiety and Depression Scale seems to be the best tool to screen depression in the non-psychiatric setting
- if indicated, treatment should be started as soon as possible

Thanks for your attention!

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