
Romanian National Neurocognitive Screening Program

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Key questions in the understanding of HAND: the interest in HIV neurocognitive impairment

| | |
|----|--|
| 1 | Which patients should be screened for HAND, and when? How often should patients be screened? |
| 2 | How can I identify patients at greatest risk of HAND? How, and to what extent, do different factors affect the risk of HAND? |
| 3 | Which tools should be used to screen for HAND? |
| 4 | How should I approach screening and differential diagnosis of HAND co-morbidities? |
| 5 | How can HAND be differentiated from neurodegenerative diseases in older patients? |
| 6 | How should NP testing be approached, in the diagnosis of HAND? |
| 7 | In addition to NP testing, which other assessments should be used in the diagnosis of HAND (e.g. psychiatric assessment, lumbar puncture/CSF analysis, imaging, exclusion of other pathologies)? In which order, and at what stage, and in which patients should these assessments be performed? |
| 8 | What is the role of lumbar puncture/CSF analysis in the monitoring of HAND, & when should it be performed? |
| 9 | When, and how often, should I monitor patients who have been diagnosed with HAND? |
| 10 | What is the natural history of ANI and MND and how should this impact patient management? |
| 11 | What interventions should I consider in treated patients with persistent or worsening NCI and CSF viral load <50 copies/mL (non-detectable)? Should I still change the ARV when the virus is not detectable in the CSF? |
| 12 | What is the risk of ARV-related neurotoxicity, and how should this risk be managed? What should I do if I suspect ARV neurotoxicity? |
| 13 | When/how should I use pharmacological agents other than ARV in the monitoring of HAND? |
| 14 | What can I do to prevent HAND? |

The Main Objectives of MIND EXCHANGE Programme

To:

- Discuss and understand the mental health issues in patients with HIV
- Understand the role of and implications of HAND
- Discuss and establish different screening and pre-screening approaches to be accepted in different areas
- Understand the differential diagnosis between:
 - HAND and depression
 - HAND and neurodegenerative diseases in old HIV patients
- Understand depression in patients with HIV

Which are the Risk Factors for HAND?

| Disease | Treatment | Co-morbidities | Demographic |
|--|---|---|--|
| <ul style="list-style-type: none">● Low CD4 nadir● High plasma, CSF VL● Low current CD4*● Longer HIV duration | <ul style="list-style-type: none">● Poor adherence● ARV interruptions● Non-optimal ARV regimen● Low ARV duration- related to treatment failure● Potential neurotoxicity● Lower CPE | <ul style="list-style-type: none">● HCV +● Hx acute CV event● CV risk factors● Anemia and thrombocytopenia | <ul style="list-style-type: none">● Older individuals● Low education● Lower socio-economic status● Lack of access to care● Poverty |

Which patients should be screened for HAND, and when?

Who to screen:

- All patients with HIV
- to assess at the baseline and monitor for all associated pathologies: cardiometabolic, osteorenal, neurocognitive, aging etc.
- to detect changes before symptoms arise
- No rationale for screening only symptomatic patients
- No rationale for screening only those patients with risk factors

How often should patients be screened?

When to screen:

- Within 6 months of diagnosis, as soon as clinically appropriate
- Before the initiation of ARV, if possible
- Insufficient data to establish best time for follow up - cognitive reserve and natural history of the disease
- However, good practice is:
 - 6–12 months in high risk patients
 - 12–24 months in lower risk patients
 - Evidence of deterioration

ROMANIAN NATIONAL NEUROCOGNITIVE SCREENING PROGRAM

Aims:

- To test a brief screening battery on a large, representative group of HIV-infected individuals
- Inclusion criteria of enrolled subjects were:
 - 715 subjects from all 9 regional Romanian reference centers
 - mainly born between 1987-1991
 - infected in their first years of life
- To compare the brief screening test to a comprehensive test battery – 150 subjects randomly selected from the initial group
- To assess possible confounders
- To evaluate the impact of exposure to ART and to different CNS penetrating regimens on neurocognitive impairment

The Screening test battery

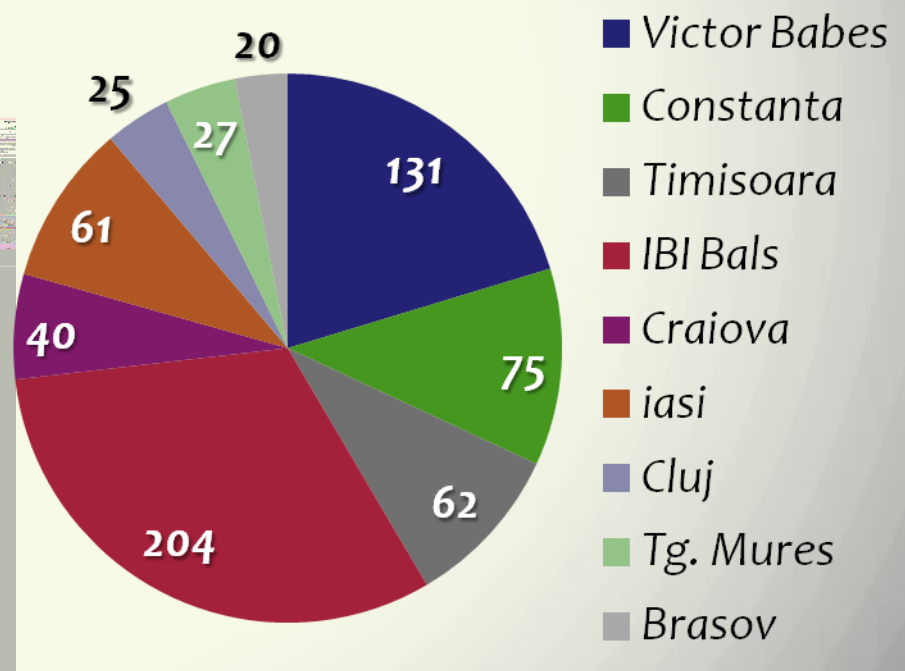
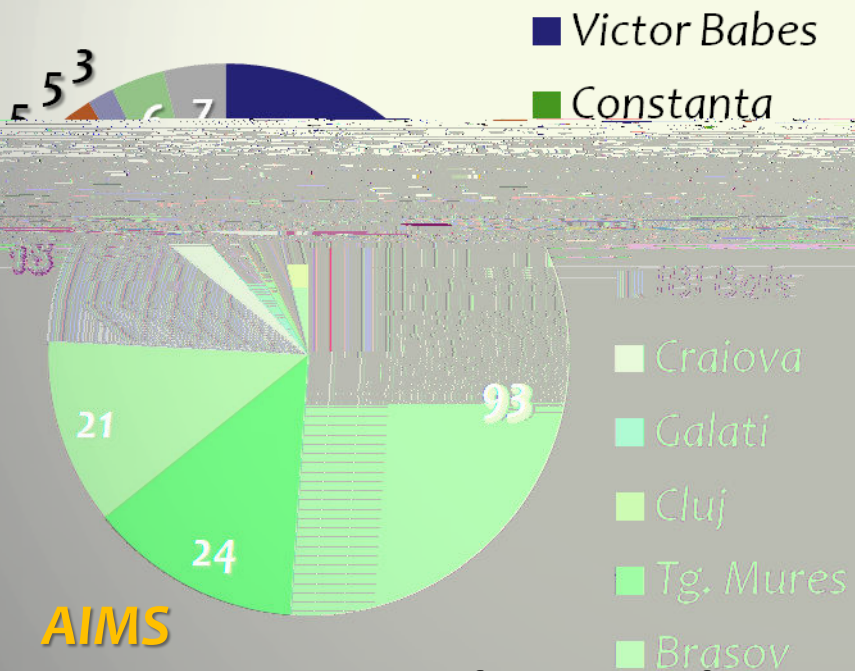
Consisted of:

- Simioni questionnaire complaints
- IHDS
- Beck depression scale
- PAOFI

Romanian National Neurocognitive Screening Program

VBH testing
n=182

National screening
N=645 enrolled patients



AIMS

1. To evaluate the performance of the NC screening battery to diagnose HAND
2. To refine the screening based on the results of the comprehensive testing
3. To extend the battery to other categories

Neurocognitive screening - conclusions

- Simioni questionnaire detected neurocognitive problems in 40% HIV patients
 - mostly memory domain
- IHDS / 40% HIV patients, some cognitive impairment, but not enough to define dementia
 - mostly motor domain
- Beck depression scale / 20% HIV patients
 - we registered surprisingly low rates of depression / self-reporting methodology vs.
 - a significant proportion of HIV patients mentioned depressive symptoms during the psychological counseling
- PAOFI / 30% HIV patients, identified at list one complain in every day functioning
 - mostly psycho-motor domain (sensory-perceptual and executive function)

Conclusions and future plans

- The brief screening battery detected neurocognitive problems in one third of HIV patients, without major confounding conditions
- The analysis of the result shows that is necessary to correlate patients' complaints with deficit in different cognitive domains
- Further refinement of the screening battery is needed in order to identify the HIV patients with subtle cognitive deficits.
- To refine the screening test battery by adding a couple of the most appropriate tests from the comprehensive test battery that demonstrated efficacy in diagnosing NCI in our Romanian HIV cohort.

The MIND EXCHANGE programme

Because of the neurocognitive issues associated with HIV, the MIND EXCHANGE consensus programme was set up to provide practical guidance in the screening, diagnosis and monitoring of HIV-associated neurocognitive disorder (HAND), which is of direct relevance to daily practice and complementary to existing guidelines

Steering Committee: Andrea Antinori, Rome, Italy (Infectologist), Gabriele Arendt, Düsseldorf, Germany (Neurologist), Igor Grant, San Diego, USA (Psychiatrist), Scott Letendre, San Diego, USA (Infectologist), Jose Muñoz-Moreno, Barcelona, Spain (Neuropsychologist)

Neurocognitive impairment in patients with HIV and depression

- Depression-related neurocognitive impairment and HAND are independent¹
- Testing for HAND may be confounded by the presence of depression
 - Evidence surrounding the impact of depression on neuropsychological functioning in patients with HIV is conflicting²⁻⁴
 - Because depression could manifest itself as cognitive impairment, it must be ruled out before diagnosing HAND¹
 - However, depression is a risk factor for HAND²

HAND, HIV-associated neurocognitive disorder.

1. Dubé B *et al. J Psychiatry Neurosci* 2005;30:237–46; 2. Cysique LA *et al. J Int Neuropsychol Soc* 2007;13:1–11;
3. Millikin CP *et al. J Clin Exp Neuropsychol* 2003;25:201–15; 4. Gibbie T *et al. HIV Med* 2006;7:112–21; 4..

Lessons learned and recommendations

- Cognitive screening instruments vary in their ability to detect the different forms of HAND
- Most screening measures perform well in detecting HIV-Associated Dementia (**HAD**) but poorly in the detection of Asymptomatic Neuropsychological Impairment (**ANI**) or Mild Neurocognitive Disorder (**MND**)
- HIV Dementia Scale is best tool currently available to detect milder forms of HAND but recommend age and education corrections to increase sensitivity
- Combination of two brief neuropsychological tests perform well in identifying HIV-associated cognitive impairment
- Comprehensive neuropsychological testing is recommended as a standard of practice, at least in specialized HIV centres where resources are available

Permission to present this slide has been kindly granted by Professor Sean Rourke, University of Toronto

Screening for HAND: Considerations with symptoms

Considerations / issues

Symptoms and subjective reporting

- How useful is the reliance on cognitive complaints by patients, or the “subjective” ratings of cognitive status to diagnose HAND?
- How does depression relate to / interact with the cognitive complaints which occur in HAND?
- How might the presence and type of neuropsychological impairment impact on reporting of cognitive complaints?

How should neuropsychological testing be approached, in the diagnosis of HAND?

Full neuropsychological evaluation may be most appropriate in:

- Patients with neurocognitive impairment at screening, if the diagnosis of HAND is in doubt
- Patients with cognitive deficits that impact everyday life
- Patients with clinical progression of HAND
- Patients at risk of HAND using a validated screening tool or evidence-supported risk factors

How should neuropsychological testing be approached, in the diagnosis of HAND?

Comprehensive testing should:

- **Test at least 6 cognitive domains**
 - Verbal; attention/working memory, executive function; learning, recall, speed of information processing, and motor skills
- Use similar tests for ANI, MND and HAD diagnosis / assess independence in activities of daily living
- Be sensitive and specific to HAND and other diagnoses in question
- Be adaptive according to the abilities of the patient
- Ideally be administered by a neuropsychologist

**The Impact of Neurocognitive
Impairment and Depression in HIV
Infection**

The IMPACT of cognitive impairment and depression in HIV infection

 ***How frequent?***

 ***How relevant?***

 ***Quality of life***




 ***Easy to recognize?***

 ***Can be cured?***






HIV neurobehavioural DISTURBANCES

HIV-associated neurocognitive disorders (HAND)

Primary HAND






-  Asymptomatic neurocognitive impairment
-  Mild neurocognitive disorder
-  HIV-associated dementia

Secondary HAND




-  Infection
-  Neoplasia
-  Cerebrovascular
-  Nutritional
-  Treatment related

Emotional and behavioral impact

New onset

-  **Depression**
-  Anxiety
-  Adjustment disorders
-  HIV mania
-  HIV psychosis

Pre-exist / recurrent / comorbid

-  Mood disorders
-  Substance use disorders
-  Other mental disorders

Depression in HIV Patients

... the hardest solitude ...

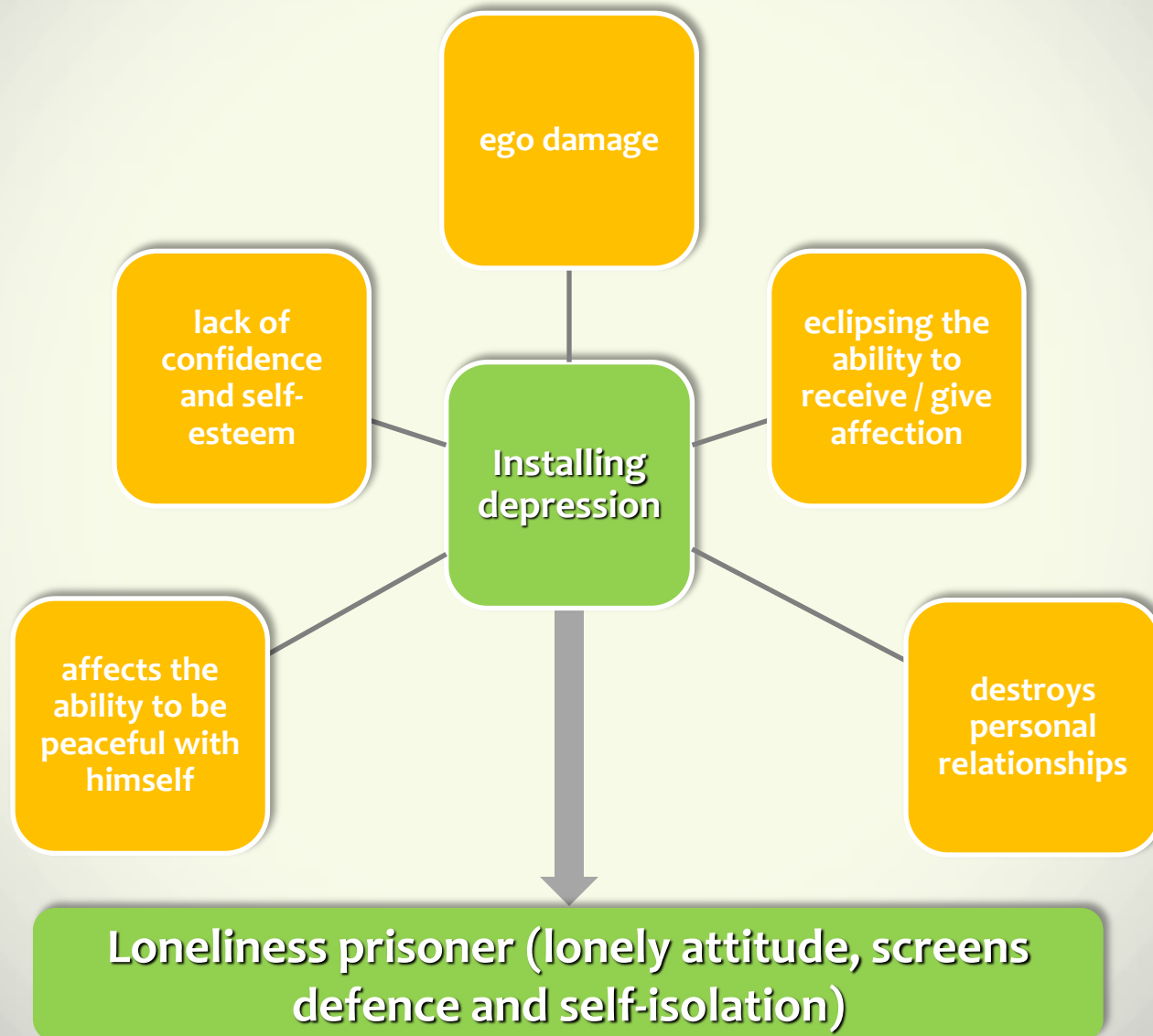


Prevalence of depression in HIV infection

Highly variable, according to:

- Assessment methodology
 - Self-reporting vs. screening tests vs. complete psy (psychologic and psychiatric) evaluation
- Studied population
 - Treatment-experienced
 - Age, gender
 - Geography, setting
- Prevalence of **DEPRESSIVE SYMPTOMS** in people living with HIV reported at **12–71%** across various studies
- Up to **23%** of HIV patients experiencing a major depressive disorder

Depressogene schemes of HIV patients



Depression in HIV patients

- Depression is **cumulative** over the years, usually lifelong of the HIV patient.
- More the HIV patient goes through several depressive episodes, the more likely to do other episodes, which, over the years are becoming more intense and closer in time.
- The depression enveloped the HIV patient: he/she believes that sees the truth, but it is lied to his/her own truth.

Depression in HIV patients

Impaired cognition is part of depression

If the initial installation of the depression is linked to an event that activates it, and the brain - which passed several times through depression, will continue to return to depression again and again

Depression: even if caused by an external event, finally changes the functional structure of the brain.

Psychological and Psychiatric disorders associated with HIV

| HIV syndromes | Co-occurring syndromes | HIV-associated syndromes with psychological and psychiatric implications |
|------------------------|---|--|
| 1. Delirium 2. HAND | 1. Adjustment disorders 2. Anxiety disorders 3. Mood disorders 4. Substance use disorders 5. Personality disorders 6. Psychotic disorders 7. Sexual disorders 8. Sleep disorders | 1. Fatigue 2. Pain syndrome 3. Wasting syndrome 4. Lipodystrophy 5. ARV-related issues |

Depression in patients with HIV

- Depression in patients with HIV is associated with^{1,2}
 - Lower quality of life
 - Affects well-being (meaning, life plans, hopes)
 - Reduced adherence to ART
 - Poorer self-care
 - Worse treatment outcomes
 - Impairment in social and vocational functioning
 - Social isolation
 - High-risk behaviour and substance abuse

ART, antiretroviral therapy.

1. New York State Department of Health. Depression and mania in patients with HIV/AIDS. New York (NY): New York State Department of Health; 2010. Available at: <http://cdn.hivguidelines.org/wp-content/uploads/depression-and-mania-posted-10-19-2010.pdf>. Last accessed July 2013;

2. Relf MV *et al.* *J Assoc Nurses AIDS Care* 2013;24(1 Suppl):S15–28;

Screening for depression in patients with HIV



- Patients may not recognise or self-report symptoms of depression¹
 - Some physicians may also be afraid to ask questions about psychological health
- A wide variety of depression screening techniques are available²
 - Most rely on self-reporting
 - Most diagnose the severity rather than presence of depression

1. New York State Department of Health. Depression and mania in patients with HIV/AIDS. New York (NY): New York State Department of Health; 2010. Available at: <http://cdn.hivguidelines.org/wp-content/uploads/depression-and-mania-posted-10-19-2010.pdf>. Last accessed July 2013.

2. Ramasubbu R *et al.* *Ann Clin Psychiatr* 2012;24:82–90.

Simple screening questions for depression

- Two questions have been shown to be effective when screening for depression:
 - During the past month, have you often been bothered by feeling down, depressed, or hopeless?
 - During the past month have you often been bothered by little interest or pleasure in doing things?
- If a patient answers “Yes” to either of these questions, further evaluation is indicated using a validated screening tool

Summary

- A significant proportion of patients with HIV suffer from depression
- Depression may be associated with a negative impact on patient outcomes and treatment adherence
- Screening for depression can be done quickly, but it is important to consider alternative diagnoses following preliminary investigations

THANK YOU !