GUIDELINE
Management of mental health disorders in HIV-positive patients

by the Southern African HIV Clinicians Society

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Disclaimer. Specific recommendations provided in this document are intended only as a guide to clinical therapy, based on expert consensus and best current evidence. Treatment decisions for patients should be made by their responsible clinicians, with due consideration for individual circumstances. The most current version of this document should always be consulted.

These guidelines are intended as a reference document to assist HIV nurse and doctor clinicians in managing mental health disorders. It is intended to improve awareness, knowledge and capacity to support patients living with HIV and mental health disorders.

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1. Introduction

'*There is no health without mental health*'.[1,2] Mental disorders are highly prevalent among people living with HIV/AIDS (PLWHA), with major depressive disorder (MDD) occurring almost twice as frequently among this group than in the general population.[3] Mental disorders may increase an individual's risk for HIV infection through increased social vulnerability, altered risk behaviour, associated substance misuse and loss of control within sexual relationships. Conversely, such disorders may also arise as a direct result of HIV neuro-invasion or psychosocial stressors, or due to complications of antiretroviral therapy (ART).[4,5]

Despite their prevalence, mental disorders are often under-diagnosed or inadequately managed in PLWHA. The impact of untreated mental disorders on health outcomes is substantial. It is imperative that clinicians caring for HIV-positive individuals actively screen for, diagnose and manage mental disorders in this population.[6]

2. Overview of the guideline

This guideline is intended to improve primary care HIV clinicians' knowledge and capacity to manage mental health disorders. It is also intended to heighten HIV clinicians' awareness of the need to integrate HIV and mental healthcare within their daily practice.[7]

The following conditions and issues are addressed here:

- HIV testing in the context of mental disorders
- common mental disorders (CMDs)
- severe mental disorders (SMDs)
- HIV-associated neurocognitive disorders (HANDs)
- grief
- healthcare worker (HCW) burnout and vicarious trauma.

These guidelines do not encompass substance use disorders or triple diagnosis (HIV/mental disorder/substance use disorder), or mental disorders among children and adolescents; these topics will be covered in separate, future guidelines.

3. Principles of HIV testing in patients with mental disorders

- All patients with mental disorders (in-/out-patients, voluntary/involuntary patients admitted under the Mental Health Care Act) should be offered HIV testing, HIV-prevention/risk-reduction education and access to condoms
- The presence of a mental disorder does not automatically equal incapacity to consent to HIV testing
- Capacity to consent to HIV testing must therefore be assessed on an individual basis, particularly in patients with SMDs
- For capacity to consent, patients should be able to:
  - understand why they are being tested
  - understand and report on the consequences of a negative or positive test result
  - report how they are likely to respond to either result
- Patients should be included in decision-making about their HIV testing, as far as possible in all cases
- If the patient is assessed as being incapable of giving informed voluntary consent (e.g. active psychosis, dementia), then proxy consent may be sought
  - Proxy consent
    - Consent is given by someone else acting in the best interests of the patient, e.g. a senior clinician in charge of the case
    - The reasons for testing and the process must be documented carefully
    - If the patient regains capacity, then disclosure of the results is paramount

  - There may be a need to disclose the results to the carer, if the patient has irreversible neurocognitive impairment, with cognisance of potential stigma/discrimination
- Disclosure
  - All medical information should be kept confidential at all times
  - Information should preferably be released only with patient consent, unless the information is relevant to clinical management/medical aid procedures
- The procedure to follow when testing for HIV in patients with mental disorders is shown in Fig. 1.[8,9]

4. Assessment and diagnosis of CMDs

The term 'common mental disorder', used to describe disorders that are highly prevalent in the general population (usually occurring at rates >10%), typically includes:

- depressive disorders
- anxiety disorders
- substance use disorders (not included in this guideline).[10]

Box 1 provides an overview of CMD prevalence. In South Africa (SA), 26 - 38% of PLWHA have a CMD (v. 12.6% of the general population).[6] CMDs have not decreased in prevalence with the introduction of ART.

Box 1. Overview of CMD prevalence

- Two-fold increase in prevalence in HIV-positive individuals[3,8]
- In SA, 26 - 38% of PLWHA have a CMD (v. 12.6% of the general population)[9]
- Some 20 - 60% of PLWHA are affected by some form of psychiatric disorder[10] (depressive disorders are most common)
- CMDs are **not** decreasing in the ART era
- CMD prevalence is influenced by viral central nervous system (CNS) pathology, concomitant psychosocial stressors and the nature of HIV as a life-threatening and stigmatised illness
- CMDs often go undiagnosed and untreated in this population

4.1 Screening

Clinicians should screen routinely for CMDs, because patients rarely volunteer information about their mental state. Box 2 includes three questions to ask patients. Due to the high prevalence of gender-based violence (GBV) in SA, we recommend clinicians also incorporate screening for GBV.[11]

Box 2. Screening for depression and GBV

Brief routine screening questions for depression

- How have you been in the past month/since your last visit?
- Have you been feeling more stressed than usual?
- Have you been feeling down, low, heart-sore or depressed?

Brief screening questions for GBV

- How are things going in your relationship with your partner?
- Have you ever been emotionally, sexually or physically victimised?

Certain patients may require more intensive screening, including:

- those at their first ART assessment
- those responding poorly to ART (detectable viral load (VL)/adherence issues)
- those exhibiting worrying behaviour (looking anxious/depressed, expressing suicidal ideation or self-harm).

Patients who respond positively to one of the brief screening questions should be administered a validated screening tool that is appropriate for primary healthcare settings, such as the Patient Health Questionnaire (PHQ)-9 (Fig. 2).[12]

4.2 Risk assessment

It is important to assess suicide risk. Clinicians should always ask about suicidal ideation in patients with depressive symptoms. High risk is indicated by:

- a clear plan for ending life
- an identified lethal method
- a previous suicide attempt
- a lack of social support
- severe (psychotic) depressive disorder.

See also the 'SAD PERSONS' scale (Fig. 3).[13]

4.3 Mental state assessment

Assessing the patient's mental state is as important as a physical examination. Clinicians should conduct and document a 'mental state examination' (Box 3) at each visit.

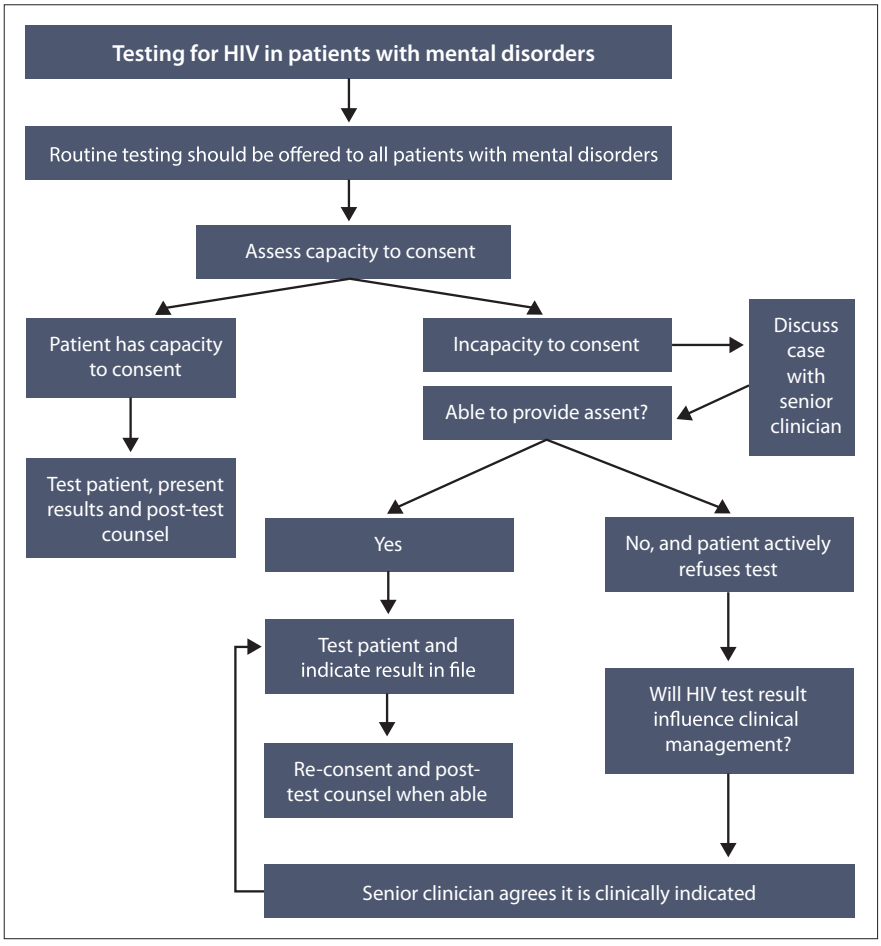

Fig. 1. Testing for HIV in patients with mental disorders.[8,9]

Box 3. Recording the mental state examination

Document the mental state examination, as for physical examination:

- appearance and behaviour: grooming, eye contact, motor activity, etc.
- level of consciousness: orientation for time, person, place
- cognitive function (see section 6: HANDs)
- mood: objectively euthymic, depressed, elevated
- speech, form and content of thinking: flow of speech, coherence and content of thinking (delusions, pre-occupations, ruminations)
- perceptual abnormalities: evidence of hallucinations
- insight into own condition

4.4 Depression in PLWHA (including MDD and less severe types)

Up to 25% of PLWHA in SA are thought to suffer from some form of depression during the course of the illness. Severe depression, also known as MDD, occurs in about 5 - 10% of patients, while minor depressive disorders are diagnosed in about 15 - 20%.[6,10] Even mild depression can lead to erratic adherence, poor care engagement and ultimately to more serious outcomes. Major depression is diagnosed by the presence of five or more of the symptoms listed in section 4.4.1 for at least two weeks, while minor depression is diagnosed when fewer symptoms are present and/or for shorter periods.

4.4.1 Symptoms of depressive disorders

Depressive disorder is characterised by five or more of the following occurring together in a two-week period:

- **EITHER:** depressed mood almost all day every day
- **OR:** loss of interest or enjoyment of usually pleasurable activities for most of the day
- **AND (occurring nearly every day):**
  - significant weight loss when not dieting or due to medical illness, or weight gain (e.g. >5% body weight change in a month), or decreased/increased appetite
  - insomnia or hypersomnia
  - psychomotor agitation or retardation (observable by others, not merely subjective feelings of restlessness or of being slowed down)
  - fatigue or loss of energy
  - feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) – not merely self-reproach or guilt about being sick
  - diminished ability to think or concentrate, or indecisiveness (either by subjective account or as observed by others)
  - recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation

Over the past 2 weeks how often have you been bothered by any of the following problems	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3
3. Trouble falling or staying asleep; or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things such as reading the newspaper or watching TV	0	1	2	3
8. Moving or speaking so slowly that others could have noticed. Or the opposite - being so fidgety and restless that you have been moving around a lot more than usual	0	1	2	3

Over the past 2 weeks how often have you been bothered by any of the following problems	Not at all	Several days	More than half the days	Nearly every day
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Add columns				
Total				
0 - 4: No depression 5 - 9: Mild depression 10 - 14: Moderate depression				
15 - 19: Moderately severe				
20 - 27: Severe				
	Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
If you checked any of the problems, how difficult have these problems made it for you to do work, take care of things at home, or get along with other people				

Total score:

Total score	Depression severity
0 - 4	No depression
5 - 9	Mild depression
10 - 14	Moderate depression
15 - 19	Moderately severe depression
20 - 27	Severe depression

Fig. 2. Patient Health Questionnaire (PHQ)-9.

S	Sex: male gender represents a higher risk
A	Age: extremes of age are at higher risk (e.g. <18 years and >55 years)
D	Depression or other psychiatric comorbidity are at higher risk
P	Previous attempts: those with a past history of [suicide] attempts are at higher risk
E	Ethanol/alcohol or other substance use/abuse
R	Rational thinking loss, e.g. psychosis with command hallucinations
S	Social support: no social support confers a higher risk
O	Organised plan
N	No spouse
S	Sickness: medical or psychiatric illness may confer a higher risk
Score card	
0 - 2 points	This patient may be sent home but one needs to ensure follow-up in the future
3 - 4 points	Close follow-up needs to be ensured and hospitalisation considered
5 - 6 points	Hospitalisation is strongly considered
7 - 10 points	Ensure hospitalisation and consider involuntary admission if necessary

Fig. 3. 'SAD PERSONS' scale (yes for any letter = 1 point).

without a specific plan, or a suicide attempt or a specific plan for committing suicide.[14]

Psychotic symptoms may occur in severe depressive disorders. These usually consist of delusions (guilt, nihilistic, of death, occasionally paranoid) and occasionally hallucinations (these are usually transient).

If the screen is positive for a CMD, conduct and document a mental state examination (see Box 3).

4.4.2 Differential diagnosis of depression

- Minor or sub-threshold depressive disorders are characterised by the presence of some symptoms, but do meet all criteria for MDD
- Major depression
- Adjustment disorder: a depressive reaction to psychosocial stressors including HIV diagnosis
- Bereavement (see section 7)
- Mood disorder secondary to a medical condition/substance, e.g. HIV, hypothyroidism, efavirenz (EFV), alcohol
- Bipolar disorder: there is usually history of a previous episode of elevated mood resulting in abnormal behaviour, e.g. reduced sleep, increased energy/libido/risk-taking, etc.

4.4.3 Management of MDD (moderate to severe depression according to the PHQ-9)

4.4.3.1 Hospitalisation

The patient requires hospitalisation:

- if there is a high suicide risk
- in complex cases: the presence of psychosis and/or minimal social support and/or a poor response to out-patient treatment and/or a diagnostic dilemma
- in complex medical comorbidity (to monitor antidepressant medication)
- in the event of severe psychomotor retardation or no eating/drinking.

4.4.3.2 Initiation of antidepressant treatment

The initiation of antidepressant therapy in patients with CMDs is based on a step-wise approach, using the PHQ-9 as a guide to diagnosis, management and follow-up (Box 4). It is essential to remember that one 'starts low and goes slow' as patients with HIV/AIDS are often more sensitive to side-effects of medication.

Box 4. Introducing an antidepressant: 'Start low and go slow'*

- Initiate 20 mg fluoxetine (or similar) at the lowest available dose and refer to psychosocial support services where available
- Reassess using the PHQ-9 at 2 - 4 weeks and for side-effects (e.g. irritability, nausea, headache, disturbed sleep patterns); most side-effects settle within 2 weeks
- If after a total of 6 - 8 weeks there is no/minimal improvement, then increase the dose and reassess with the PHQ-9 in 4 - 6 weeks
- If after reassessment there is still no improvement, then up-refer

* Fluoxetine and amitriptyline are the only antidepressants on the primary-level essential drugs list. Nurses are not currently permitted to prescribe – refer to a doctor. If unsure at any point, then phone the referral centre for advice. If the depression worsens at any point, or if suicide risk increases, then refer the patient.

4.4.5 Psychotherapy[15]

- If available, patients should be referred for psychological assessment and treatment
- Evidence-based psychotherapy interventions for PLWHA and depression include:
  - cognitive-behavioural therapy (CBT): a form of psychotherapy addressing dysfunctional emotions and maladaptive ideas through a goal-directed systematic process
  - interpersonal therapy (IPT): a form of psychotherapy that is time-limited and encourages patients to regain control of mood and functioning through the therapeutic alliance
  - group IPT (IPT-G): a form of therapy that employs the same basic structure and focus of individual IPT, though modified to capitalise on the group format
- Key determinants of successful therapy include the motivation of patients to attend multiple sessions and the access to clinics/times.

4.5 Anxiety disorders

Anxiety disorders in PLWHA are common. Some studies report that between 20% and 60% of HIV-positive adults suffer from some form of psychiatric disorder. The most recent general population study of the prevalence of mental disorders in SA was the SASH study, which reported a combined 12-month prevalence of depressive and anxiety disorders of 12.6%.[6] It is important to recognise and treat anxiety disorders as they have been associated with increased rates of poor treatment compliance and high-risk behaviour. Quality of life is also adversely affected by anxiety disorders (Table 1).

5. SMDs and HIV/AIDS

These disorders occur less frequently in the general population (usually at rates <5%) and include:

- schizophrenia
- bipolar mood disorder
- MDD with psychotic features.

Box 5 describes the prevalence and impact of SMDs.

Box 5. Prevalence and impact of SMDs

Prevalence

- HIV among those with SMDs: 2.6 - 59.3% in sub-Saharan Africa[8]
- SMDs in the HIV-positive population: up to 15%
- New-onset psychosis among the HIV-positive population: 0.2 - 15.2%[16]

Impact

- SMDs lead to an increased risk of acquiring and transmitting HIV
- SMDs may impact adherence to psychiatric treatment and ART
- HIV disease progression can be associated with secondary psychiatric disorders, which often improve with ART
- **Integrated** care of both conditions improves outcomes[7]
- Successful ART is more likely if there is:
  - no substance abuse
  - no history of homelessness/incarceration
  - retention in psychiatric care
  - adherence to psychiatric treatment[16]
- Regular mental health visits decrease the risk of ART discontinuation

5.1 Diagnosis of SMDs

SMDs in PLWHA can often be classified as 'primary' or 'secondary'. Primary SMDs often occur prior to HIV infection while secondary

Table 1. Common anxiety disorders

Anxiety disorder*	Features	Medication options	Psychotherapy
GAD	• Pervasive physical and psychological symptoms of anxiety interfere with normal functioning (work, studying, activities of daily living, socialising) and/or cause significant distress	Medication options for all anxiety disorders include: • SSRI antidepressant at doses as for MDD • short-term (2 weeks) benzodiazepines, e.g. 1 - 2 mg lorazepam nocte/prn, 10 - 30 mg oxazepam daily	• CBT
PD	• Recurrent panic attacks (acute severe anxiety/panic: palpitations, sweating, tremor, feelings of choking, inability to breathe, feelings of impending doom, fear of death from symptoms) • First panic attack often unexpected and unrelated to external stimulus • Subsequent attacks may become associated with particular situations, leading to avoidance, e.g. fear of crowded places (agoraphobia) • Isolated panic attacks can occur as part of GAD and depressive disorders • Frequently associated with substance use disorders	• As above	• CBT
PTSD	• Onset after experiencing or witnessing a serious traumatic event (rape, assault, accidents) • Symptoms may occur soon after the event or with delayed onset: intrusive memories (reliving, flashbacks, nightmares), hyper-arousal (increased startle response, anxiety symptoms) and avoidance (avoiding situations which remind the person of the traumatic event, numbing, and feelings of a foreshortened future)	• As above	• Trauma counselling • CBT • Note: those recently exposed to trauma should not receive once-off debriefing or prescription benzodiazepines as these may increase the risk of PTSD
OCD	• Irrational thoughts or fears which are intrusive (obsessions), commonly fears of contamination or of not having completed an activity correctly, which results in compulsive rituals, e.g. repeated hand-washing, checking of activities	• As above	• CBT

SSRI = selective serotonin reuptake inhibitor; MDD = major depressive disorder; CBT = cognitive-behavioural therapy; GAD = generalised anxiety disorder; PD = panic disorder; PTSD = post-traumatic stress disorder; OCD = obsessive compulsive disorder.

SMDs arise as a consequence of HIV infection. Both are responsive to a combination of psychotropic medication and ART.

A careful approach will help to differentiate primary SMDs (with comorbid HIV) (Fig. 4a) from secondary SMDs resulting directly from HIV or an opportunistic infection (Fig. 4b).

Clinicians must:

- conduct a thorough history: presenting symptoms, temporal relationship to HIV diagnosis, family/past psychiatric history
- conduct a comprehensive physical and neurological examination: this is essential to exclude underlying medical causes for psychiatric symptoms, e.g. opportunistic infections (particularly CNS pathology – toxoplasmosis/tuberculosis or cryptococcal meningitis), delirium or medication side-effects
- perform the following investigations: vital signs, urine dipstix, blood glucose, full blood count (FBC), creatinine and estimated glomerular filtration rate (eGFR), $CD4^+$ count, lumbar puncture; may also perform alanine transaminase (ALT)/liver function tests (LFTs), syphilis serology, thyroid stimulating hormone (TSH), VL testing and a computed tomography (CT) scan, if these are indicated on the basis of history and examination findings.

5.2 Management of SMDs

- Requires a multidisciplinary team approach, and where possible, integrated care including the involvement of community members and allied professionals
- Adherence support via treatment supporter/support groups and careful monitoring are key; patients should be educated/counselled regarding mental disorders and HIV to improve insight
- Poly-pharmacy (antidepressants, anticonvulsants, antipsychotics and ART): try as far as possible to rationalise to once daily dosing; patients on complex regimens should be reviewed regularly with a view to simplification
- Patients are more vulnerable to medication side-effects (e.g. extra-pyramidal side-effects while receiving antipsychotics) and should be monitored closely.
- See Table 2.

5.3 Starting ART in SMD: Use of EFV

Clinicians should follow standard national guidelines when initiating patients with SMDs on ART. EFV can often be used safely in patients with CMDs and in most with SMDs.[17] Routinely avoiding EFV for fear

Table 2. Commonly used drugs and their interactions[19,20]*

Class and drug	Dosage	Possible side-effects	Possible drug interactions
SSRIs			
Fluoxetine	20 - 60 daily	Headache, nausea, vomiting, irritability (initially), sexual dysfunction	EFV: potential increase in EFV levels Monitor for worsening of neuropsychiatric conditions
Citalopram/ Escitalopram	10 - 20/5 - 10 mg daily	Headache, nausea, vomiting, irritability (initially), sexual dysfunction	Generally nil clinically significant drug interactions PIs: potential for decrease citalopram dose
Sertraline	50 - 100 mg daily	Headache, nausea, vomiting, irritability (initially), sexual dysfunction	Generally nil clinically significant drug interactions; however, EFV may decrease dose of sertraline so titrate to effect
TCAs			
Amitryptaline	25 - 100 mg nocte	Sedation, anticholinergic side-effects – urinary retention, worsening confusion in older patients, constipation Fatal in overdose	Amitryptaline and PIs may increase the concentration of amitryptaline; potential cardiac arrhythmia abnormalities due to increased dose of amitryptaline
SNRIs			
Venlafaxine	75 - 225 mg daily	Potential for withdrawal syndrome if stopped quickly Initial irritability and GI side-effects Sexual side-effects	Generally well tolerated EFV and NVP may decrease venlafaxine concentration PIs may increase venlafaxine concentration
Tetracyclic antidepressants			
Mirtazepine	30 - 60 mg nocte	Sedation, weight gain	NVP and EFV potentially increase mirtazepine clearance
Trazodone	50 - 150 mg nocte	Sedation	NB: PI/r may increase trazodone dramatically – monitor carefully
NDRIs			
Bupropion XL	150 - 300 mg daily	Irritability, anxiety, tremulousness, paraesthesias, insomnia, seizures	EFV and PIs: potential for decreasing the dose of bupropion
Antipsychotics			
FGAs			
Haloperidol	0.5 - 5 mg nocte	EPSEs (dystonia, tremor, akathisia, cogwheeling, bradykinesia), NMS	PI/r may increase haloperidol concentration EFV may decrease haloperidol concentration
Chlorpromazine	25 - 200 mg in divided doses	Sedation, anticholinergic side-effects, NMS	PI/r may increase chlorpromazine concentrations
SGAs			
Risperidone	0.5 - 4 mg nocte	EPSE, sedation	Risperidone levels may increase with PIs Monitor for EPSEs and NMS EFV and NVP may decrease risperidone concentrations
Quetiapine	25 - 600 mg	Sedation, cardiac issues (QT prolongation – rare)	PI/r: potentially increased levels of quetiapine with increased sedation EFV and NVP may decrease levels of quetiapine
Olanzapine	5 - 20 mg	Sedation, metabolic syndrome – recommend lipogram if available	Probable interactions with PIs PIs: decreased concentration of olanzapine, may need to increase dose or choose alternative agent
Aripiprazole	5 - 30 mg	Akathisia, sedation	PI/r could potentially increase aripiprazole concentrations EFV and NVP could decrease aripiprazole concentrations
Clozapine	25 - 250 mg	Neutropaenia Best to avoid without specialist support	Probable interactions with PIs Possible increased concentration with PIs and possible increased risk of sedation and seizures EFV and NVP may decrease clozapine concentrations

continued...

Table 2 (continued). Commonly used drugs and their interactions[19,20]*

Class and drug	Dosage	Possible side-effects	Possible drug interactions
Mood stabilisers			
Lithium	400 - 800 mg	Lithium toxicity that may be life-threatening Monitor levels regularly once steady state is reached	Relative contraindication to avoid with TDF Potential risk for increased acute kidney injury
Sodium valproate	200 - 800 mg	Sedation, thrombocytopenia, toxic valproate levels if not monitored regularly	Interaction with AZT (increased AZT levels) PI/r may decrease valproate and increase PI Monitor levels closely
Lamotrigine	25 - 200 mg	SJS	Possible interactions with PIs; decreased dose of lamotrigine May need to increase/titrate doses of lamotrigine
Carbamazepine	100 - 200 mg bd	Sedation, syndrome of inappropriate ADH, skin rash, cognitive dulling, decreased white cell count	NVP and EFV: decreased carbamazepine, decreased EFV PI/r: increased carbamazepine, decreased PI
Benzodiazepines			
Alprazolam	1 - 2 mg daily	Sedation, dependence	PIs increase concentration of alprazolam
Diazepam	10 - 30 mg/day	Sedation, respiratory depression and ataxia	PIs increase diazepam

SSRIs = selective serotonin reuptake inhibitors; TCAs = tricyclic antidepressants; SNRIs = serotonin noradrenaline reuptake inhibitors; GI = gastrointestinal; NDRIs = noradrenaline dopamine reuptake inhibitors; FGAs = first-generation antipsychotics; SGAs = second-generation antipsychotics; EPSEs = extra pyramidal side-effects; NMS = neuroleptic malignant syndrome; ADH = antidiuretic hormone; EFV = efavirenz; NVP = nevirapine; AZT = zidovudine; TDF = tenofovir; PIs = protease inhibitors; PI/r = ritonavir-boosted PI; SJS = Stevens-Johnson syndrome.

* See http://www.druginteractions.org

of worsening psychosis/depression is not warranted, especially since EFV has a more favourable side-effect profile, lower pill burden and fewer drug-drug interactions with psychiatric medications than other available alternatives (nevirapine and lopinavir/ritonavir).

Milder neuropsychiatric side-effects of EFV (vivid dreams, dizziness), which typically resolve within 2 - 4 weeks, can be managed with reassurance.[18] Should a patient develop new-onset or worsening of pre-existing psychosis with a temporal relationship to EFV introduction, and the psychosis persists despite psycho-pharmacological management, then the clinician should consider switching from EFV to an alternative agent. If a patient cannot tolerate EFV side-effects, then it may be necessary to switch to an alternative ARV.

The use/initiation of EFV in patients who are currently psychotic or severely depressed remains controversial. If available, consider alternative regimens as there currently is no published literature on the outcomes of EFV in psychotic/depressed individuals. If alternatives are unavailable, contraindicated or involve significant drug-drug interactions, then initiate EFV and monitor carefully.

5.4 Diagnosis and management of secondary SMDs

It is helpful to establish whether the SMD (psychosis or manic episode) is due to an underlying primary mental disorder or is secondary to HIV infection. Primary disorders require the initiation of psychotropic treatment and an assessment of whether HIV disease is currently contributing to the disorder. If patients do not meet National Department of Health (NDoH) criteria for ART initiation and are not considered to have HIV-associated SMD, then they can be referred to out-patient HIV services when discharged. Where the SMD is either thought to be secondary to HIV or where a primary SMD is being aggravated by HIV, ART and psychotropic treatment should be given in hospital.

5.5 SMDs secondary to HIV infection

- SMDs secondary to HIV infection are often associated with:
  - cognitive impairment (memory deficits and psychomotor slowing)
  - significant immune-compromise: stage III/IV WHO disease, $CD4^+$ counts <350 cell/µl and/or high VLs
  - some atypical mental state features, e.g. irritability, non-auditory hallucinations (i.e. visual or other), and a lack of personal or family history of mental disorders (i.e. no or little genetic loading)
  - no/poor response to psychotropic treatment.
- Management includes:
  - commencing ART in line with the NDoH guidelines
  - using low-dose anti-psychotics (haloperidol, risperidone, quetiapine) for psychosis
  - patients with mania due to HIV may respond well to second-generation antipsychotics (SGAs) (risperidone, quetiapine, olanzapine, aripiprazole)
  - considering mood stabilisers in persistently manic patients (consult with a psychiatrist).

6. HIV-associated neurocognitive disorders

HIV-associated neuropathological disease presents with a characteristic sub-cortical deficit pattern including: psychomotor slowing, impaired memory, attention, language, executive functioning and behavioural apathy. In patients receiving ART, a mixed cortical-subcortical picture is observed (less psychomotor slowing, more executive function, language and visuo-spatial difficulties). Classification into various HAND categories (Box 6) is determined by the extent of neurological and functional impairment:

- mild neurocognitive disorder (MND)
- HIV-dementia (HIV-D).[21]

Box 6. MND v. HIV-D

Incidence

- HIV-D in untreated HIV: 35/1 000 person years
- HIV-D in patients receiving ART: 3/1 000 person years

Prevalence (SA)

- MND, pre-ART: 42.4%
- MND, while receiving ART: 25.4%[22]

Impact

- HIV-associated neuro-invasion results in a spectrum of neurological effects, ranging from subclinical to advanced dementia
- Milder (or subclinical) HAND, which often persists during ART, has significant effects on functional outcomes, e.g. poor adherence, unemployment
- Increasing HIV testing uptake, earlier access to ART and adherence support will positively impact rates of HAND in HIV-positive populations

6.1 Screening

- Without screening (excluding HAND sufferers presenting to hospital with confusional states/psychosis), many patients with gradual neurodegenerative changes are undiagnosed due to infrequent self-reporting of functional impairment/ decline
- Such milder HAND needs to be detected as it may precede to further neurodegeneration that can potentially be prevented by ART
- In pre-ART patients with CD4$^+$ counts >350 cells/μl, screening should be performed in wellness clinics approximately annually; patients with clear neurocognitive disorder should be referred for confirmation and initiation of ART
- At ART initiation, patients with cognitive problems may require additional treatment support; a baseline assessment allows tracking over time of progress/recovery
- Once receiving ART, patients with HAND may require additional adherence support
- HAND may progress or fail to recover despite ART
- Should be offered as part of adherence support or may be offered annually, or where resources are limited, reserved for those with clinical problems (treatment failure, poor adherence, on-going depression, self-reported functional impairment).

6.2 Approaches to screening for HAND

- There is no globally accepted screening policy or practice

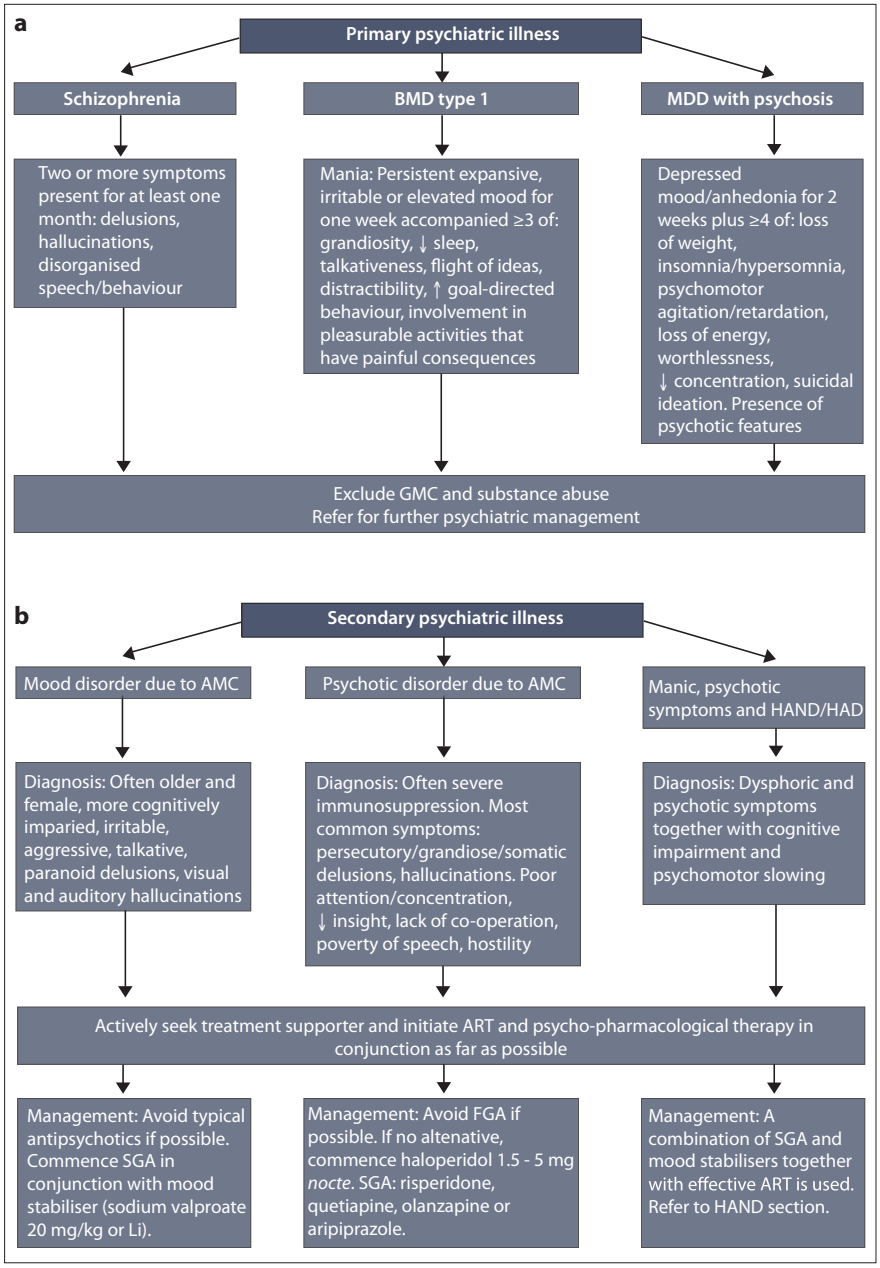

Fig. 4. Recognising (a) primary and (b) secondary SMDs. (BMD = bipolar mood disorder; SMD = severe mental disorder; HAD = HIV-associated dementia; AMC = another medical condition; HAND = HIV-associated neurocognitive disorder; ART = antiretroviral therapy; MDD = major depressive disorder; SGA = second-generation antipsychotic; FGA = first-generation antipsychotic.)

- An ultra-brief symptoms-based tool[23] may detect more severe cases (see Table 3)
- Other tools proposed for use include:
  - International HIV Dementia Scale (IHDS) (validated in SA) (http://www.europeanaidsclinicalsociety.org/Guidelines/G2_pC.htm)
  - Montreal Cognitive Assessment (MOCA) (http://www.mocatest.org)
  - the HIV-Dementia scale (http://www.turkpsikiyatri.org/arsiv/category/3-eng.html?...93:hiv-dementia)
  - Cognitive Assessment Tool – Rapid Version (awaiting validation) (http://www.hivmentalhealth.co.za/.../Cognitive-Assessment-Tool-paper-version2.pdf)
- A positive screen does not equate to a diagnosis of HAND; three further steps are required for clinical confirmation (Table 4).

6.3 Management (Fig. 5)

- Pre-ART, with confirmed HAND: commence ART, irrespective of CD4$^+$ count; engage family/partner for treatment support; and diagnose and treat confounding conditions
- Receiving ART, with HAND: usually mild/

Table 3. Simioni Neurocognitive Symptom Questions[23]

Ask the patient the following questions. Each answer should include one of 'never', 'hardly ever', or 'yes, definitely'. Any one 'yes, definitely' answer equals a positive screen.

Question	Never	Hardly ever	Yes, definitely
Do you experience frequent memory loss (e.g. do you forget the occurrence of special events, even more recent ones, appointments, etc.)?	☐	☐	☐
Do you feel that you are slower when reasoning, planning activities or solving problems?	☐	☐	☐
Do you have difficulties paying attention (e.g. to a conversation, a book or a movie)?	☐	☐	☐

Table 4. Three-step diagnostic approach to HAND in clinical practice

Step*	None	Mild - moderate	Severe
1. Is neuropsychological impairment present? (use symptom questions and at least one brief objective measure e.g. IHDS, MMSE, HDS, MoCA)	☐	☐	☐
2. To what extent are confounding illnesses contributing to the neurocognitive disorder? (depression, alcohol abuse, head injury, epilepsy, nutritional deficiency, CNS OI and neurosyphilis)	☐	☐	☐
3. Is functional impairment present? (measure basic daily activities including pill-taking and complex tasks, e.g. cleaning, cooking, shopping, money management, work tasks or driving)	☐	☐	☐

IHDS = International HIV Dementia Scale; MMSE = mini mental state examination; HDS = HIV dementia scale; MoCA = Montreal Cognitive Assessment; CNS = central nervous system; OI = opportunistic infection; HIV-D = HIV-dementia; MND = mild neurocognitive disorder; NP = neuropsychological; HCWs = healthcare workers; CT = computed tomography.

Clinicians then need to confirm whether HIV-D or MND is present:
- HIV-D: severe NP impairment + at least mild - moderate functional impairment +/- mild - moderate contribution from confounders.
- MND: either Severe NP impairment + no reported functional impairment, or mild - moderate NP impairment + at least mild - moderate functional impairment.

* Notes: Step 1: Clinicians may perform more advanced neuropsychological testing or combine bedside tests. Primary HCWs may refer patients for such detailed assessment.
Step 2: If clinical examination reveals no focal abnormality or comorbid medical conditions, lumbar puncture, CT scanning and blood tests rarely add diagnostic information. If delirium, confusion or psychiatric/behavioural symptoms are present, these further investigations are mandatory. Actively manage underlying confounding conditions.
Step 3: The extent of functional impairment is often under-rated – seek objective measures including third-party reports and clinical assessment of simple tasks where possible.

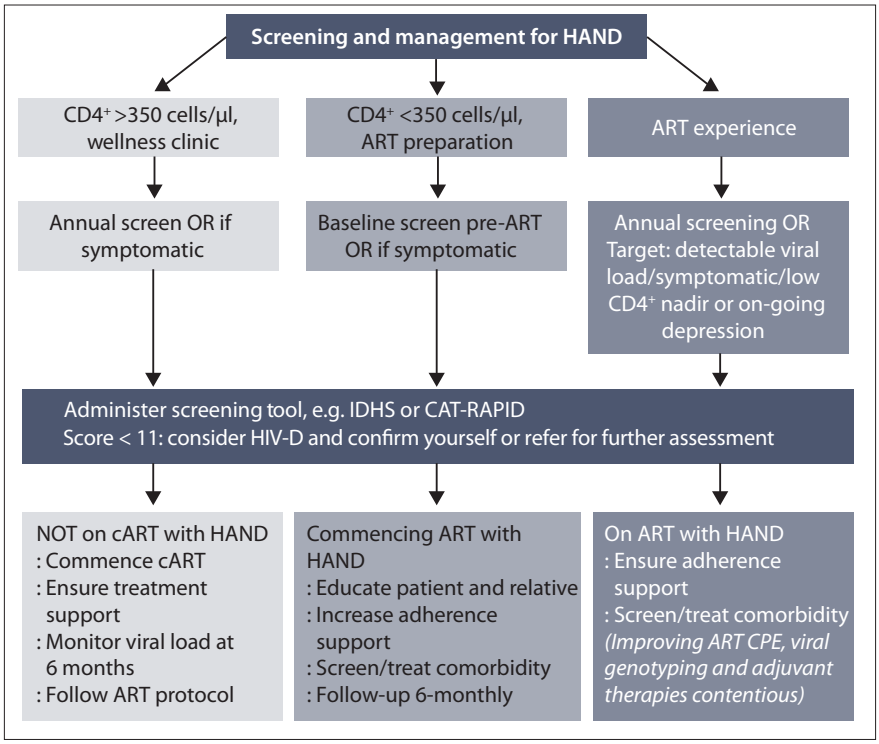

Fig. 5. Screening and management of HANDs. (CPE = CNS penetration effectiveness.)

moderate disease but, with ageing populations, more advanced disease may develop
- Routine VL monitoring with enhanced support, if adherence is poor
- Screen and treat comorbidities including age-related dementia
- Adjusting the ARV regimen to enhance CNS penetration (CPE) is not recommended, as the evidence in this regard is conflicting
- Measure the cerebrospinal fluid VL if viral compartmentalisation is suspected (low CD4+ nadir, severe impairment, confusional symptoms, increased tone and psychomotor slowing despite viral suppression in plasma)
- Augmentation strategies, including memantine, are not recommended due to the lack of robust supporting evidence and cost
- Sodium valproate or lithium may be used if there is neuropsychiatric comorbidity.

7. Grief and loss in the context of HIV

Grief is a normal, non-pathological response to any type of loss, not just death. The grief response is highly individualised as it is influenced by individual, cultural, religious, familial, community and societal factors. Grief arising from a loss related to HIV may be particularly complicated; complicated grief is defined as a prolonged period of intensified grief symptoms that disrupt daily functioning.[24]

7.1 Screening

- Screen for common symptoms of grief:
  - emotional: enduring sadness, shock, anger, anxiety, loneliness, yearning, guilt,

Table 5. Differentiating grief/bereavement from depression[25]

Grief/bereavement	Depression
Expected, culturally accepted response to loss	Only diagnose depression if the griever experiences depressive symptoms persisting for ≥2 months
Guilt is focused on an aspect of loss	Guilt is preoccupied with a negative self-image
Moments of pleasure/happiness	Feelings of emptiness and despair are constant
Preoccupation with deceased	Preoccupation with self
Not demoralising or humiliating	Demoralising and humiliating
Overt expression of anger	Anger not as pronounced
Diminishes in intensity over time	Consistent sense of depletion
Suicidal gestures are rare	Suicidal gestures are not unusual
Responsive to support	Unresponsive to support
Elicits sympathy, concern and desire to embrace	Elicits irritation, frustration and a desire to avoid from others
Usually functions	Inability to function at work, home and/or school

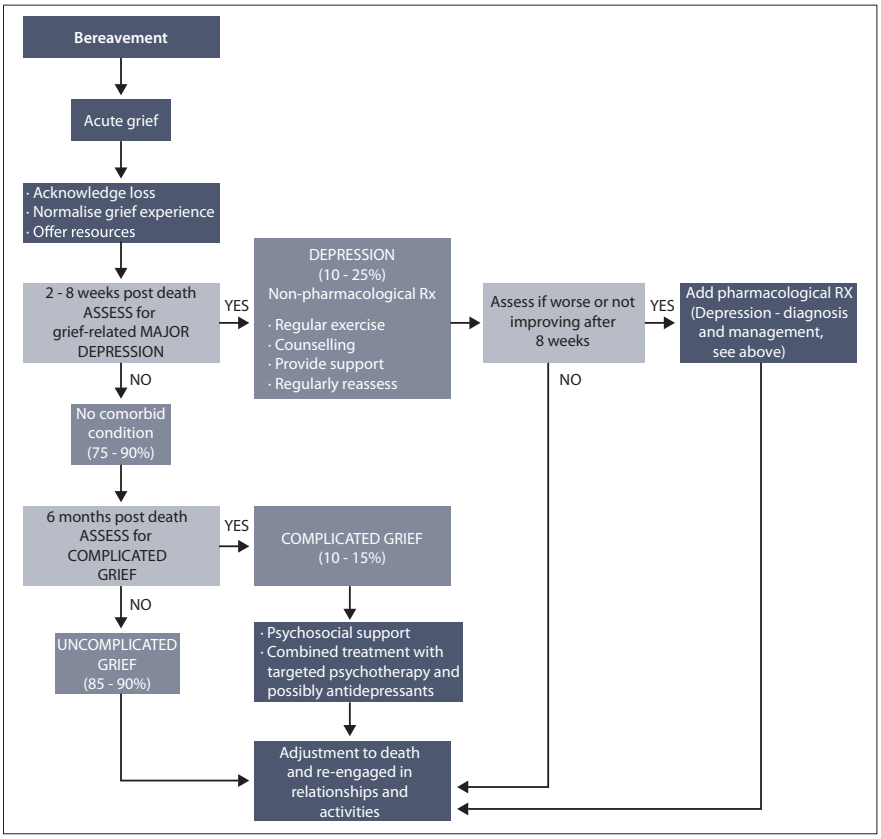

Fig. 6. Management of grief and bereavement.[26]

fear, withdrawal, feeling worthless, apathy, irritability, appetite disturbances
- physical: fatigue, tightness in the chest, shortness of breath, lack of energy, numbness, nausea, body aches, panic attacks, insomnia
- psychological/cognitive: disbelief, confusion, sense of presence, lack of concentration, auditory hallucinations (hearing the voice of the deceased), intrusive thoughts, anxiety about death, mental fatigue
- spiritual distress: questioning faith or the meaning of being a survivor
- Explore the nature and relationship of the loss/death and its impact
- Assess if the grief reaction is appropriate for the setting/cultural context
- Assess the griever's coping style, support network, and previous experiences of loss or death
- Assess for barriers to effective grieving, e.g. a lack of support, multiple losses, mental health issues, a complex relationship with the deceased, the manner of death, etc.
- The screening of children and adolescents needs to be age-appropriate and cognisant of the multiple subsequent losses that can arise following parental/caregiver death, e.g. separation from siblings, new school/friends, new home, etc.
- Clinicians may have trouble distinguishing grief and bereavement from depression (see Table 5; refer to Fig. 6 for the management of acute grief and bereavement)

8. Burnout and vicarious trauma

HCWs may also experience emotional and psychological effects from exposure to cumulative challenges within the health sector. While taking care of oneself is a prerequisite to taking good care of others, stigma persists for HCWs acknowledging burnout and vicarious trauma. Table 6 highlights key symptoms indicative of burnout and vicarious trauma.[29]

8.1 Burnout

- Prolonged involvement in emotionally demanding situations results in gradual progression towards: (*i*) emotional exhaustion; (*ii*) depersonalisation; and (*iii*) a reduced personal accomplishment and commitment to one's profession
- Risk factors include: a high patient load; difficult patient circumstances; HCW empathy, own experiences, age, training, lack of control and failure to care for oneself; and organisational characteristics (a lack of support/recognition/fairness, low salaries)
- Failure to recognise burnout may lead to depression or chronic fatigue[27]
- Burnout can be assessed officially using the Maslach Burnout Inventory (MBI) (http://www.mindgarden.com/products/mbi.htm) or the Oldenburg Burnout Inventory (OBI) (http://www.bma.org.uk/burnoutquestionnaire).

Table 6. Symptoms of HCW burnout and vicarious trauma

Burnout	Vicarious trauma
Individual level	**Individual level**
• Overextended emotionally and physically by his/her work environment	• Feeling overwhelmed/helpless when hearing patients' trauma stories
• Responds to colleagues/patients in an impersonal way	• Feeling ineffective, unskilled and/or powerless
• Feels no sense of accomplishment in anything that he/she does	• Intrusive imagery of the trauma stories that they hear about
• Physical exhaustion: fatigue; insomnia; weight fluctuations	• Hyperarousal
• Emotional exhaustion: feeling responsible; psychosomatic symptoms	• Avoidance of places, people or work
• Psychological exhaustion: compassion fatigue	• Feeling angry and irritable
• Absenteeism	• Disconnect from other staff members
Organisational level	**Organisational level**
• Absenteeism and high staff turnover	• Impact of trauma stories on staff not acknowledged/recognised
• Disengaged from colleagues/patients	• Disengaged from colleagues/patients
• Increased team conflict	• Increased team conflict/poor teamwork
• Insufficient staff training/technical ability and lack of resources	• Insufficient training of staff to manage emotional impact of trauma

8.2 Vicarious trauma

Repeated exposure to patients' traumatic stories may result in intrusive imagery, avoidance/hyperarousal, experiencing symptoms similar to the patients' trauma response (confusion, tearfulness, isolation, anger, irritability, powerlessness, hopelessness), increased vulnerability and/or survivor guilt.[28]

8.3 Management

- The individual clinician can manage burnout by following the 3 'r' approach:[30]
  - **r**ecognise: watch carefully for signs of burnout
  - **r**everse: undo damage by using stress-management techniques and employing support from fellow HCW and family
  - **r**esilience: build resilience to stress by looking after your physical and mental health
- When recovering from burnout: slow down; re-evaluate goals and priorities; and get support.

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